**Kundina V. V., Babkina T. M. Myocardial stunning in patients with coronary artery disease before and after treatment by method of coronary artery bypass grafting (own studies). Journal of Education, Health and Sport. 2022;12(1):43-54. eISSN 2391-8306. DOI**
**http://dx.doi.org/10.12775/JEHS.2022.12.01.004**
**https://apcz.umk.pl/JEHS/article/view/JEHS.2022.12.01.004**
**https://zenodo.org/record/5838417**

**The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 1, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).**

**Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 1 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe:Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).**



**Received: 15.12.2021. Revised: 25.12.2021. Accepted: 11.01.2022.**

UDC: 616.127: 616.132.2–005.4-089

# Myocardial stunning in patients with coronary artery disease before and after treatment by method of coronary artery bypass grafting (own studies)

**V. V. Kundina, T. M. Babkina**

**Shupyk National Healthcare University of Ukraine, Kyiv**

**Vyktoriia Valeryivna Kundina**, Assistant of the Department of Radiology, Shupyk National Healthcare University of Ukraine, Kyiv,
**Tetiana Mykhailivna Babkina**, Dr. Sc., Full Professor, Head of the Department of Radiology, Shupyk National Healthcare University of Ukraine Kyiv.
Vyktoriia Valeryivna Kundina, home address: Kyiv, 3 Puluia Str., Apt. 253; e-mail: vika.kundina@gmail.com; tel. 0674010710

## Abstract

**Aim of the study:** Determination of quantitative radiological indicators of myocardial revascularization effectiveness in patients with coronary artery disease in the early postoperative period.

**Materials and methods of research:** For the implementation of the clinical objectives, 62 patients with coronary artery disease, heart failure, with preserved systolic function and systolic dysfunction were examined in the early postoperative period (up to 7 days). The patients' age ranged from 40 to 79 years, the average age of the examined was 59.6 ± 8.2 years. 35 (56%) patients had HF with LV systolic dysfunction with EF of 49% or less.

27 (44%) patients had preserved systolic function - ejection fraction greater than or equal to 50%.

**Results:** In the group before treatment, the average value of MV was 69.4% CI 95% [65.3%; 73.5%], and after treatment the value of MV was 75.0% CI 95% (70.8%; 79.3%], p = 0.0000. Percentage of RFP inclusion in the anterior wall was 69.5% CI [66.2%; 72.8%] before treatment and significantly improved to 72.3% CI [69.1%; 75.4%] after treatment (p = 0.023). Lateral wall had a parameter value of 73.9% CI [70.7%; 77.1%] before treatment and improved perfusion up to 77.2% CI [74.3%; 80.2%] (p = 0.018). Parameter values for the intraventricular septum were 64.5% CI [60.7%; 68.3%] before treatment and 69% CI [65.2%; 72.8%] after treatment (p = 0.000034) and for the inferior wall those were 54.0% CI (49.7%; 58.3%] and 61.7% CI (57.9%); 65.6%] before and after treatment respectively (p = 0.000032).

**Conclusion:** The determination of quantitative radiological parameters proposed as a result of this study is extremely important for the early postoperative period (7-10 days) for determination of stunned myocardial reserve and late stage of patients` management (1-1.5 years) for determination of hibernation reserve and final assessment of CABG effectiveness.

**Key words: coronary artery disease; revascularization; myocardial scintigraphy; myocardial viability; coronary artery bypass grafting**

**Introduction**. Insufficient myocardial blood supply caused by ischemia leads to a decrease in blood flow in the subendocardial layers, an increase in intramyocardial tension and to myocardial dysfunction as a result [1]. It has been experimentally proven, that myocardial ischemia is accompanied by a decrease in the left ventricle systolic function immediately after its occurrence [2].

In cases of minor or short-term ischemia, there is a temporary appearance of "stunned" myocardium - living typical cardiomyocytes with reduced contractile function restored after normalization of blood supply, and show no signs of metabolic and histological changes.

In 1975, Heyndrickx and co-authors experimentally proved in dogs, that after the reversible episode of 5-15-min coronary ischemia there was a prolonged depression of regional myocardial regions for several days, which gave rise to finding a mechanism for temporary cell contractility violation[3].

In 1982, Braunwald and Kloner defined stunned myocardium as a condition of prolonged, postischemic ventricular dysfunction resulting from short-term blood supply impairment. The hypothesis of stunned state occurrence was proposed: hit - the most acute

episode of blood supply impairment, run - gradual restoration of blood supply and stun - reversible changes in regional segments of the ventricle, which can last for several days, but most importantly, leads to complete recovery of contractile function [4].

To date, scientists are considering two main hypotheses of the pathophysiology of stunned myocardium. The first is the hypothesis of damage caused to the contractile elements of typical cardiomyocytes by oxygen free radicals, which wavily occurs in the first seconds of myocardium reperfusion. In support of this theory, Zweier and co-authors conducted research using paramagnetic resonance spectrometry and proved that a large amount of oxygen free radicals are released in the first 10 seconds of reperfusion [HYPERLINK "https://doi.org/10.3892/etm.2018.7089"5], also the use of dismutase and catalase as free radicals scavengers significantly reduced the degree of muscle attenuation in animal experiments conducted by Przyklenk and co-authors [4].

The second theory is intracellular overload of a typical cardiomyocyte with calcium ions, which leads to a change in the sensitivity of myofilaments and a decrease in cell contractility. In support of this hypothesis, Przyklenk refers to facts of myocardial stunning reducing and reducing the time of its complete functional recovery with the use of drugs (calcium antagonists, verapamil and nifedipine). In 2006, a study on stunned animal myocardium using ranolysin as an late INa inhibitor in typical cardiomyocytes also showed a decrease in myocardial stunning, which may also be included in the pathophysiological factors of reversible changes [4].

Not the least role is played by the reticulum of cells dysfunction, which slows down the transmission of impulses and dyschronizes muscle fiber cells, causing a state of myocardial stunning [6]. Clinical manifestations of myocardial stunning depend on the muscle fibers mass in the pathological condition, the segment of the lesion and are characterized by left ventricular dysfunction. Myocardial stunning was observed in coronary angioplasty [7] and contractile function was restored 2-3 days after reperfusion.

The same fact is supported by a study on significant recovery of myocardial perfusion and cardiac function parameters (ejection fraction and left ventricle systolic thickening) in patients with acute coronary syndrome [8] by method of single-photon emission computed tomography.

The state of stunned myocardium is accompanied by the appearance of cardiac troponins in the blood, which is classically considered a sign of acute coronary syndrome (ACS) [9], but studies in animals have shown that in short-term coronary occlusion, the state of stunned myocardial occurs, serum troponin increases in an hour and remains stable for 24

hours from the moment of blood supply impairment occurance, while the study of stained histological macro and microslides did not reveal any necrotic changes.

Therefore, Weil and co-authors hypothesized that some cells in stunned state undergo apoptosis, which is associated with an increase in cardiac troponins [10]. Given all the above, the scientific community of cardiology faces the question of the mechanism of occurrence and restoration of contractility in such a pathological myocardium condition, which is becoming increasingly important in today's conditions.

**Aim of the study**. Determination of quantitative radiological indicators of myocardial revascularization effectiveness in patients with coronary artery disease in the early postoperative period.

**Materials and methods**

The study has a parallel-group open design, is retrospective. All patients were operated by surgical teams with highly qualified cardiac surgeons (more than 15 years of practice, the highest medical category) in order to minimize medical error. Randomization was not used in the sample formation.

For the implementation of the clinical objectives, 62 patients with coronary artery disease, heart failure, with preserved systolic function and systolic dysfunction , who underwent clinical and instrumental examinations and inpatient treatment in the Department of Cardiology, were examined on the basis of the State Institution ‘Heart Institute of the Ministry of Health of Ukraine’.

Patients were sequentially examined and selected for myocardial revascularization. The diagnosis of coronary artery disease was established on the basis of a set of examinations, which included measurement of blood pressure, ECG in 12 leads, laboratory tests, echocardiography, coronary ventriculography. The diagnosis of coronary artery disease was established according to the standards of the European Society of Cardiology (2013) [11].

All patients were examined in the dynamics of the pathological process before and after surgery.

The patients' age ranged from 40 to 79 years, the average age of the examined was 59.6 ± 8.2 years. (Fig.1).

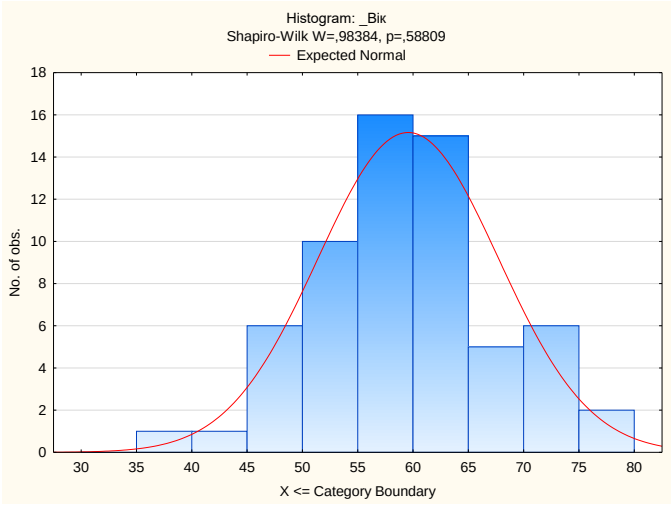


Fig. 1. "Normal" age distribution among patients. EMBED STATISTICA.Graph \s

All patients signed a Voluntary Consent to participate in a clinical trial, approved by the Ethics Committee of the National Healthcare University, Kyiv, Ukraine, and were informed of the possible consequences of radiopharmaceuticals (RFPs) administration.

CABG was identified as a priority treatment method in patients with the following coronary bed lesion areas: clinically significant anterior interventricular branch (AIV) of left coronary artery (LCA) stenosis with single- and two-vessel lesions of the coronary artery; LCA trunk lesions greater than 50% with any SYNTAX score [12] and all patients with multivessel lesions.

MSG was performed on Infinia Hawkeye TM combined gamma-camera (GE, USA) with integrated CT and a special cardiac software package. The studies were performed in single-photon emission computed tomography (SPECT) and SPECT/ CT with ECG synchronization (Gated SPECT) modes according to the recommendations of the European Association of Nuclear Medicine [13-14] with a high-resolution, low-energy collimator. 99mTc-MIBI (methoxyisobutylisonitrile) RFP (Polatom, Poland) was used. 99mTc-MIBI was administered intravenously with an activity of 555-740 MBq. All patients underwent MSG in the dynamics of treatment (before CABG and after CABG). One-day protocol (One Day Rest) was used [15]. A total of 124 scintigraphic studies were performed.

MSG data processing was performed using Xeleris workstation applying Myovation and ECToolBox cardiology software packages. A test of 50% and above RFP accumulation was used to determine the quantity of VM (viable myocardium) [16]. If RFP fixation was greater than or equal to 50%, such myocardium was considered viable (Fig. 2). After assessing RFP accumulation in the myocardium, a semi-quantitative analysis was performed

in the ‘bull`s eye’ coordinate system using a 17-segment model of the left ventricular myocardium (Fig. 3). The evaluation was performed in points from 0 to 4 for each segment, then the data were summed.

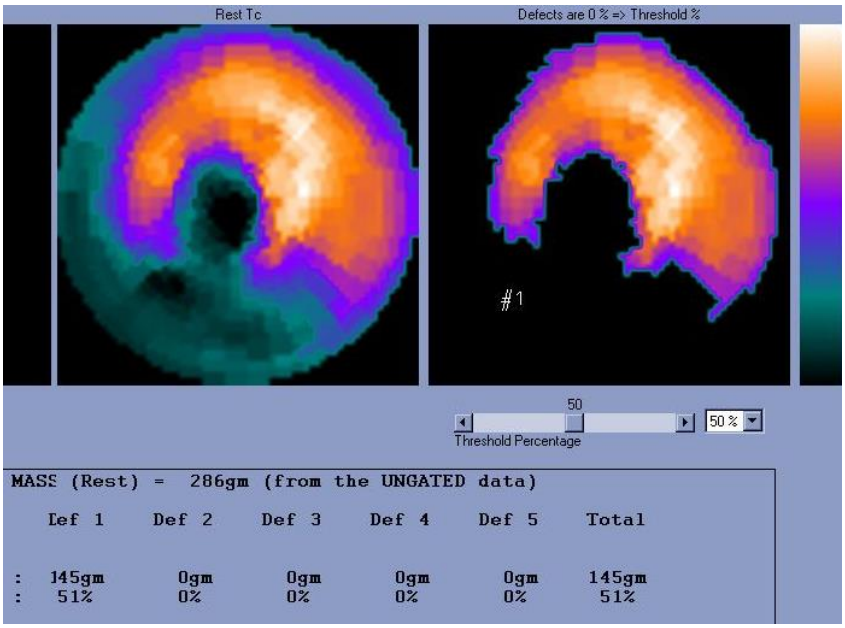


Fig. 2. Determination of VM quantity using Myovation and ECToolBox cardiac programs (MV limit is 50% or greater RFP fixation ; 51% of patient`s myocardium accumulates RFP below the established level; VM is 49% respectively)

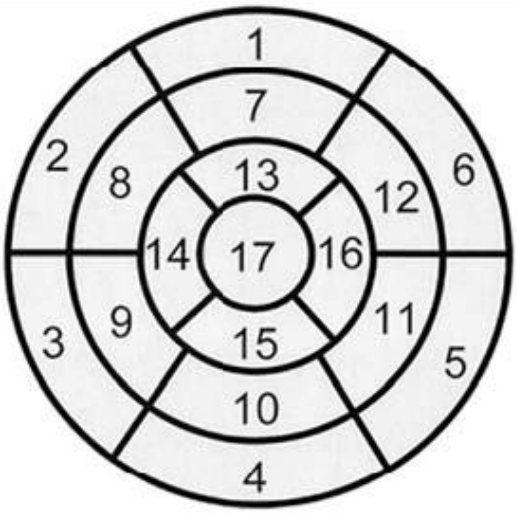


Fig. 3. ‘Bull`s eye’ coordinate system in the semi-quantitative analysis of MSG results. Segments: 1 - basal anterior, 2 - basal anteroseptal, 3 - basal inferoseptal, 4 - basal inferior, 5 - basal inferolateral, 6 - basal anterolateral, 7 - mid anterior, 8 - mid anteroseptal, 9 - mid inferoseptal, 10 - mid inferior, 11- mid inferolateral, 12 - mid anterolateral, 13 - apical anterior, 14 - apical septal, 15 - apical inferior, 16 - apical lateral, 17 - apex

ECG synchronization allowed to calculate functional parameters of the left ventricle, such as EDV, ESV, EF, SV, left ventricle systolic thickening, used in the next stage of MSG results processing [17].

After reconstruction, radionuclide (emission) images were combined with CT images. During SPECT reconstruction, CT transmission information was used to correct emission information for corrections for attenuation of radioactive signals (correction for attenuation) [18].

The results of calculations and graphs are generated directly from the industrial statistical complex Statistica 10 by StatSoft [19].

**Obtained results and their discussion.** According to the objective, we assessed RFP accumulation as a whole, separately in each wall of the left ventricle (taking apical region into account) and in the basal and medial regions of the left ventricular wall separately. The percentage of RFP accumulation indicates the completeness of different LV regions perfusion.

In the group of patients before treatment, the average value of MV was 69.4% CI 95% [65.3%; 73.5%], and after treatment the value of MV was 75.0% CI 95% (70.8%; 79.3%], which allows us to make a conclusion about the positive effect of myocardial revascularization in patients with coronary artery disease with significant statistical assurance ($p = 0.0000$) (Table 1).

Table 1. Statistical difference of comparative parameters before and after CABG

| Comparative parameters of % RFP inclusion | **T** | **Z** | **p-value** |
|---|---|---|---|
| Anterior wall before & after | 584 | 2.271941 | 0.023091 |
| IVS before & after | 320.5 | 4.142156 | 0.000034 |
| Inferior wall before & after | 318 | 4.161512 | 0.000032 |
| Lateral wall before & after | 574 | 2.347421 | 0.018905 |
| Apical segment before & after | 294 | 3.988189 | 0.000067 |
| Myocardial vulnerability before & after | 136 | 5.39999 | 0.00000 |

Note: T - test statistics in the designation of Sidney Siegel; Z - Wilcoxon test; p -statistical probability.

When evaluating the effectiveness in each wall, the following results were obtained. The anterior and lateral walls of the left ventricle restored perfusion worse in the early postoperative period, although they had a registered statistically significant difference. Before treatment, the percentage of RFP inclusion in the anterior wall as a whole was 69.5% CI [66.2%; 72.8%] and accurately improved after treatment up to 72.3% CI [69.1%; 75.4%] - p =

0.023 (Table 1). The lateral wall, in turn, had a value of 73.9% CI [70.7%; 77.1%] before treatment and improved perfusion up to 77.2% CI [74.3%; 80.2%] - p = 0.018 (Table 1). Registered parameters of the anterior and lateral walls in the form of the Wilcoxon test are presented in Fig. 4a and Fig. 4b, respectively.

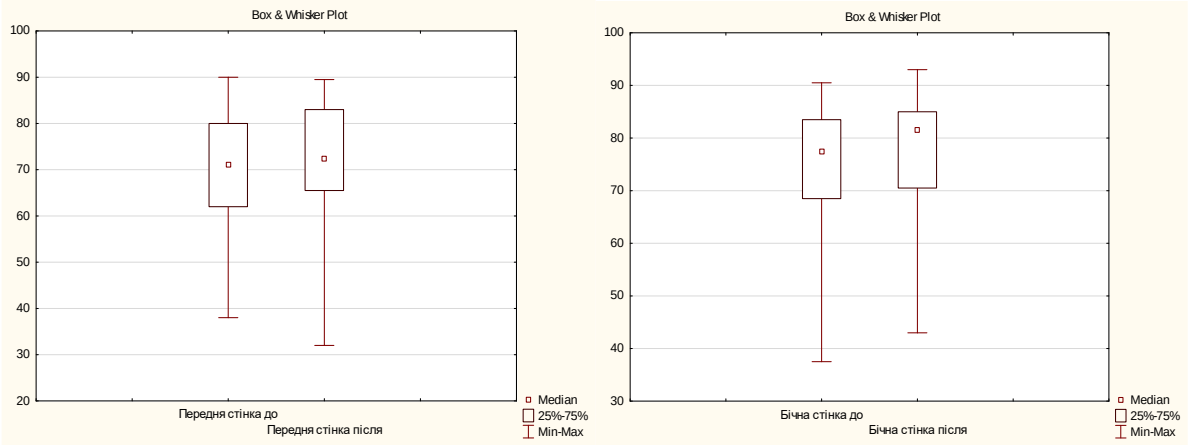


Fig. 4. Wilcoxon test for % accumulation of RFP in the anterior (4a) and lateral (4b) walls of the left ventricle

Note that perfusion impairment in these walls was quite moderate in the study group of patients and figures restored to normal (75% or more) in some patients after surgery

Parameters of% RFP inclusion in the intraventricular septum (IVS) and the inferior wall showed a more significant perfusion impairment, which was caused by significant circulatory disorders in RCA area in most patients.

Parameter values of the interventricular septum were 64.5% CI [60.7%; 68.3%] before treatment and 69% CI [65.2%; 72.8%] after treatment (p = 0.000034) and for the inferior wall those were 54.0% CI (49.7%; 58.3%] before and 61.7% CI (57.9%); 65.6%] after treatment respectively (p = 0.000032) (Table 1).

The registered parameters of IVS and inferior wall in the form of the Wilcoxon test are presented in Fig. 5a and Fig. 5b respectively.

The same statistical significance in the restoration and improvement of blood supply was registered in the apical region of the left ventricle (Fig. 6). Blood supply impairment was 59.5% CI [55.1%; 64.0%] before treatment and 64.5% CI [60.1%; 68.9%] after treatment- p = 0.000067 (Table 1).

When evaluating the basal and medial regions, only three parameters did not show registered significance: medial and basal segments of the anterior wall and basal region of the lateral wall, which is shown in table. 2.

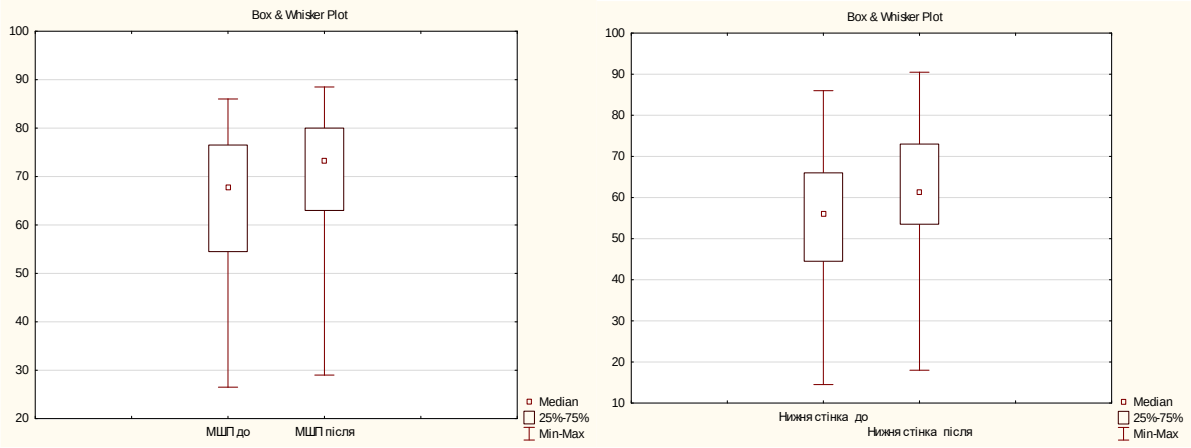


Fig. 5. Wilcoxon test for% accumulation of RFP in IVS (2a) and inferior (2b) LV wall

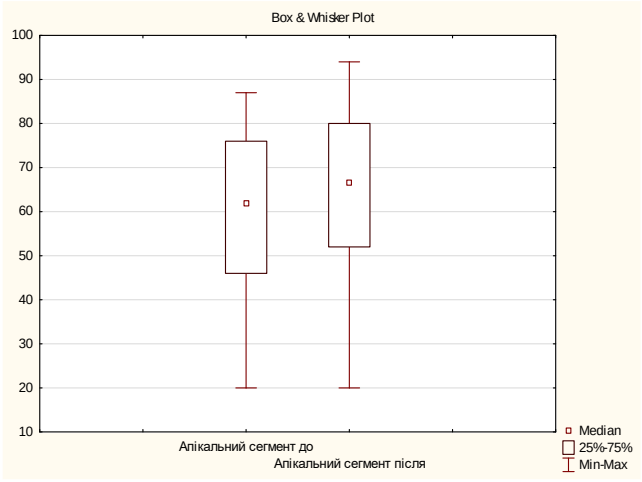


Fig. 6. Wilcoxon test for% accumulation of RFP in the apical LV region

Table 2 Statistical difference of comparative parameters before and after CABG

| RFP inclusion parameters | T | Z | p-value |
|---|---|---|---|
| IVS basal region before & after | 336 | 3.065124 | 0.0022 |
| IVS medial region before & after | 230.5 | 4.054024 | 0.0001 |
| IW basal region before & after | 366.5 | 3.654796 | 0.0003 |
| IW medial region before & after | 343 | 4.091003 | 0.0000 |
| LW medial region before & after | 544.5 | 2.240549 | 0.0251 |
| Apical segment before & after | 294 | 3.988189 | 0.0001 |
| Apex before & after | 465.5 | 3.019516 | 0.0025 |
| AW basal region before & after | 496.5 | 1.753081 | 0.0796 |
| AW medial region before & after | 643 | 1.82661 | 0.0678 |
| LW basal region before & after | 508.5 | 1.64798 | 0.1002 |

Note: T - test statistics in the designation of Sidney Siegel; Z - Wilcoxon test; p - statistical probability.

**Conclusions.** Restoration of blood supply or improvement of perfusion in the walls and regions of the left ventricle in the early postoperative period up to 7 days clearly demonstrates the amount of stunned myocardium and allows to assess the effectiveness of myocardial revascularization as a whole and segmentally using non-invasive techniques - SPECT / CT. The determination of quantitative radiological parameters proposed as a result of this study is extremely important for the early postoperative period (7-10 days) for determination of stunned myocardial reserve and late stage of patients` management (1-1.5 years) for determination of hibernation reserve and final assessment of CABG effectiveness.

**Conflict of interest.** There are no conflicts of interest of any kind concerning commercial, financial, copyright relations, relations with organizations or individuals that could be related to the research in any way, and the relationship between the co-authors of the article.

**References**


1. V. P. Ivanov, O. V. Shcherbak, O.F. Bilonko; Pathophysiological mechanisms of development and progression of myocardial dysfunction in patients with acute myocardial infarction; Ukrainian Medical Journal, 4 (108) - VII / VIII 2015

2. T.A. Nechesova, I. Yu. Korobko, N.I. Kuznetsova, Left ventricular remodeling: pathogenesis and assessment methods, Belarus, Medical News. - 2008. - No. 11. - P. 7-13

3. Vaidya Y, Cavanaugh SM, Dhamoon AS. Myocardial Stunning and Hibernation. [Updated 2021 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK537026/

4. HYPERLINK "https://www.ahajournals.org/doi/10.1161/JAHA.119.015502" \o "Robert A. Kloner" Robert A. Kloner, Stunned and Hibernating Myocardium: Where Are We Nearly 4 Decades Later?, 4 Feb 2020 Journal of the American Heart Association. 2020;9:e015502 HYPERLINK "https://doi.org/10.1161/JAHA.119.015502" https://doi.org/10.1161/JAHA.119.015502

5. Cheng, B., Zhong, J., Wu, F., Li, G., Ruan, Q., Luo, G., Jiang, H."Ebselen protects rat hearts against myocardial ischemia-reperfusion injury". Experimental and Therapeutic Medicine 17, no. 2 (2019): 1412-1419. https://doi.org/10.3892/etm.2018.7089

6. Andrea Igoren Guaricci, Gabriella Bulzis; Current interpretation of myocardial stunning, Trends in Cardiovascular Medicine,Volume 28, Issue 4, 2018, Pages 263-271, ISSN

1050-1738, HYPERLINK "https://doi.org/10.1016/j.tcm.2017.11.005" https://doi.org/10.1016/j.tcm.2017.11.005.

7. HYPERLINK "https://onlinelibrary.wiley.com/action/doSearch?ContribAuthorRaw=Wdowiak-Okrojek%2C+Katarzyna" Katarzyna Wdowiak-Okrojek, HYPERLINK "https://onlinelibrary.wiley.com/action/doSearch?ContribAuthorRaw=Wejner-Mik%2C+Paulina" Paulina Wejner-Mik, HYPERLINK "https://onlinelibrary.wiley.com/action/doSearch?ContribAuthorRaw=Kasprzak%2C+Jaros%C5%82aw+D" Jarosław D. Kasprzak, Recovery of regional systolic and diastolic myocardial function after acute myocardial infarction evaluated by two-dimensional speckle tracking echocardiography, Clinical physiology and functional imaging, 2019, 177-181, https://doi.org/10.1111/cpf.12553

8. Calabretta R, Castello A, Linguanti F; Prediction of functional recovery after primary PCI using the estimate of myocardial salvage in gated SPECT early after acute myocardial infarction. Eur J Nucl Med Mol Imaging. 2018 Apr;45(4):530-537. doi: 10.1007/s00259-017-3891-1. Epub 2017 Dec 1. PMID: 29196789.

9. George Stavroulakis, Exercise-induced release of troponin, Clinical Cardiology, V.43, August 2020, Pages 872-881, https://doi.org/10.1002/clc.23337

10. Weil BR, Young RF, Shen X, Suzuki G, Brief Myocardial Ischemia Produces Cardiac Troponin I Release and Focal Myocyte Apoptosis in the Absence of Pathological Infarction in Swine. JACC Basic Transl Sci. 2017 Apr;2(2):105-114. doi: 10.1016/j.jacbts.2017.01.006. Epub 2017 Mar 29. PMID: 28979949; PMCID: PMC5624553.

11. 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the management of stable coronary artery disease of the European Society of Cardiology / T. F. HYPERLINK "javascript:;" Members, HYPERLINK "javascript:;" _G. Montalescot, HYPERLINK "javascript:;" _U. Sechtem et al. // Eur. Heart J. 2013. Vol. 34, no 38. – P.2949–3003, HYPERLINK "https://doi.org/10.1093/eurheartj/eht296" https://doi.org/10.1093/eurheartj/eht296

12. Prognostic value of site SYNTAX score and rationale for combining anatomic and clinical factors in decision making: Insights from the SYNTAX trial / Y. J. Zhang, J. Iqbal, C. M. Campos et al. / J. Am. Coll. Cardiol. 2014. Vol. 64, no 5. P. 423–432. doi: HYPERLINK "https://doi.org/10.1016/j.jacc.2014.05.022" \t "_blank" 10.1016/j.jacc.2014.05.022.

13. https:/www.nucmed-guide.app/#!/chapter/209.

14. Gated SPECT Myocardial herfusion imaging, intraventricular synchronism, and cardiac events in heart failure / A.Peix, J.Karell, L.Rodriges et al. / Cl. Nucl. Med. 2014. Vol. 39, no. 6. P. 498-504. Doi: 10.1097/RLU.0000000000000428.

15. Paul A.K. Gated Myocardial Perfusion SPECT: Basic Principles, Technical Aspects, and Clinical Applications / A.K. Paul, H.A. Nabi / J. Nucl. Med. Technol. 2004. Vol. 32, no.4. P. 179–187. PMID: 15576339.

16. Loffler A.I. Myocardial viability testing to guide coronary revascularization / A. I. Loffler, C. M. Kramer / Interv. Cardiol. Clin. 2018. Vol. 7, no. 3. P. 355-365. doi: 10.1016/J.iccl2018.03.005.

17. Paul A.K. Gated Myocardial Perfusion SPECT: Basic Principles, Technical Aspects, and Clinical Applications / A.K. Paul, H.A. Nabi / J. Nucl. Med. Technol. 2004. Vol. 32, no.4. P. 179–187. PMID: 15576339.

18. Dvorak R.A. Interpretation of SPECT/CT Myocardial Perfusion Images: Common Artifacts and Quality Control Techniques / R. A. Dvorak, R. K. Brown, J, R, Corbett / RadioGraphics. 2011. Vol. 31. P. 2041–2057 doi: 10.1148/rg.317115090

19. Statistica 10. HYPERLINK "https://www.tibco.com/products/data-science"https://www.tibco.com/products/data-science