Comparison of Echocardiography, Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography/Computed Tomography (PET/CT) and Cardiac Magnetic Resonance Imaging (MRI) diagnostic value while choosing treatment strategies after acute myocardial infarction (AMI)

Povilas Žudys, Eglė Kazakauskaitė, prof. habil. dr. Renaldas Jurkevičius

Lithuanian University of Health Sciences, Department of Cardiology

ABSTRACT

Background and aim. The adrenal tumors are a reasonably common pathology. Radiologic imaging detects an adrenal Aim. Evaluate myocardial viability, volumes of heart chambers and systolic function with different modalities: echocardiography, SPECT, PET/CT, and MRI.

Objectives. 1) Assess and compare myocardium movement, perfusion, and viability with echocardiography, SPECT, PET/CT, and MRI.

2) Compare ejection fraction (EF), end-diastolic volume (EDV), and end-systolic volume (ESV) results between different modalities.

3) Establish which diagnostic method is similar to PET/CT („gold standard“) the most.

4) Compare MRI („gold standard“) EF, EST, EDT results with results of other modalities.

Methods. Prospective trial. The statistical analysis was performed by SPSS software.

Study participants. Thirty patients who were treated in the Department of Cardiology, Hospital of Lithuanian University of Health Sciences Kaunas Clinics in 2012-2016. They have significantly lowered EF (EF ≤40%), severely damaged coronary arteries after acute myocardial infarction, that is why the benefit of revascularization for these patients is questionable because myocardium could have scars.

Results. Average patient age was 67,8 (interval 43–84 year), there was 25 (83,3%) men and 5 (16,6%) women. All patients had risk factors. Between echocardiography and PET/CT paired t test results of EF (OR 0,73 [95% CI -2,04-3,51], p=0,59), EDV (OR 13,36 [95% CI -10,18-36,92], p=0,25), ESV (OR 0,76[95% CI -16,93-18,46], p=0,93) were not significantly different (p>0,05). Although SPECT compared with PET/CT (paired t test) between EF (OR 2,76 [95% CI 0,88-4,64], p<0,05), EDV (OR 37,7 [95% CI 20,08-55,39], p<0,05), ESV (OR 23,26 [95% CI 11,34-35,19], p<0,05) and paired t test results between CMR and PET/CT (OR 3,43 [95% CI -5,68-(-1,18)], p<0,05), GDT (OR -43,23 [95% CI -66,82 (-19,64)], p<0,05) ir GST (OR -23,13 [95% CI -40,35-(-5,90)], p<0,05), it is clear that difference is significant. While evaluating miocard segment with Spearman corelation coeficient (r>0,05) and tested with McNemar test (p>0,05) it is clear, that in thirteen from sixteen miocardium segments there was found no significant difference between different modalities. Calculated Kappa coeficient shows agreement from fair to great. On the other hand, three of rest segments (lateral basal (18), lateral middle (12) and upper anterior(1)) statisticaly significantly were different (r<0.05, κ<0.20), McNemar test was negative with only few PET/CT with ultrasound and PET/CT with SPECT (p<0.05).

Conclusion. 1) Non-invasive cardiovascular imaging modalities (echocardiography, (99mTc)-MIBI SPECT, (18F)-FDG PET/CT and MRI) correlate well because 13 of 16 segment parameters match between types of examination. Spearman correlation coefficient (r>0,05) and Kappa value (κ>0,05) was counted, McNemar test was performed (p>0,05).

2) The agreement is seen between ultrasound and PET/CT when EF, ESV, and EDV is compared. Agreement between MRI and SPECT is seen too. Only EF (without EDV and ESV) agreement is seen between echocardiography and MRI. A paired t-test was performed (p>0,05).

3) PET/CT (“gold standard”) and CMR damage of segments (viability) correlate best of all because most of the segments (10 of 16) Spearman coefficients and 11 of 16 segments Kappa values are close to one.

4) Comparing MRI (“gold standard”) EF, EDV, ESV with other modalities, significantly similar data could be obtained only with MRI and SPECT. EF (without EDT and ESV) agreement is seen between echocardiography and MRI alone (p>0,05).

Keywords: PET/CT, MRI, SPECT, myocardial infarction

INTRODUCTION

The number of people who are prevalent to have ischemic heart disease (IHD), angina pectoris (AP), or myocardium infarction (MI) is increasing, and this trend is growing worldwide [33, 38]. Ischemic heart disease is a dysfunction of myocardium because of the decreased flow of oxygen to heart contractile cells. The cause of the disease is atherosclerotic coronary artery stenosis or spasms, which causes various length or localization myocardium ischemia [15]. IHD can expose as the sudden death of heart muscle, myocardium infarction, angina pectoris, heart rhythm, and conduction disorders or heart failure [33, 34]. According to the Lithuanian Institute of Hygiene, coronary artery disease-related deaths comprise more than half cases of death in Lithuania [33]. This is one of the biggest social, economic, and health issues not only in Lithuania but in the world as well [34]. In Europe, 4,25 million people die because of coronary artery disease annually [32]. More women die (55% of all deaths) than men (43%), the condition is more prevalent between the lower-income population, because people and society health depend on finance and budget [32, 33].

Left ventricle (LV) ejection fraction (EF), end-diastolic volume (EDV), and end-systolic volume (ESV) are used to diagnose and evaluate heart and coronary artery disease [35]. Moreover, these parameters provide useful diagnostic information during heart failure or when heart valves are damaged [36].

Various diagnostic modalities are used to evaluate EF, EDV, ESV, and condition of heart muscle segments: echocardiography, Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET/CT), heart Magnetic Resonance Imaging (MRI) [37]. Those modalities should give the same results with comparable errors [38, 39]. Diagnostic methods are convenient because all necessary information can be acquired in a single procedure.

SPECT shows LV function and myocardial perfusion [41], PET/CT – LV function, and viability (evaluation of functional parameters), although MRI with late gadolinium enhancement precisely shows EF, EDV, ESV and myocardial viability (anatomical parameter (scar) evaluation) [42]. With echoscope LV function, volumes and movement could be easily evaluated [40]. Previous studies show that there is a good correlation of LV parameters between those four methods, although there are some problems while myocardium perfusion defects, hibernating myocardium, or scars are found [43]. Moreover, there are specific problems with patients who have a small heart or because of poor video resolution and decreased quality of LV endocardium view because of image fusion at the end of systole [44, 45 46].

Firstly, if doctors want to increase patient prognosis, and outcomes of the disease, the precision of radiologic modalities should be evaluated. Looking at the world literature, only two modalities are being analyzed. Moreover, this is the first time in Lithuania when all four modalities are compared together.

In this article, main LV parameters (EF, ESV, EDV) and function of damaged heart segments (contraction, perfusion, and viability) are compared using echocardiography, SPECT, PET/CT, and heart MRI. PET/CT is a “gold standard” evaluating myocardial viability [13] while MRI – LV volumes and function [3]. It is essential to compare the match level between all four modalities (echocardiography, SPECT, PET/CT, and MRI). Differences between results can occur because of the type of myocardial damage or the size of the heart [39]. The reason why big errors were seen while evaluating LV viability, function, and volumes was because of doctor’s subjectivity and time between examination (procedures took place not the same day). All different diagnostic modalities are used to evaluate anatomical heart structure, although PET/CT (being expensive) is partly harmful to the patient because of exposure to radiation, shows myocyte morphology what helps to determine myocardial viability more precisely. Four chosen modalities are discussed not only that it shows myocardial damage precisely but is increasingly being used in clinical practice (PET/CT and MRI first were introduced in LUHS KC in autumn of 2012).

It is expected that this article will help to answer the question of which modality is the best to evaluate different parameters of the heart, but will help to choose which one to use (most precise, fastest and cheapest, less harmful) to examine patient. According to all mentioned reasons, the aim of this article is clear – to evaluate myocardium viability, heart volumes, systolic LV function using different modalities: echocardiography, SPECT, PET/CT, and heart MRI.

POSITRON EMISSION TOMOGRAPHY

PET scanners were introduced in 1970 and were used only for scientific purposes. After 1990 all body PET scans were started to be used in clinical practice. Firstly, it was used only for neoplastic processes, later for cardiologic patients. There was a problem related to the lack and availability of radionuclide material. Lack of computer software was an issue, too, so PET examinations were not performed daily.

PET is a radionuclide related examination method in which detectors are used to discern positron-emitting particles. This allows scientists and doctors to observe various biological events. There is no stable matter in nature which emits positrons, that is the reason why radionuclides must be produced in a particle accelerator – cyclotron (for example 18 F-fluor-2-deoxyglucose, which has a half-life of 110 seconds). PET scanners just visualize radionuclide existence in tissue, and physiologic signal depends on radioactive substance characteristics. The main disadvantage is that the half-life of a substance is low, which leads to high procedure costs [1, 2].

When positron leaves the atom's nucleus, it travels few millimeters and meets an electron, collides with it, and emits two photons, who travel in two opposite directions and are seen in circular detectors. Trail of two photons draws a line between two detectors and is called response line (sinogram). With the help of a computer, all response lines are combined, and a three-dimensional image is made dependent on radioactive material presence in tissue [3, 4].

Radiotracers attenuation correction is produced using computed tomography, which leads to lesser artifacts, and it leads to less negatively positive perfusion defects, which result in higher specificity. High PET resolution allows us to evaluate small perfusion defects and lowers false-negative results. Moreover, short radiotracer half-life reduces radiation dose and enables to produce tension and relaxation phases with the same scan.

PET compared to SPECT has more advantages because it has higher spatial resolution and attenuates correction more precisely, which leads to lesser numbers of tissue artifacts. Many studies proved that PET specificity and sensitivity is more than 90% [50, 51, 52].

Using outer detectors and PET radiotracking technique, it is possible to get in vivo radiotracer dispersion views. Just as the same as in CT scans, cross-sectional views are produced. View quality and type depend on radiotracer. PET allows evaluating blood flow, heart function, and metabolism using biological substrates not invasively with radionuclides such as carbon, oxygen, nitrogen, or fluoride. These radionuclides have a shorter half-life than those used in SPECT. Moreover, fluoro-deoxy-glucose (FDG) metabolizes fast, which means that stress test with adenosine or dobutamine could be proceded quite fast [24].

PET radiotracers acquire a stable stance when they emit positron, which is electron antimatter. Positrons have the same resting mass as electrons but are charged positively. When positron collides with an electron, they annihilate each other and emits 511-keV gamma radiation. Gamma radiation is colinear and flies in the opposite direction, so PET scanner could be programmed to detect only that kind of rays. This method allows us to reach higher spatial resolution than SPECT. Also, PET is stationary, while SPECT rotates [5, 7]. PET allows for correcting attenuation too [6].

Myocardium blood flow speed evaluation provides diagnostic and prognostic value sooner than it could be evaluated with SPECT, that is the main disadvantage of SPECT. Also, perfusion, substrate metabolism, and heart innervation in vivo can be monitored with PET noninvasively. That allows scientists to examine heart physiology and pathophysiology. FDG is the most common radiotracer used in examining myocardium viability [5].

HYBRID PET/CT

Ability to evaluate CAD, myocardium perfusion, metabolic activity, and function of the ventricle with hybrid PET/CT makes it inextinguishable

in clinical practice [8]. Heart PET/CT is quite a new modality for patients with CAD. The myocardium is evaluated coronary anatomy and function with a single scan; that is the reason why it has huge potential for cardiac patients. Hybrid PET/CT allows evaluating the location of the stenosis, level, and functional myocardium damage [10]. Moreover, the calcium index could be computed to patients with CAD and to proceed noninvasive angiography with contrast [9].
Production of PET/CT scanners starts with adding a CT system (which can produce 64 or more sections) to the PET scanner. These integrated systems work together to help the patient. All software is combined into a mechanical part of the PET device. One universal gantry is used with integrated software with PET/CT interface. CT portal is used in front of the device or back of it. Originally CT component in PET/CT device was used to correct attenuation and to see the patient's anatomy more precisely. Other more modern tomographs are able not only to correct attenuation but evaluate coronary calcium index and make CT angiography. All information about CT could be found in SNMMI/ASNC/SCCT guidelines [11].
Multiple layer CT angiography improved fast and became the most promising noninvasive heart artery examination method. Because of PET/CT scanners and improved software, multidisciplinary methods came to life with whom coronary arteries can be evaluated thoroughly using coronary artery calcium index and coronary angiography [12]. Moreover, PET/CT allows evaluating myocardium viability and metabolism [13].
Hybrid PET/CT helps to evaluate risk level and helps to make a decision about which CAD treatment strategy to choose. Compared studies showed that half of angiographically significant stenoses are not related to perfusion defects and are not hemodynamically significant. In contrast, coronary anomalies are found to patients with normal perfusion; First clinical trials were presented by Namdar et al., using PET with [13N]NH3 and four-layer CT angiography for 25 patients with CAD. Sensitivity, specificity, positive and negative, and predictive values foreseeing significant stenoses were 90%, 98%, 82%, and 99% respectively compared to golden standard – PET and angiography. This research shows that hybrid heart examination is crucial non-invasive for CAD and choice of treatment strategy [14, 15, 16].
Previous studies show that if perfusion defects are not found with PET/CT, then the probability for a patient (who has a moderate or high risk for CAD) to die is very low (1%). Also, patients who have less recurrent ischemia are treated with medication more effectively than a revascularization procedure. Although patients with large ischemia regions treated with invasive procedures receive better outcomes. Discussed methods allow specialists to decide which treatment strategy to use [2].
Diagnostic PET accuracy for CAD is high (sensitivity and specificity are more top than 90%). It is unique that with the help of PET, scientists can measure blood flow mL/min/g in the active and resting phase. Studies show that blood flow analysis with PET significantly reveals CAD incidence. Moreover, hybrid PET/CT is developing fast and can examine patients in the 45-minute interval in one session [2, 18].

GLUCOSE METABOLISM IN MYOCYTE

In specific surroundings, myocyte uses glucose for proper function for energy production and survival. In the aerobic environment, myocyte uses long-chain fatty acids, and this provides 70% of all energy demand. About 20% is received from glucose. Postprandial glucose rise is used for energy production firstly; this fast adaptation is crucial for normal heart function and is independent of lack of substrate, hormone imbalances, heart work, or other factors.
Chronic adaptation for substrate metabolism is seen after abnormal stimuli are observed. For example, if there is a chronic insufficiency of myocardial blood flow when the myocardium is hybernated leads to excessive dependability from plasma glucose. That is the mechanism of protection against hypoxia. On the other hand, if diabetes mellitus is present, then fatty acids are used more, and glucose is becoming not that necessary. This way of receiving energy is harmful to heart cells, which lead to heart dysfunction [19].

FDG is used for the detection of viable myocardium because glucose metabolism is a sign of biological activity. Also, FDG is used to diagnose patients with heart sarcoidosis, moderate or intense vasculitis, and heart implant infection where inflammation is the primary pathogenetic process.
Myocardial glucose intake depends on serum glucose and insulin level. Patient preparation also plays a crucial role in the need of getting an accurate view of myocardial viability. There are specific protocols that advises how to cope with a patient who has diabetes and those who do not [5, 20].
PET/CT is an essential procedure for diagnosing CAD because it allows detecting atherosclerotic damage (CT) and its‘ effect on blood flow (PET) in a single scan. It provides essential CAD diagnostic value and has a considerable advantage compared to CT or PET separately [18].

ECHOCARDIOGRAPHY

Echocardiography is cheap, convenient, and is easy to do. This diagnostic method can show heart function and hemodynamics. It is the most common diagnostic modality after cardiography and chest x-ray. For patients with acute heart pain, transthoracic echocardiography is made to evaluate myocardial movement and to diagnose acute coronary events. It is easy to find some dyspnea reasons such as dissection of the aorta or heart tamponade [47].

CARDIAC MAGNETIC RESONANCE IMAGING

Magnetic Resonance Imaging procedure in cardiology is making progress significantly fast, especially when there is a possibility to combine and synchronize it with electrocardiography. Using intravenous contrast agents, it is possible to evaluate myocardial structure changes. MRI is a noninvasive diagnostic method that allows examining a patient while he is laying on his back. MRI has better soft tissue differentiation ability than CT even without contrast agent.
MRI similarities compared to other radiologic methods – there is no radiation, the procedure is noninvasive, and there is no known negative effect to the human body, only that tissue collects radio waves, and body temperature may increase to around 1 degree Celsius during the procedure. To have quality images, 1,5 T MRI is required. 3 T MRI machines are better only at evaluating myocardial perfusion. While diagnostics with MRI is evolving and progressing, ventricle general and segmental functions could be evaluated easily (resolution is better than CT). Valve and vessel blood flow analysis could be performed because of great video resolution, and MRI is the easiest method to evaluate right ventricle function compared to other modalities. MRI disadvantages are excessive patient cooperation during the long phase of the examination, which takes 1,5 hours, is expensive, and requires a long time to proceed [21].
Heart muscle evaluation for patients with CAD and left ventricle insufficiency is crucial. Many methods are being used in clinical practice to evaluate heart morphology, function, and metabolism. Every method and procedure has its‘ own diagnostic advantage for measuring myocardial viability, although no one of each can show heart wall damage. MRI with contrast was presented as an alternative for evaluating heart damage. Few experimental studies show a comparison of histologic and contrast MRI views of muscle necrosis, moreover, contrast MRI allows to detect reversible and permanent myocardium defects with the help of contrast agent, which accumulates transmurally. Depending on the radiotracer’s presence in heart muscle contractile function, prognosis can be predicted after revascularization of infarcted myocardium in the presence of CAD [22, 23].
Late gadolinium enhancement (LGE) is a unique feature of MRI and is related to different gadolinium contrast agent presence in normal and damaged myocardium. When a marked gadolinium agent is introduced into the bloodstream, it moves to expanded intracellular space of infarcted heart cells and shows scientists which parts are affected by necrosis. Maximal signal strength is received 10-20 minutes after contrast agent introduction [23]. Late gadolinium enhancement test has a high sensitivity level and can detect

CAD caused scars. Using the late gadolinium enhancement technique, small scars that were not identified with cine MRI were found [24]. It is calculated that the scar area must cover more than 50% of muscle for wall movement anomaly to occur. Also, using late gadolinium enhancement technique, infarctions can be found, which were not seen with SPECT. Surprisingly, microinfarctions are found created with percutaneous angiography and a slight increase of creatine kinase [25].
LGE MRI correlates well with PET/CT findings of myocardium blood flow and metabolism and is more sensitive to endocardial infarctions. Studies also show importance in examining myocardium after revascularization [26]. Moreover, there is a vast amount of information showing MRI benefits, that is the reason why many think MRI with LGE is the golden standard in examining myocardial viability better than PET/CT [23, 27].
Using MRI high-resolution myocardium images is received, and the high contrast between tissue and blood allows doctors to evaluate heart chambers more precisely. CAD is usually diagnosed when abnormal heart movement is observed using an echoscope with dobutamine or myocardium perfusion method after injection of gadolinium radiotracer. Detecting scars or necrosis with the LGE technique is a unique MRI ability [14]. On the other hand, chronic ventricle insufficiency with altered blood flow and metabolism can be evaluated using PET/CT, though tissue composition (a scar or normal tissue) with MRI [28]. MRI is much better for evaluating subendocardial or transmural damage because of its high image resolution. In addition, it is used to evaluate wall scaling during ventricular contraction. When a viable myocardium shows a distortion of the marked magnetic lines through the systole, the myocardial scar will not show such differences [29]. In one study, scientists compared MRI and PET with FDG. He discovered that MRI with late gadolinium enhancement closely agrees with PET/CT data as a myocardial scar marker. However, MRI has more often identified a scar than PET/CT, with a higher resolution [29].

Single Photon Emission Radionuclide Computed Tomography (SPECT)
SPECT is a radionuclide test where gamma rays are used to obtain an object's two-dimensional image. The SPECT machine consists of a gamma camera, a bed for the patient, a computer that produces tomographic reconstruction, software, and interface.
Various radiotracers (usually (99m Tc) -MIBI) are used for examination. Unlike PET, gamma photons are released directly from the radioactive material. PET radiotracers annihilate positrons to electrons a few millimeters away and emit two gamma photons that are thrown in the opposite direction.
Radiated photons are "captured" by the collimators, which leave scintillation (glow) in scintillation crystal. The photoelectric multiplier is sensitive to that glare, which is captured and processed by the computer. From 1 to 3, gamma chambers are used in SPECT. You need to scan at a 360° angle to get more accurate images.
SPECT is about three times cheaper than PET/CT, and one of the most sensitive cardiac perfusion modality (83% accuracy - 85%, sensitivity, 72% specificity). Disadvantages of SPECT: inadequate image due to scattered gamma rays compared to PET/CT, last long, the image quality decreases if the patient moves and artifacts are possible due to the random distribution of radiotracer. The sensitivity of the SPECT to detect angiographically proven CAD is high (87-89%), and specificity is 89%. SPECT not only identifies a lesion but shows where and what size it is [48]. Also, patients with less reversible ischemia have been shown to have a greater chance of survival while receiving medication than a revascularization procedure, whereas, in patients with high ischemic zone, invasive revascularization procedures are more necessary [49]. These SPECT properties are useful for selecting patients for percutaneous coronary intervention and possible revascularization.
Myocardial perfusion reserve data obtained with MRI and PET/CT correlate well in the evaluation of myocardial blood flow. Both methods show myocardial damage accurately and similarly [30]. Volumes of the heart were measured

by PET/CT, left ventricle EF and wall movement corresponds well to the parameters determined by MRI [3]. In addition. Higher resolution images are obtained with MRI compared to PET/CT. MRI should be an alternative method for the assessment of patients with CAD in centers where it is not possible to study myocardial viability with PET/CT, or it is just too expensive [31]. Similar results are observed when comparing PET/CT with SPECT and PET/CT with echocardiography [23, 45, 47, 48].

RESEARCH OBJECT

Patients who are examined and treated in Lithuanian University of Health Sciences Kaunas Clinics Department of Cardiology after acute myocardial infarction with significantly decreased left ventricular ejection fraction (LV EF ≤40%) and serious coronary artery damage which revascularization is compromised because of myocardial scarring.

SELECTION OF SUBJECTS

Participant selection was performed according to disease (CAD, MI), present heart insufficiency, and examination technique (echocardiography, SPECT, PET/CT, and MRI). There were 30 participants who were examined in Lithuanian University of Health Sciences Kaunas Clinics from 2012 to 2016.

RESEARCH ORGANIZATION AND METHODS

There is not a daily routine to perform all mentioned radiologic examination procedures to patients after acute myocardial infarction even in specialized Lithuanian hospitals. This was the reason for choosing a prospective trial. Patient information was examined (case histories and records). Some patients decided not to participate in the trial or had contraindications for MRI.

Left ventricle EF, EDV, ESV, and sixteen heart segment damage was evaluated with four different modalities:

1) Echocardiography
2) Single Photon Emission Computed Tomography (SPECT) using (99mTc)-MIBI radiotracer.
3) Positron Emission Tomography/Computed Tomography (PET/CT) using (18F)-FDG radiotracer.
4) Heart Magnetic Resonance Imaging (MRI) using late gadolinium enhancement with Gd-DO3A-butrol radiotracer.

Heart segments were numbered from heart apex to base. Sixteen segments are: basal anteroseptal (14) basal anterior (13), basal lateral (18), basal posterior (17), basal inferior (16), basal inferioseptal (15), mid anteroseptal (8), mid anterior (7), mid lateral (12), mid posterior (11), mid inferior (10), mid inferoseptal (9), apical anterior (1), apical lateral (5,6), apical inferior (4), apical septal (2,3).

Using echoscope, myocardium segments were marked by doctor and movement evaluated in scale by a number. If the segment value is three or more, that means that the segment is not functioning well and has akinetic zones. Examining with SPECT significant perfusion defect was considered if the index value is 3,5 or more. Segment examined using PET had little viability if glucose accumulation in heart muscle was lower than 50%, and segments that were examined with MRI and had transmural scar were considered to be not viable at all.

METHODS OF DATA ANALYSIS

Statistical data analysis was performed using SPSS (Statistical Package for the Social Sciences) program („IBM," Armonk, New York, USA). Data belonging to the normal distribution was checked by Kolmogorov-Smirnov and Shapiro-Wilk criteria. Distributed values are given as averages with standard deviation (SD) in brackets. Data is given in absolute value.

While analyzing the relationship between different cardiac testing methods chi-square, ($\chi 2$) probability criterion was performed. Myocardial segment damage was checked by the McNemar test and a paired t-test was performed for EF, EDV, and EST. The results were considered statistically significant when p is lower than 0.05.

GENERAL DATA OF THE SUBJECTS

The mean age of subjects (n=30) during the study was 67.8 years (range 43-84 years). Distribution by sex - 25 males (83.3 %) and five females (16.6 %). Patients had risk factors: six (20 %) were obese (BMI ≥30 kg/m2), ten (33 %) had overweight (BMI 25-29,99 kg/m2), presence of dyslipidemia – twenty-five (83.3 %), twenty-one patient (70 %) had arterial hypertension, seven patients (23.3%) were smoking, two (6.6%) had diabetes, and fourteen had a family history of CAD (46.6%).

Table 1. Risk factors

Risk factor	N	%	Risk factor	N	%
BMI ≥30 kg/m2	6	20	Smoking	7	23,3
BMI 25–29,99 kg/m2	10	33.3	Diabetes	2	6,6
Dislipidemia	25	83.3	Family history	14	46,6
Arterial hypertension	21	70	Age >45 male, >55 female	29	96,6
Male	25	83,3			

According to anamnesis, atrial fibrillation was diagnosed in five (16.6%) patients and atrial flutter in one (3.3%). Ventricular extrasystoles were found in five (16.6%) and ventricular tachycardia to four (13.3%) patients — the weakness of the sinoatrial node diagnosed to (3.3%) patient. According to NYHA (New York Heart Association) heart failure criteria, two subjects (6.6%) had class II heart failure, nineteen (63.3%) had grade III, and nine (30%) had grade IV. Six patients (20%) had a stroke. The oncologic process has been previously recorded for one patient (3.3%). One (3.3%) patient had the chronic obstructive pulmonary disease (COPD), and two (6.6%) were diagnosed with anemia. The first stage of chronic kidney disease (CKD calculated by glomerular filtration rate) was diagnosed to one (3.3%), the second stage CKD to four (13.3%), the third stage - to three (10%). Coronary artery bypass graft (CABG) operation was conducted on six (20%) subjects.

It was evaluated how many drugs were used. The most common drug was adrenal blockers, 28 patients used it (93.3%), no one used calcium channel blockers, ACE inhibitors was prevalent to 21 (70%) patients, Aldosterone receptor blockers - 5 (16.6%), ivabradine - 8 (26.6 %), digoxin - 3 (10%), torazemide - 20 (66.6%), spironolactone - 20 (66.6%), aspirin - 27 (90%), clopidogrel - 10 (30%), vitamin K antagonists - 9 (30 %), nitrates - 17 (56.6%), statins - 28 (93.3%), one patient (3.3%) treated with oral drugs and another one (3.3%) with insulin. Allopurinol was taken by 6 (20%) patients.

Almost all patients were treated with the best possible treatment because they were treated with beta-adrenergic blockers (93.3%), ACE inhibitors, or aldosterone receptor inhibitors (70 + 16.6 = 86.6%). These three drugs are adequate treatment for patients with CAD and heart insufficiency. Statins (93.3%) are also used to achieve the optimum treatment result, while aspirin is always given after an acute myocardial infarction, although two patients (6.6%), aspirin was contraindicated because of a high risk of bleeding from the gastrointestinal tract. Despite the best available treatment, symptoms continued, and patients still contacted doctors. After advanced radiological examinations, the treatment regimen for CAD and heart failure was chosen: to continue medication, to prescribe interventional, or to treat surgically.

Table 2. Anamnesis

Anamnesis		**N**	**%**	**Anamnesis**		**N**	**%**
Atrial fibrillation		5	16.6	CKD	I	1	3.3
Atrial flutter		1	3.3		II	4	13.3
Ventricular extrasystoles		5	16.6		III	3	10
Ventricular tachycardia		4	13.3	Anemia		2	6.6
The weakness of the sinoatrial node		1	3.3	Stroke		6	20
HF, NYHA	I	0	0	Cancer		1	3.3
	II	2	6.6	COPD		1	3.3
	III	19	63.3	Heart bypass surgery		6	20
	IV	9	30				

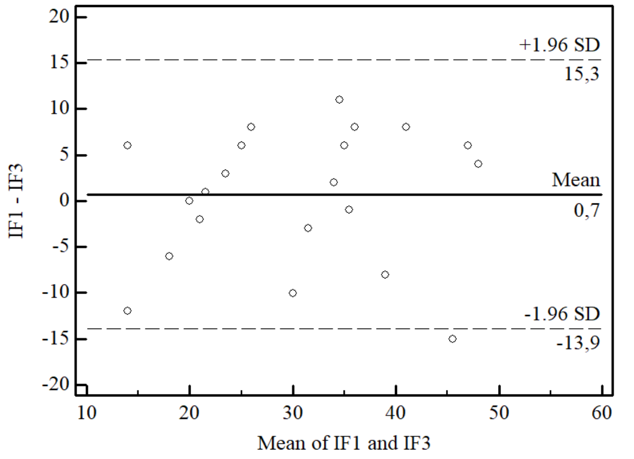
Table 3. Drug use among patients

Medication	**N**	**%**	**Medication**	**N**	**%**
Beta adreno blocker	28	93.3	Alopurinol	6	20
Calcium channel blocker	0	0	Aspirin	28	93.3
ACE inhibitor	21	70	Clopidogrel	10	30
Aldosterone receptor blocker	5	16.6	Vit. K antagonist	9	30
Ivabradine	8	26.6	Nitrates	17	56.6
Digoxin	3	10	Statins	28	93.3
Torazemide	20	66.6	Injections of insulin	1	3.3
Spironolactone	20	66.6	Metformin	1	3.3

While assessing the history of past or existing arrhythmias, it was observed that the left bundle branch block occurred in most cases - 14 patients (46.6%), while other arrhythmia monitored less often: sinus rhythm - 4 (13.3%), atrioventricular block - 4 (13.3%), premature complexes - 1 (3.3%), while the right bundle branch block have occurred to nobody (0%). Resynchronization therapy has not been applied to anyone. Moreover, patients with intracardiac defibrillators are not included in the study because MRI is contraindicated for them. Coronary angiography was performed to all 30 (100%) patients. Right coronary artery stenosis was found to (RCA> 75%) 21 (70 %) patients, anterior interventricular branch (AIB> 75%) to 28 (93.3 %), circumflex branch (Cx> 75%) to 23 (76.6 %).

Pair Differences Of Ejection Fractions (EF) Between Test Methods

Paired t-test checks whether test value t is close to zero. If so, the difference between results of the two modalities EF, EDV, and ESV values is negligible. It was found that only paired difference between echocardiography and PET/CT in EF, EDV and ESV was negligible. However, comparing the SPECT with PET/CT, and MRI with PET/CT differences between the EF, EDV, and ESV is significant. If 95% of normal distribution includes a zero value, the differences between the methods are considered to be statistically insignificant.



The paired difference between echocardiography (EF1) and PET/CT (EF3).

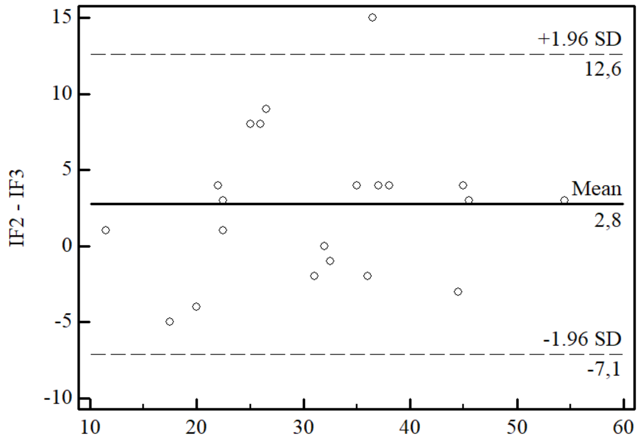
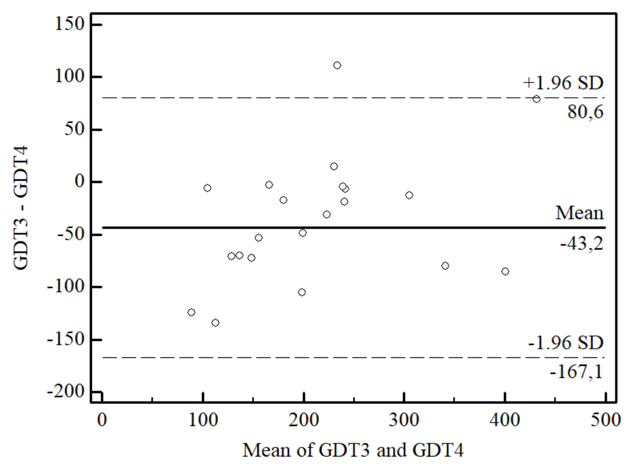


Fig. 2. Paired EF difference of SPECT (EF2) and PET/CT (EF3).

PAIRED END-DIASTOLIC VOLUME (EDV) DIFFERENCES BETWEEN TEST METHODS



4 Fig. The paired difference between echocardiography and PET/CT (EDV3).

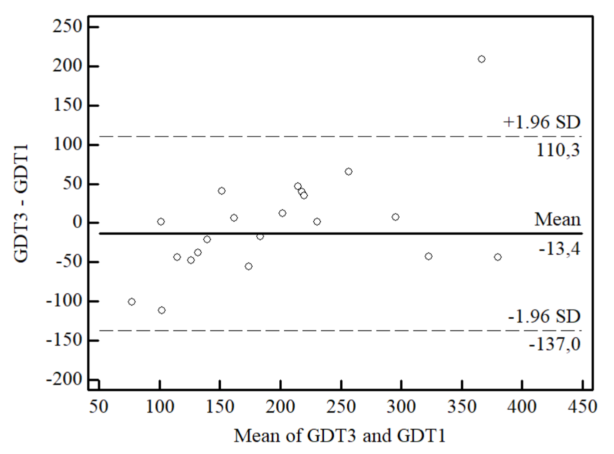


Fig.5. Paired GDT difference of SPECT (EDV1) and PET/CT (EDV3)

EDV difference between echocardiography and PET/CT was not significant (OR 13.36 [95% CI -10,18-36,92], p=0.25), but paired GDT difference between SPECT and PET/CT study techniques - significant (OR 37.7 [95% CI 20.08-55.39], p <0.05), same result with MRI and PET/CT modalities (OR 43.23 [95% CI -66.82-(-19.63)], p <0.05).

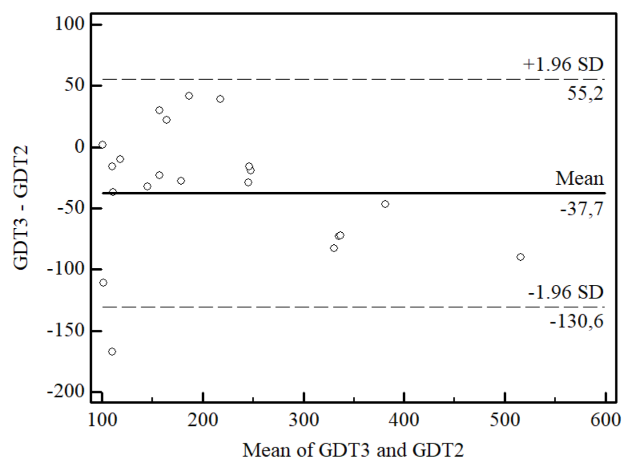
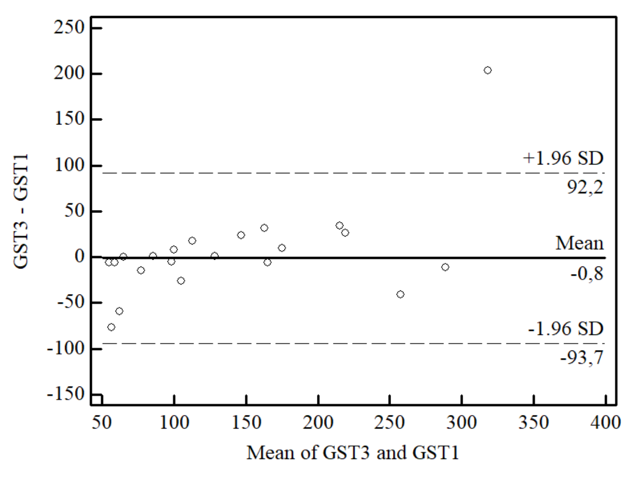
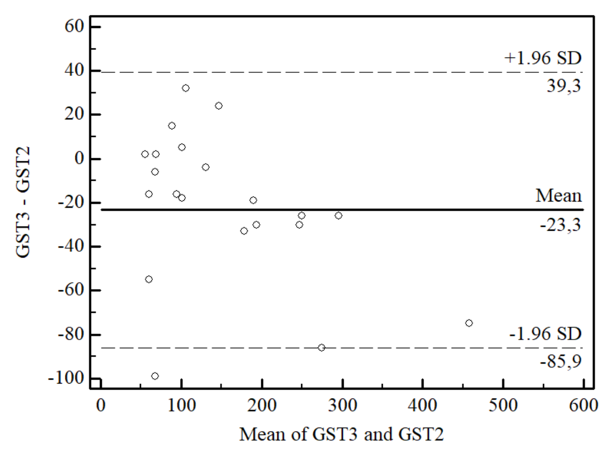


Fig. 6. Paired EDV difference between MRI (EDV2) and PET/CT (EDV3)

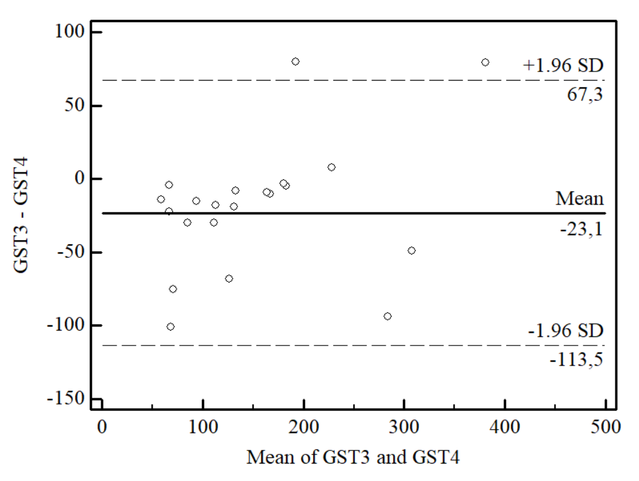


7. Paired ESV Difference of Echoscope (ESV1) and PET/CT (ESV3)



8. Paired ESV difference between SPECT (ESV2) and PET/CT (ESV3)

PAIRED END-SYSTOLIC VOLUME (ESV) DIFFERENCES BETWEEN TEST METHODS



9 Fig . Paired ESV difference between MRI (ESV4) and PET/CT (ESV3).

Pair ESV difference between echocardiography and PET/CT modalities was not significant (odds ratio 0.76 [95% CI -16,93-18,46], p=0.93), but paired ESV difference between SPECT and PET/CT was significant (odds ratio 23.267 [95% CI, 11.34-35.19], p<0.05) together with ESV difference between MRI and PET/CT (odds ratio - 23.13 [95% CI-4 0.35-(-5.90)], p<0.05).

STATISTICAL ANALYSIS OF DAMAGED SEGMENTS

Four hundred eighty myocardium segments were analyzed with four different methods in total. Hibernating myocardium areas larger than 10% was found in a combination of SPECT and PET/CT for eight (26.6%) patients.

It was calculated after examination with each diagnostic method of how many damaged segments were detected. Independent data was examined, results were reported, and the Pearson Chi-square criterion checked their significance.

Most of the damaged myocardial segments showed the statistically insignificant difference (p> 0.05), a significant difference was observed only between lower apex (4), and lateral apex (5, 6) segments (p<0.05). That is the reason why we can say that segment damage is detected similarly with different methods.

While comparing the studies, the values of apical lateral (5, 6) and apical septal (2,3) segment lesion detection difference was statistically significant between echocardiography, SPECT, PET/CT and MRI (p <0.05). There is no complete correlation between echocardiography, SPECT, PET/CT, and MRI in evaluating myocardial damage.

TABLE 4. NUMBER OF DAMAGED MYOCARDIAL SEGMENTS

Segment	Number of damaged myocardial segments (out of 30 patients)				P-value
	Echoscopy	GNP	PET / CT	IHR	
14	12	10	9	10	0.88
13	10	6	5	7	0.46
18	4	1	2	2	0.52
17	4	6	5	7	0.78
16	9	7	4	7	0.48
15	3	4	6	9	0.2
8	22	16	15	18	0.26
7	19	17	15	16	0.76
12	4	3	2	3	0.86
11	7	8	4	5	0.56
10	11	11	7	9	0.64
9	9	6	5	7	0.64
1	20	22	17	17	0.43
5.6	20	16	9	13	<0.05
4	20	15	9	12	<0.05
2.3	20	13	14	18	0.22

STATISTICAL ANALYSIS OF DEPENDENT DATA

Dependent data analysis was performed, and Spearman correlation coefficients (r) and kappa value (κ) were determined, data were checked with the McNemar test.

The greater the Spearman correlation factor is, the greater the segment damage correlation is, using different diagnostic methods.

When Spearman correlation coefficients were identified (r> 0.05), and values of McNemar test checked (p <0.05), It was found that there is a correlation in the detection of thirteen (from sixteen) myocardial segments damage with all four different modalities. Kappa (κ) value indicates a higher or lower coincidence level.

5 table. Interpretation of Kappa value

Kappa (κ) value	Compliance
<0.20	Bad
0.21-0.40	Enough
0.41-0.60	Average
0.61-0.80	Good
0.81-1.00	Very good

Table 6. Myocardial segments coincidence analysis

Segment of myocardium		Modality	Spearman correlation rate (r)	Kappa (κ) value	McNemar test value
basal anteroseptal (14)	PET/CT	Echocardiography	0,65	0,64	0,38
		PET/CT	0,72	0,77	1,00
		MRI	0,93	0,92	1,00
basal anterior (13)	PET/CT	Echocardiography	0,44	0,40	0,13
		SPECT	0,89	0,89	1,00
		PET/CT	0,81	0,79	0,50
basal lateral (18)	PET/CT	Echocardiography	-0,06	-0,05	0,63
		SPECT	-0,13	-0,13	1,00
		MRI	0,80	0,78	1,00
basal posterior (17)	PET/CT	Echocardiography	0,38	0,38	1,00
		SPECT	0,45	0,44	0,69
		MRI	0,58	0,58	1,00
basal inferior (16)	PET/CT	Echocardiography	0,76	0,74	0,25
		PET/CT	0,91	0,90	1,00
		MRI	0,91	0,90	1,00
basal inferoseptal (15)	PET/CT	Echocardiography	0,44	0,40	0,13
		SPECT	0,53	0,50	0,22
		PET/CT	0,37	0,37	0,73
mid anteroseptal (8)	PET/CT	Echocardiography	0,34	0,31	0,11
		SPECT	0,33	0,33	1,00
		MRI	0,60	0,6	0,69
mid anterior (7)	PET/CT	Echocardiography	0,42	0,40	0,18
		SPECT	0,94	0,93	1,00
		MRI	0,94	0,93	1,00
mid-lateral (12)	PET/CT	Echocardiography	-	-	0,25
		PET/CT	-	-	0,25
		MRI	-	-	0,25
mid posterior (11)	PET/CT	Echocardiography	0,35	0,35	1,00
		SPECT	0,71	0,67	0,25
		MRI	0,88	0,87	1,00
mid inferior (10)	PET/CT	Echocardiography	0,68	0,63	0,06
		SPECT	0,61	0,6	0,38
		MRI	0,92	0,91	1,00
mid inferoseptal (9)	PET/CT	Echocardiography	0,38	0,38	1,00
		SPECT	0,51	0,51	1,00
		MRI	0,32	0,31	1,00
apical anterior (1)	PET/CT	Echocardiography	-	0,35	<0,05
		SPECT	-	0,05	0,12
		MRI	-	0,54	0,13

apical lateral (5,6)	PET/CT	Echocardiography	0,34	0,21	<0,05
		SPECT	0,48	0,38	<0,05
		MRI	0,35	0,29	0,07
apical inferior (4)	PET/CT	Echocardiography	0,4	0,27	<0,05
		SPECT	0,39	0,36	0,18
		MRI	0,59	0,59	1,00
apical septal (2,3)	PET/CT	Echocardiography	0,76	0,74	0,13
		SPECT	0,73	0,73	1,00
		MRI	0,46	0,46	1,00

While comparing echocardiography with PET/CT, and SPECT with PET/CT basal lateral (18) segment results completely divides, as Spearman coefficient, Kappa value is negative (ultrasonographically observed only one lesion, with PET/CT – 3 and with SPECT - 4). The coincidence level is very low. A similar trend has been observed, and with mid-lateral (12) segment, as with PET/CT procedure, any mid-lateral (12) segment lesion was observed. Spearman correlation coefficient and Kappa value cannot be calculated because some PET/CT test result is constant (not any specific myocardial zone lesion was found). It is also impossible to count the Spearman correlation coefficient of the apical frontal segment (1), as neither one patient examined with PET/CT had myocardial damage. This data can be considered as completely unfamiliar.

It seems that the segments of PET/CT and MRI have the most significant similarities, as the majority (10 out of 16) segments Spearman ratio and 11 out of 16 segments Kappa values are closest to one.

If the McNemar test value is > 0.05, then we can reject the hypothesis that the results of the different test methods are significantly different when evaluating segment damage. All damaged myocardium segments examined with PET/CT coincided with echocardiography, SPECT and MRI tests, except apical frontal segment (1) of the PET/CT and echocardiography (McNemar - <0.05) and PET/CT with echocardiography (McNemar - <0.05) and PET/CT with MRI (McNemar <0.05) for apical lateral (5, 6) segment. Also, a value that not passed McNemar test was calculated by examining the apical inferior (4) segment with PET/CT and echocardiography.

In conclusion, it could be said that if we get McNemar test value is <0.05, then there is no coincidence between the test methods. While investigating patients, only two segments lesion diagnosis mismatched between methods.

Analysis of heart EF, EDV, and ESV

A comparison of PET/CT with echocardiography, SPECT, and MRI revealed that there is no statistical reliability of significant errors in EF, EDV, and ESV between the same methods (p>0.05).

Using echocardiography, it was found the most damaged segments compared with PET/CT, SPECT, and MRI - the biggest mismatch result. The biggest viable myocardial area was calculated using PET/CT.

While examining EF, EDV, and ESV detected with MRI and comparing it with other modalities; it was clear that significantly similar data was received only using MRI and SPECT (p>0.05). The difference is insignificant if using a paired Student t-test for dependent samples change close to 0, and 95% CI includes 0.

Table 10. MRI EF , EDV and ESV P values for comparison

Couple of modalities (EF)		P value (EF)	P value (EDV)	P value (ESV)
MRI	Echocardiography	0.77	<0.05	<0.05
	SPECT	0.57	0.69	0.99
	PET/CT	<0.05	<0.05	<0.05

MRI is a 'golden standard' for cardiac volume and function. This study found that using MRI and SPECT EF, EDV, and ESV coincide well ($p>0.05$). EF also coincides with echocardiography ($p=0.77$). MRI and PET/CT EF, EDV, and ESV were compared, and results do not match ($p<0.05$).

Patients who have more than 10% of hibernated myocardium found with SPECT perfusion and PET/CT metabolism tests coronary artery bypass grafting (CABG) would be useful because revascularized hibernated myocardium recovers to the previous stage. However, if the scar is already formed and the hibernating myocardial area is less than 5%, the CABG would not be beneficial to the patient. While comparing SPECT and PET/CT images, the hibernating left ventricular zone was found to be more than 10% in 8 (26.6%) patients, CABG is recommended for them.

DISCUSSION

In this study, heart muscle motility, perfusion, and metabolism were evaluated by various modalities in patients after acute myocardial infarction (MI). The most important results were found by comparing the levels of segment damage. It has been observed that segmental damage is well seen by methods of echocardiography, SPECT, PET/CT, and MRI.

In one study, after PET/CT and MRI evaluation of left ventricle EF, EDV and ESV were found a good correlation between function parameters, but some variation was seen, so these two studies cannot be used as a replacement for each other [59]. Although after the assessment of echocardiography and MRI results, there was found proper matching in EF [57]. Other studies showed similarities between methods for evaluating EF, cardiac volumes, and vitality [53, 54, 55, 56, 57, 58].

In another study, 289 segments were evaluated with PET/CT, and 82% of the segments were identified as damaged while with MRI, only 72.6%. Both methods correlated with 75% precision [60]. Similar situations observed with echocardiography and MRI modalities [61]. Another study showed that PET/CT and MRI correlate carefully evaluating left ventricular volumes and EF [58], although this article shows discrepancies in EDV and ESV between the two methods of examination.

Transmural heart defects closely correlate between MRI and PET/CT. Due to the high image resolution, MRI identifies even subendocardial scars. However, more research is required to find out whether MRI is more useful than PET/CT in assessing myocardial recovery after revascularization because there is still not enough data if MRI could replace PET/CT as a starting point in the investigation of myocardial viability [62].

PET/CT research is getting more available, and its accuracy is higher than SPECT. PET/CT sensitivity and specificity for CAD diagnosis are 89 % and 90%, respectively [4, 63]. PET/CT accuracy is achieved through improved video resolution, overlay matching, and attenuation correction. This gives an advantage to studying obese patients, who are particularly prone to increasing the chance of artifacts. Echocardiography is also not the best study for patients who have a BMI of more than 30. Scientists have researched and found that PET/CT is very similar but slightly more accurate than SPECT (89% and 79%) in myocardial injury determination, including obese patients. Also, researchers have shown that the quality of the images was better with PET/CT (78%) than with SPECT (62%) [51]. Accurate diagnosis and prognosis for the patient are important, and various heart examination techniques accurately detect cardiac lesions. That helps to determine the appropriate treatment for the patient. Moreover, the probability of another cardiovascular event must be evaluated for each patient [66]. The PET/CT study is not an extremely frequent study, as it is costly for the healthcare system [64].

The accuracy of echocardiography is heavily dependent on investigating physicians because it is difficult to assess wall movements without a large margin of error objectively. Besides this, the patient's physique and the acoustic window have influence [65]. Due to examined reasons, echocardiography correlates not so well with PET/CT while assessing myocardial segments,

but EF, EDV, and ESV results correlate well with those from PET/CT study. As echocardiography develops, it is assumed that in the future, the echocardiographic examination will be used to evaluate myocardial movements more precisely.
To asses ideally, echocardiography, SPECT, PET/CT, and MRI should be proceeded in a period of a few days, because over time, myocardial structure changes, which may change cardiac parameters. The data compared in this study may also have been different because echocardiography, SPECT, PET/CT, and MRI were not performed on the same day.
Coronary artery bypass graft may be needed for those with more than 10% of hibernating myocardium in the left ventricle, believing that post-operative heart muscle viability, movement, and function will be restored. Although further research is needed to optimize this procedure [67].

CONCLUSIONS

1) Non-invasive cardiovascular imaging modalities (echocardiography, (99mTc)-MIBI SPECT, (18F)-FDG PET/CT and MRI) correlate well because 13 of 16 segment parameters match between types of examination. Spearman correlation coefficient (r>0,05) and Kappa value (κ>0,05) was counted, McNemar test was performed (p>0,05).
2) The agreement is seen between ultrasound and PET/CT when compared to EF, ESV, and EDV. Agreement between MRI and SPECT is seen too. Only EF (without EDV and ESV) agreement is seen between echocardiography and MRI. The paired t-test was performed (p>0,05).
3) PET/CT ("gold standard") and CMR damage of segments (viability) correlate best of all because most of the segments (10 of 16) Spearman coefficients and 11 of 16 segments Kappa values are close to one.
4) Comparing MRI ("gold standard") EF, EDV, ESV with other modalities, significantly similar data could be obtained only with MRI and SPECT. EF (without EDT and ESV) agreement is seen between echocardiography and MRI alone (p>0,05).

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