

*Original article*

## Myocardial Perfusion Scintigraphy in the Prediction of the Existence of Hemodynamically Significant Coronary Artery Stenosis

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### SUMMARY

**Introduction/Aim.** Anatomically insignificant stenosis of coronary arteries obtained on coronary angiography, in numerous cases can show hemodynamic significance and as such cause ischemic myocardial changes. The goal was to assess the diagnostic accuracy of myocardial perfusion scintigraphy (SPECT MPI) in the detection of hemodynamically significant coronary artery stenosis in patients with moderate risk for ischemia, without previously detected coronary disease.

**Patients and methodology.** The study included 258 patients, of which 54% females and 46% males, with an average age of  $59.0 \pm 10.1$  years. SPECT MPI was done by a two-day protocol with 99 mTc-MIBI. The pathological finding was the existence of perfusion defects. The physical stress test was done by Bruce protocol. Coronary angiography (CA) was performed according to a standard protocol in patients with pathological SPECT MPI findings ( $n = 128$ ). Anatomically significant coronary artery narrowing was  $> 70\%$ . Stenoses from 30% to 69% were considered hemodynamically significant in patients with reversible perfusion defects on SPECT MPI.

**Results.** The sensitivity (SE) of SPECT MPI was 89%, specificity (SP) 42%, positive predictive value (PPV) 86%, negative predictive value (NPV) 50%, and total diagnostic accuracy (ACC) was 74% when the results were compared with stenosis  $> 70\%$ . By including stenosis from 30% to 69%, the obtained values of diagnostic indicators of SPECT MPI reliability were: SE 91%; SP 100%; PPV 100%; NPV 50% and ACC 91%.

**Conclusion.** With CA only, it is not possible to prove the existence of hemodynamic significance of coronary artery stenoses from 30% to 69%, which represents a recruitment range for developing ischemia. SPECT MPI shows high SE, SP, PPV, and ACC in detecting the existence of left ventricular myocardium perfusion disorder in either stenosis of coronary arteries with or without anatomically significant value.

**Keywords:** myocardial perfusion scintigraphy, coronary disease, hemodynamics of coronary artery stenosis, anatomical significance of coronary stenosis

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## INTRODUCTION

A strict pathophysiological division into primary myocardial ischemia - ischemic heart disease – coronary artery disease (CAD), which occurs as a result of coronary artery spasm, or secondary ischemia, that occurs as a result of coronary artery stenosis, practically does not exist in everyday clinical practice. However, in the vast majority of cases, it is represented by mixed ischemia of the myocardium, which implies the existence of pathophysiological mechanisms of both vasospasm and the existence of stenotic lesions of the coronary arteries (1). A normal heart rate at rest enables the complete extraction of oxygen by cardiomyocytes from the blood of the coronary arteries, therefore, oxygen extraction under conditions of increased oxygen demand is not possible. According to this oxygen extraction mechanism, a healthy heart compensates for increased demands simply by increasing the coronary flow. A failure to increase coronary flow for any reason, spasm, or stenosis will lead to ischemia (2).

The result of all pathophysiological processes is the remodeling of the coronary arteries, either positive or negative, which, in case of progression, inevitably leads to a decrease in the lumen of the coronary artery and thus to disruption of the hemodynamics of blood flow (3).

The existence of disturbed balance in the supply of oxygen to the myocardium and its current needs for the same can lead to various manifestations: occurrence of anginal discomfort, changes in the ECG's ST segment, regional or global contractility disorders, i.e. reduced uptake of radiopharmaceuticals by the myocardium during perfusion scintigraphy.

CA is one of the ways of visualizing coronary blood vessels after radiopaque contrast is applied with a catheter. In terms of morphology, this method represents the gold standard for assessing the presence of stenoses and their severity on coronary artery blood vessels (4, 5).

The method is invasive, and as such it carries certain risks, i.e. discomfort for the patient.

The combination of physical load tests with myocardial perfusion scintigraphy is a non-invasive method, with considerably lower risk for the patient. The results obtained by a combination of these two methods, within the framework of myocardial perfusion imaging (MPI) with single-photon emission tomography, play a significant role in the selection of

patients, who should be referred to invasive diagnostic and therapeutic procedures in the framework of detection and treatment of ischemic myocardial disease.

## AIM

The aim of the study was to assess the diagnostic accuracy of myocardial perfusion scintigraphy with single-photon emission tomography (SPECT MPI), in the early detection, assessment of severity and treatment of coronary disease in patients suspected of having ischemic heart disease, at moderate risk for ischemia, but without previously detected coronary disease.

## PATIENTS AND METHODS

This study included patients at moderate risk for CAD according to the pretest probability calculated using the Duke Clinical Sum without previously detected coronary artery disease. The clinical score of CAD prediction was made in the program package according to the ACC/AHA/ACP-ASIM (6) protocol, through the Duke test (7), that is, by calculating the Duke clinical sum (DCS). The prediction only applied to patients without previously verified CAD. A total of 258 patients were examined, of which 140 women (54%) and 118 men (46%), with average age of  $59.0 \pm 10.1$  years (range 23 - 79 years). SPECT-MPI was performed according to a two-day protocol (7), on a two-detector gamma camera (Ecam, Siemens, Germany) equipped with high-resolution (Hi-Res) collimators. The radiopharmaceutical used was Tc – 99 m methoxyisobutylisonitrile (MIBI) (Tc-99 m MIBI). On the first day, a study was performed with the application of radiopharmaceuticals immediately after the end of the physical load test, in the dose of 20 mCi, while on the second day, a study was done at rest with the same dose of radiopharmaceutical. In patients in whom perfusion defects were recorded on the stress study, when performing the study at rest, 5 minutes before the application of radiopharmaceuticals, the diagnostic application of a coronary dilator (Nitrolingual-Spray, G. Pohl-Boskamp GmbH & Co, KG, Kieler Strasse 11, Hohenlockstedt, Germany) in the dose of 0.4 to 0.8 mg was done to assess the viability of the myocardium affected by ischemia (8, 9).

The dilator was applied sublingually. The reconstruction of the scintitomogram through the

myocardium of the left heart chamber was done along the coronal, sagittal, and transverse axes both for the study after the physical load test and for the study at rest.

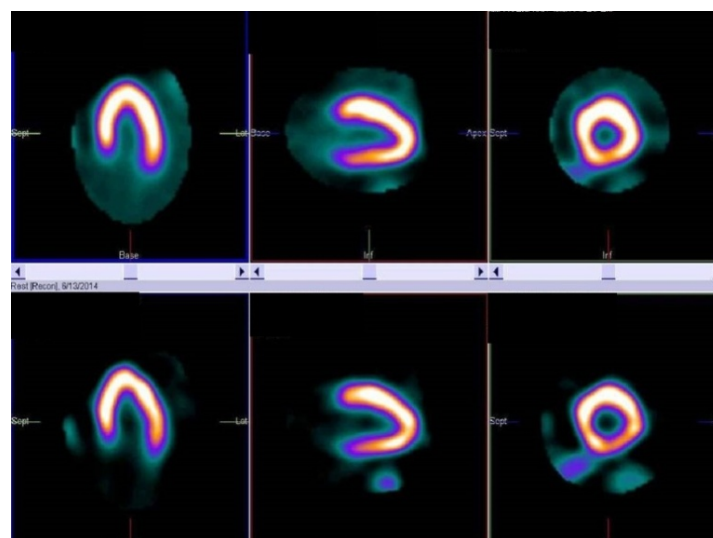
All patients underwent a stress test with a physical load on a treadmill, after adequate preparation, which included the exclusion of beta-blockers, calcium channel antagonists, and nitrates. The treadmill exercise test was performed using the Bruce protocol (10, 11). It is understood that there are load levels that increase every three minutes from the start of the test. In all subjects, the test was completed after reaching 85% of the heart rate value (12, 13). The calculation of the target heart rate (THR) was done according to a modified formula that allows for avoiding differences in training and differences brought about by belonging to the biological sex (14).

$$\text{THR} = (209 - 0.7 \times \text{patient years})$$

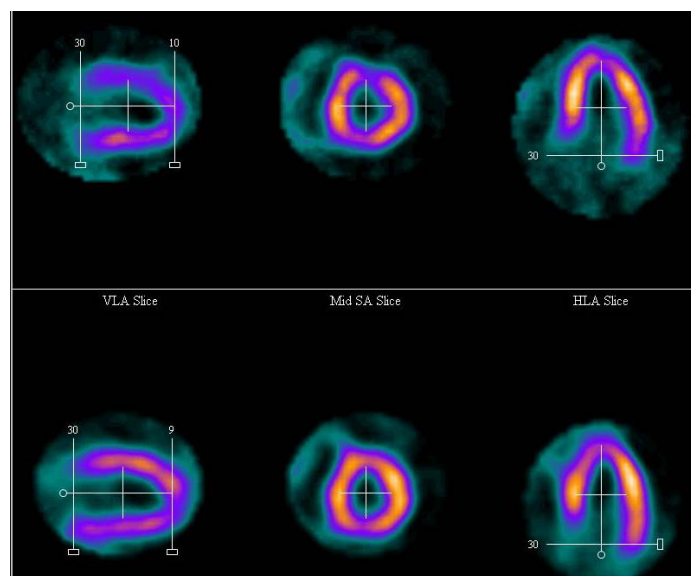
In patients in whom perfusion defects were recorded on the stress study, during the study at rest, 5 minutes before the application of the radiopharmaceutical, the diagnostic application of the coronary dilator was preceded to assess the viability of the ischemia-affected myocardium. The dilator was applied sublingually. The obtained scintomograms were qualitatively evaluated in terms of the exis-

tence of perfusion defects, the presence of which represented a pathological finding. Coronary angiography was performed in 128 subjects, in whom the presence of perfusion defects was observed on SPECT MPI. Coronary angiography was performed in the angio rooms of the Clinic for Cardiology and Vascular Diseases of the Clinical Center in Niš, using devices (Axiom Artis, Siemens, Germany) according to the protocol for this diagnostic procedure (15).

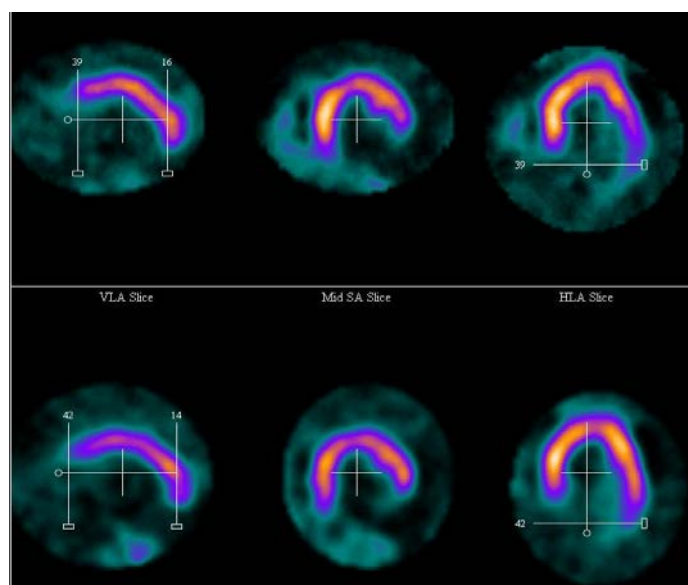
A retrograde femoral approach according to Seldinger (16) was applied. Coronary artery stenosis > 70% was considered anatomically significant stenosis and confirmation of myocardial ischemia. Values of coronary artery stenosis from 30% to 69% in patients with reversible perfusion defects on SPECT MPI were taken into consideration for hemodynamic significance. A comparison of the findings was done by statistical data processing in the program package IBM® SPSS® Statistics 20. The values were presented as mean value ± standard deviation or as individual values. The analysis of variance (ANOVA) method was used to test the significance of the differences in the mean values of independent samples. Student's paired t-test was used to test the differences in mean values of the same groups in repeated measurements. Pearson's  $\chi$



**Figure 1.** The normal finding of SPECT MPI with Tc-99m MIBI. The first row presents the transversal, sagittal, and coronal scintitomograms obtained from the reconstruction of the left chamber of the heart from the stress study, while the second row shows reconstructed scintitomograms from the rest study



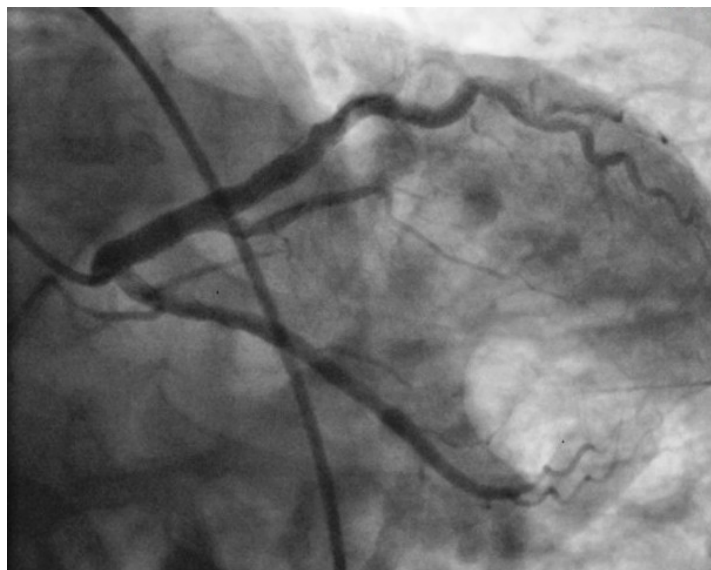
**Figure 2.** Reversible perfusion defect in a 70-year-old female patient with Tc-99m MIBI. The first row shows the transversal, sagittal, and coronal scintitograms obtained from the reconstruction of the left chamber of the heart from the stress study, while the second row presents the reconstructed scintitograms from the rest study. Myocardial ischemia



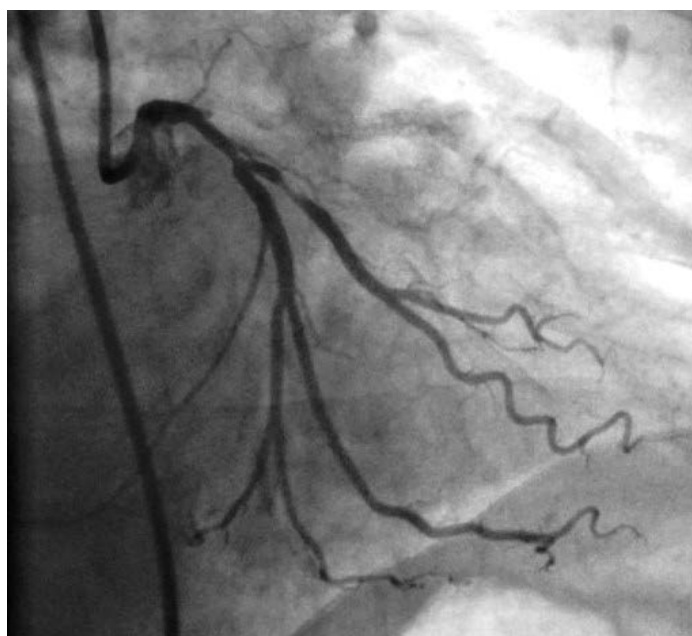
**Figure 3.** Fixed perfusion defect in a 60-year-old male patient. The first row shows the transversal, sagittal, and coronal scintitograms obtained from the reconstruction of the left chamber of the heart from the stress study, while the second row shows the reconstructed scintitograms from the rest study. Myocardial infarction

2 test was used to test for differences in proportions. In correlation to coronary angiographic findings, the sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and total diagnostic accuracy (ACC) of SPECT MPI findings were calculated. The category of normal findings on SPECT MPI included a homogeneous distribution of radiopharmaceuticals, without scintigraphically detectable perfusion defects (Figure 1).

The pathological finding in SPECT MPI studies implied the existence of perfusion defects in the myocardium of the left heart chamber (17, 18), which were categorized as reversible or fixed perfusion defects. Reversible perfusion defects were categorized as an indicator of myocardial ischemia of the left heart chamber, while fixed perfusion defects had the character of fibrosis or myocardial infarction of the left heart chamber (Figure 2 and 3).



**Figure 4.** Normal coronary angiographic findings



**Figure 5.** LAD stenosis over 75% on coronary angiography

A normal finding on coronary angiography was represented by coronary arteries without stenoses (Figure 4), while a pathological coronary angiographic finding corresponded to the presence of one or more stenotic coronary arteries on the obtained coronary angiograms (Figure 5).

All patients signed an informed consent before the study, and all diagnostic procedures were done according to the declaration of Helsinki.

## RESULTS

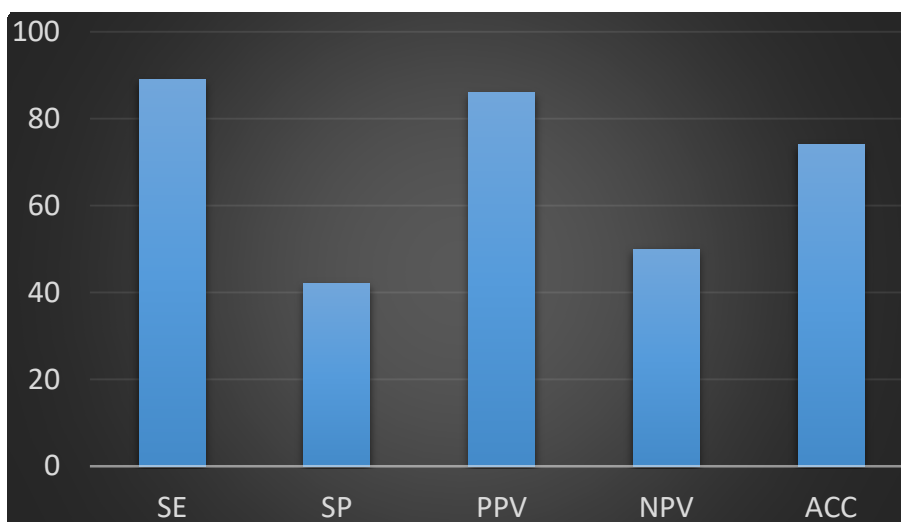
Comparing SPECT MPI and CA findings in case of coronary artery narrowing  $\geq 70\%$ , the following results were obtained: SPECT MPI was truly positive in 63.3%, truly negative in 20.0%, false positive in 16.7%, and false negative in 0%. The existence of perfusion defects and coronary artery stenosis with anatomical significance were considered to be truly positive SPECT MPI findings. SPECT MPI

findings without perfusion defects with normal coronary angiographic findings were considered a truly negative finding. Perfusion defects on SPECT MPI without significant stenosis on coronary angiography, or with stenosis less than 70%, were considered false positive findings. A finding without perfusion defects but with the presence of anatomically significant stenosis on coronary angiography was considered a false negative finding.

By comparing the results obtained in this way, the diagnostic indicators of the reliability of the SPECT MPI method concerning the coronary findings were obtained, with the premise that a value of 70% was taken as the limit for the anatomical sig-

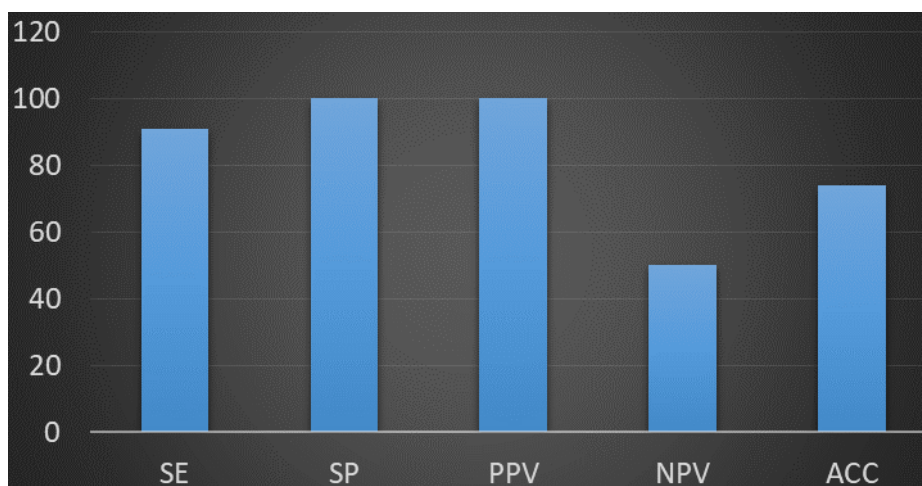
nificance of coronary artery stenosis. The sensitivity (SE) of SPECT MPI was 89%; specificity (SP) 42%; positive predictive value (PPV) 86%; negative predictive value (NPV) 50% and overall diagnostic accuracy (ACC) 74% (Chart 1).

However, when taking into account the presence of coronary artery stenoses on CA with the values from 30% to 69%, together with anatomically significant stenoses, with the value of  $\geq 70\%$  on CA, in a comparison of SPECT MPI and CA findings, the following values of diagnostic reliability indicators of SPECT MPI were obtained: SE 91%; SP 100%; PPV 100%; NPV 50% and ACC 91% (Chart 2).



**Chart 1.** Diagnostic reliability indicators of the SPECT MPI method

SE – Sensitivity; SP – Specificity; PPV – Positive predictive value; NPV – Negative predictive value; ACC – Diagnostic accuracy



**Chart 2.** Diagnostic reliability indicators of the SPECT MPI method

SE – sensitivity; SP – specificity; PPV – positive predictive value; NPV – negative predictive value; ACC – overall accuracy

## DISCUSSION

In a large number of cases, ischemic changes in the heart are not accompanied by the existence of usual anginal symptomatology (19, 20). A large number of patients in whom ischemic changes of the myocardium were detected due to the presence of coronary artery stenosis report a pronounced existence of fatigue as the leading symptom (21).

In our research, the pretest probability for the presence of coronary disease was calculated using the Duke's test (22), by calculating the Duke's clinical sum. This approach of calculating the probability of the existence of CAD is applicable only in patients who have not previously been diagnosed with the existence of flow disorders in the coronary arteries.

Duke's algorithm in calculating the pretest CAD probability uses both the presence and characterization of pain in patients suspected of having CAD. The characterization of chest pain as angina is of great importance for the correct choice of diagnostic methods to which the patient is subjected to achieve optimal diagnosis and timely treatment (23).

Ischemic heart disease occurs when there is significant stenosis of one or more coronary arteries. Anatomically significant stenosis is considered to be the one that reduces the diameter of the coronary artery by 70% compared to the diameter of the intact coronary artery. Stenoses localized on the main trunk of the left coronary artery are considered significant if they reduce the lumen by 50%. Patients with this reduction of the lumen of the coronary artery usually have chronic anginal complaints. However, it is interesting to note that most acute coronary syndromes are caused by stenoses of the order of 50% of the initial diameter of the coronary artery (24). Such patients are mostly without significant symptoms, and as such unlike those with chronic anginal complaints. At first glance, they do not represent the target population for non-invasive or invasive tests aimed at detecting coronary disease.

Due to all of the above, the group of patients with a moderate pretest probability of having CAD, obtained by Duke's clinical score, represents the target group for conducting further diagnostic testing (6).

It should be noted that this approach corresponds to the existence of ischemic disease caused by coronary artery stenosis and does not apply to cases of ischemia caused by the existence of microvascular disorders.

In our research, the group of patients was fully positioned as a group with a moderate probability of having CAD, which fully justified their additional clinical testing.

In our study, the physical load test was performed on all patients, using the standard protocol according to Bruce (25, 26). The load achieved by the patients on TFO was quantified by metabolic equivalents (27), and the target heart rate was determined by the Karvonen method (28). The test was stopped after reaching the target heart rate, that is before there was a need to stop the test. Indications for interrupting the physical stress test are the appearance of ST-T dynamics on the ECG, block of the left bundle branch of Hiss, the appearance of cardiac arrhythmias, i.e. the inability of the patient to continue the test due to individual reasons (fatigue, dizziness, fainting...). In the subjects of our study, there were no cases of interruption of the test due to physical exertion, i.e. only subjects in whom the TFO was completed after reaching the maximum heart rate were included in the study.

The positive predictive value of functional tests can be expressed by the frequency with which patients with positive functional tests have angiographically demonstrable CAD, while the negative predictive value is expressed by the frequency of patients with negative functional tests who do not have angiographically demonstrable CAD.

The pretest probability for the existence of CAD practically represents one of the very important parameters for choosing the right functional test for the detection of CAD (29).

Moderate-probability patients are the target group for performing SPECT MPI studies using a treadmill exercise test (27).

Confirmation of the previous claims can be found in the study by Melin et al. (29).

In patients with a low pretest probability, a negative finding on the functional test will practically only confirm the previous exclusion of the existence of CAD, while a positive finding on the functional test will have a higher degree of probability of belonging to the group of false positive findings (6).

According to the recommendations of the ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guidelines for the selection of functional testing in patients to detect CAD, SPECT MPI with a treadmill exercise test belongs to category Ib. According to this guide, SPECT MPI studies are recommended in patients

with a moderate pretest probability of having CAD, with an uninterpretable or normal ECG at rest, at least a medium-high degree of physical functioning, and the absence of aggravating factors, i.e. of comorbidities for performing TFO.

Reversible perfusion defects by their scintigraphic characteristics indicate the existence of myocardial ischemia, therefore, in our study, they were an expected finding in patients suspected of having CAD. On the other hand, the finding of a fixed perfusion defect, which according to its scintigraphic characteristics corresponds to the existence of a heart attack or scarred myocardium in the groups of patients with AP and DM, in which the diagnosis of coronary disease was not previously established, can be a surprising finding at first glance.

Gutterman DD (30), in his review report, provides data on the thirty-year follow-up of 5,127 patients, where it was determined that unrecognized myocardial infarction, i.e. myocardial infarction which in its genesis did not give characteristic symptoms, was found in 28% of men and 35% of women. Practically, such patients have their first clinical presentation as an acute myocardial infarction, that is, as sudden cardiac death, without prior detection of characteristic anginal pain which would clinically warn of the existence of myocardial ischemia. This clinical presentation corresponds to the existence of "silent" ("silent") myocardial ischemia, that is, clinically silent myocardial infarction. In the same paper, monitoring of the presence of myocardial ischemia with an ECG monitor in 30 patients is described, where it was observed that episodes of ST depression were much more frequent without pronounced anginal symptomatology and that episodes of ischemia without pain had a much longer duration compared to ST depression on the ECG, which was accompanied by anginal pain.

In the study conducted by Stramba-Badiale et al. (31), a total of 414 patients with elevated blood pressure were examined ten days after stopping antihypertensive therapy. The assessment of the presence of "silent" myocardial ischemia was made using TFO and ECG holter monitoring for 48 hours. Out of a total of 411 patients examined by TFO testing, ST depression was found in 6.1% of subjects, which indicated the existence of myocardial ischemia. In these patients, all the observed episodes of myocardial ischemia on ECG were not accompanied by the existence of symptomatology. Out of the total number of patients, 396 of them underwent

ECG Holter monitor testing. In 10.9% of the examined patients, at least one episode of ST depression was observed while wearing a Holter ECG. The overall results of the study show that 15% of patients with moderate hypertension had episodes of ST depression consistent with myocardial ischemia. Most of the described ST depressions were asymptomatic and were not related to the level of hypertension, in terms of its gradation to moderate or severe.

The coronary examination enables an insight into the anatomy of the coronary arteries, assessment of the presence of coronary artery stenosis, the character of coronary artery stenosis, assessment of the existence of collateral blood flow, i.e. assessment of blood flow through the myocardium of the left heart chamber. Despite the existence of more modern non-invasive techniques for evaluating the mentioned anatomical, pathoanatomical, and morphological-functional characteristics of coronary blood vessels, such as coronary angiography using CT diagnostics, coronary angiography remains the "gold standard" (32).

Even though coronary angiography is recognized as the "gold standard", this does not mean that this diagnostic method does not have its limitations. One of the shortcomings of coronary angiographic findings lies in the technical quality of coronary angiograms obtained by this methodology. The technically poor quality of coronary angiograms can make interpretation difficult to the extent that it affects the accuracy of the method or even leads to inconclusive results. In a study conducted by Leape et al. (33), 308 coronary angiographic findings were re-evaluated in patients who had previously undergone PTCA or CABG therapeutic approaches. The examination of these coronary angiograms was done by three experienced doctors, and the results of the re-reading of the angiograms were compared with the initial ones. Technical deficiencies of coronary angiography were found in 52% of the reviewed studies. Panel interpretation of coronary angiography showed a lower percentage of significant coronary disease by 16%, lower severity of stenosis by 43%, and a lower expansion of CAD by 23%. The classification of the recommendation for CABG was changed from the category necessary/appropriate to uncertain/inadequate in 17% to 33% of patients examined.

Angiographic methodology belongs to the anatomical procedures for assessing the condition of

the coronary arteries. The presence of stenosis that does not belong to the pathological findings (less than 70%) does not allow the evaluation of its hemodynamic significance. Assessment of the hemodynamic significance of any coronary angiographic finding that does not belong to the category of pathological findings is possible only by applying techniques such as fractional flow reserve. In a study conducted by Nakazato et al. (34), 58 patients with an intermediate degree of stenosis from 30% to 69% were examined. All patients underwent coronary angiography, that is, FFR. Values of  $FFR \leq 0.80$  were considered pathological in the sense of causing hemodynamically significant disturbance for the onset of CAD. Twenty-two lesions out of a total of 58 examined (38%) were hemodynamically significant in terms of causing ischemia. This approach, i.e. the assessment of FFR greatly changes the significance of lesions about the result when the percentage of stenosis is assessed as an individual parameter.

It is not possible to see the very structure of the atherosclerotic plaque in the coronary artery with the coronary angiographic method. The existence of a vulnerable atherosclerotic plaque, with a thin fibrous cap, a large lipid core, and an increased content of macrophages, cannot be detected by the coronary angiographic method. By comparing previous coronary angiographic findings, in patients who had unstable angina pectoris or myocardial infarction, it was observed that the lesions that caused the current coronary event on previous coronary angiograms were characterized as insignificant, with lumen involvement, often less than 50%. In the coronary view, these lesions were "silent" in terms of causing a coronary event (35).

In our study, a comparison was made between the findings obtained on SPECT MPI studies with the findings of the "gold standard" obtained by coronary angiography. The comparison was made at two levels. In the first case, a coronary artery stenosis of over 70% was considered significant, while in the second case, a narrowing of 30 to 69% as well as over 70% was considered significant. Narrowing up to 30% of the lumen of the coronary artery was con-

sidered a normal, i.e. insignificant coronary angiography finding. A study designed in a similar way to our research was published in the New England Journal of Medicine in 2010, including the analysis of a large group of subjects, almost four hundred thousand of them, from 663 hospitals in America where coronary angiography was performed and in whom no previous diagnosis was made. The findings of coronary angiography were retrospectively compared with the findings of demographic characteristics, the presence of risk factors, and the findings of non-invasive tests. In this paper, as in our research, a sensitivity testing model was applied, taking as relevant the narrowing of the coronary artery below 70% percent, i.e. a degree of narrowing of 20% of coronary artery lumen stenosis was considered a normal finding (36).

## CONCLUSION

The pathological finding of SPECT MPI was detected in a high percentage of subjects of the medium-risk group in whom coronary artery disease was not previously proven.

1. SPECT MPI shows high sensitivity, specificity, and overall diagnostic accuracy in the detection of anatomically significant coronary artery stenoses.

2. It is not possible to prove or rule out the existence of hemodynamic significance of coronary artery stenoses, which take the values from 30% to 69%, only by CA.

3. Coronary artery stenoses from 30% to 69% represent a recruitment range for the occurrence of major coronary events such as ischemia or myocardial infarction.

4. SPECT MPI shows high sensitivity, specificity, positive predictive value, and overall diagnostic accuracy in terms of detecting the presence of left ventricular myocardial perfusion disorders even in stenoses that do not show an anatomically significant value.

## References

1. Hung MJ, Hu P, Hung MY. Coronary Artery Spasm: review and update. *Int J Med Sci* 2014;11:1161-71.  
<https://doi.org/10.7150/ijms.9623>
2. Crossman DC. The pathophysiology of myocardial ischemia. *Heart* 2004;90:576-80.  
<https://doi.org/10.1136/hrt.2003.029017>
3. Dangas G, Mintz GS, Mehran R, et al., Preintervention arterial remodeling as an independent predictor of target lesion revascularization after non-stent coronary intervention. An analysis of 777 lesions with intravascular ultrasound imaging. *Circulation* 1999;99:3149-54.  
<https://doi.org/10.1161/01.CIR.99.24.3149>
4. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography: a report of the American college of Cardiology/ American Heart Association Task Force on practice guidelines (Committee on coronary angiography). *J Am Coll Cardiol* 1999;33:1756-824.  
[https://doi.org/10.1016/S0735-1097\(99\)00126-6](https://doi.org/10.1016/S0735-1097(99)00126-6)
5. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA Guideline update for the management of patients with unstable angina and non-ST segment myocardial infarction - Summary article: *J Am Coll Cardiol* 2002;40:1366-74.  
[https://doi.org/10.1016/S0735-1097\(02\)02336-7](https://doi.org/10.1016/S0735-1097(02)02336-7)
6. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease. *J Am Coll Cardiol*; 2012;60:44-164.  
<https://doi.org/10.1016/j.jacc.2012.07.013>
7. Hesse B, Tägil K, Cuocolo A, et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. *Eur J Nucl Med Mol Imaging* 2005;32:855-97.  
<https://doi.org/10.1007/s00259-005-1779-y>
8. Kula M, Tutuş A, Unal S, et al. Technetium-99m-tetrofosmin imaging with incremental nitroglycerin infusion to detect severely ischaemic but viable myocardium: a comparative study with thallium-201. *Nucl Med Commun* 2003;24:987-94.  
<https://doi.org/10.1097/00006231-200309000-00007>
9. Niyaz K, Niaz K, Zaman MU, et al. Assessment of viable myocardium by nitrate augmented 99mTc MIBI myocardial perfusion imaging. *J Pak Med Assoc* 2007;57:83-7.
10. Bruce AR, Lovejoy FW Jr, Pearson R, et al. Normal respiratory and circulatory pathways of adaptation in exercise. *J Clin Invest* 1949;28: 1423-30.  
<https://doi.org/10.1172/JCI102207>
11. Bruce AR, Lovejoy FW Jr, Pearson R, et al. Variability of respiratory and circulatory performance during standardized exercise. *J Clin Invest* 1949; 28:1431-8.  
<https://doi.org/10.1172/JCI102208>
12. Cohn JN, ed. Quantitative exercise testing for the cardiac patient: the value of monitoring gas exchange: introduction. *Circulation* 1987;76:1-58.
13. Londeree BR, Moeschberger ML. Influence of age and other factors on maximal heart rate. *J Cardiac Rehabil* 1984;4:44-9.
14. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol* 2001;37:153-6.  
[https://doi.org/10.1016/S0735-1097\(00\)01054-8](https://doi.org/10.1016/S0735-1097(00)01054-8)
15. Spellberg RD, Ungar I. The Percutaneous Femoral Artery Approach to Selective Coronary Arteriography. *Circulation* 1967;36:730-3.  
<https://doi.org/10.1161/01.CIR.36.5.730>
16. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/ SCAI guideline for percutaneous coronary intervention: a report of the American college of Cardiology Foundation/American Heart Association Task Force on practice

- guidelines and the society for cardiovascular angiography and interventions. *J Am Coll Cardiol* 2011;58:44-122.  
<https://doi.org/10.1016/j.jacc.2011.08.007>
17. Klocke FJ, Baird MG, Lorell BH, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging- executive summary: a report of the American college of Cardiology/American Heart Association Task Force on practice guidelines (ACC/AHA/ASNC Committee to revise the 1995 guidelines for the clinical use of cardiac radionuclide imaging). *Circulation* 2003;108:1404-18.  
<https://doi.org/10.1161/01.CIR.0000080946.42225.4D>
  18. Shaw LJ, Hachamovitch R, Peterson ED, et al. Using an outcomes-based approach to identify candidates for risk stratification after exercise treadmill testing. *J Gen Intern Med* 1999;14:1-9.  
<https://doi.org/10.1046/j.1525-1497.1999.00273.x>
  19. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. *Circulation* 2004;109:1101-7.  
<https://doi.org/10.1161/01.CIR.0000118498.35499.B2>
  20. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease. *Eur Heart J* 2013;34:2949.  
<https://doi.org/10.1093/eurheartj/eh296>
  21. Nakanishi R, Rana JS, Rozanski A, et al. Relationship of dyspnea vs. typical angina to coronary artery disease severity, burden, composition and location on coronary CT angiography. *Atherosclerosis*. 2013;230:61-6.  
<https://doi.org/10.1016/j.atherosclerosis.2013.06.008>
  22. Diamond GA, Forester JS. Analysis of probability as an aid in the clinical diagnosis of coronary artery disease. *NEJM* 1979;300:1350-8.  
<https://doi.org/10.1056/NEJM197906143002402>
  23. Pepine CJ, Balaban RS, Bonow RO, et al. Women's Ischemic Syndrome Evaluation: current status and future research directions: report of the National Heart, Lung, and Blood Institute workshop: October 2-4, 2002: Section 1: diagnosis of stable ischemia and ischemic heart disease. *Circulation* 2004;109:44-6.  
<https://doi.org/10.1161/01.CIR.0000116206.77324.5B>
  24. Bugiardini R, Bairey Merz CN. Angina with "normal" coronary arteries: a changing philosophy. *JAMA* 2005;293:477-84.  
<https://doi.org/10.1001/jama.293.4.477>
  25. Cohen-Solal A, Zannad F, Kayanakis JG, et al. Multicentre study of the determination of peak oxygen uptake and ventilatory threshold during bicycle exercise in chronic heart failure: comparison of graphical methods, interobserver variability and influence of the exercise protocol: the VO2 French Study Group. *Eur Heart J* 1991;12:1055-63.  
<https://doi.org/10.1093/oxfordjournals.eurheartj.a059837>
  26. Douglas PS. Is noninvasive testing for coronary artery disease accurate? *Circulation* 1997;95:299-302.  
<https://doi.org/10.1161/01.CIR.95.2.299>
  27. Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. *JAMA* 1998;280:913-20.  
<https://doi.org/10.1001/jama.280.10.913>
  28. Karvonen MJ, Kental E, Mustala O. The effects of training on heart rate a longitudinal study. *Ann Med Exp Fenn* 1957;35:307-15.  
<https://doi.org/10.1002/j.2164-4918.1957.tb01772.x>
  29. Melin JA, Wijns W, Vanbutsele RJ, et al. Alternative diagnostic strategies for coronary artery disease in women: demonstration of the usefulness and efficiency of probability analysis. *Circulation* 1985;71:535-42.  
<https://doi.org/10.1161/01.CIR.71.3.535>
  30. Gutterman DD. Silent myocardial ischemia. *Circ J* 2009;73:785-97.  
<https://doi.org/10.1253/circj.CJ-08-1209>
  31. Stramba-Badiale M, Bonazzi O, Casadei G, et al. Prevalence of episodes of ST-segment depression among mild-to-moderate hypertensive patients in northern Italy: the Cardioscreening Study. *J Hypertens* 1998;16:681-8.

<https://doi.org/10.1097/00004872-199816050-00016>

32. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/ SCAI guideline for percutaneous coronary intervention: a report of the American college of Cardiology Foundation/American Heart Association Task Force on practice guidelines and the society for cardiovascular angiography and interventions. *J Am Coll Cardiol* 2011;58:44 -122.  
<https://doi.org/10.1016/j.jacc.2011.08.007>
33. Leape LL, Park RE, Bashore TM, et al. Effect of variability in the interpretation of coronary angiograms on the appropriateness of use of coronary revascularization procedures. *Am Heart J* 2000;139:106-13.  
[https://doi.org/10.1016/S0002-8703\(00\)90316-8](https://doi.org/10.1016/S0002-8703(00)90316-8)
34. Nakazato R, Shalev A, Doh JH, et al. Aggregate plaque volume by coronary computed tomography angiography is superior and incremental to luminal narrowing for diagnosis of ischemic lesions of intermediate stenosis severity. *J Am Coll Cardiol* 2013;62:460-7.  
<https://doi.org/10.1016/j.jacc.2013.04.062>
35. Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographic progression of coronary artery disease and the development of myocardial infarction. *J Am Coll Cardiol* 1988;12:56-62.  
[https://doi.org/10.1016/0735-1097\(88\)90356-7](https://doi.org/10.1016/0735-1097(88)90356-7)
36. Patel MR, Peterson ED, Dai D, et al. Low diagnostic yield of elective coronary angiography. *N Engl J Med* 2010;362:886-95.  
<https://doi.org/10.1056/NEJMoa0907272>

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## Perfuziona scintigrafija miokarda u predikciji postojanja hemodinamski značajnih stenoza koronarnih arterija

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### SAŽETAK

**Uvod/Cilj.** Anatomski nesignifikantna stenoza koronarnih arterija dobijena na koronarnoj angiografiji u velikom broju slučajeva može biti hemodinamski signifikantna i, kao takva, izazvati ishemijske promene miokarda. Cilj rada bio je proceniti dijagnostičku tačnost perfuzione scintigrafije miokarda (SPECT MPI) u detekciji hemodinamski značajne stenozе koronarnih arterija kod bolesnika sa umerenim rizikom od ishemije i bez prethodno otkrivene koronarne bolesti.

**Pacijenti i metodologija.** Istraživanjem je obuhvaćeno 258 pacijenata (54% žena i 46% muškaraca, prosečne starosti  $59,0 \pm 10,1$  godina). SPECT MPI je urađen dvodnevним protokolom sa 99mTc-MIBI. Patološkim nalazom smatrano je postojanje perfuzionih defekata. Test fizičkog opterećenja urađen je po Bruceovom protokolu. Koronarna angiografija (CA) urađena je po standardnom protokolu kod bolesnika sa patološkim SPECT MPI nalazom ( $n = 128$ ). Anatomski značajnim suženjem koronarne arterije smatrala se stenoza  $> 70\%$ . Stenoze od 30% do 69% smatrane su hemodinamski značajnim kod bolesnika sa reverzibilnim defektima perfuzije na SPECT MPI-ju.

**Rezultati.** Kada su rezultati upoređeni sa stenozom  $> 70\%$ , osetljivost (SE) SPECT MPI-ja bila je 89%, specifičnost (SP) 42%, pozitivna prediktivna vrednost (PPV) 86%, negativna prediktivna vrednost (NPV) 50%, a ukupna dijagnostička tačnost (ACC) 74%. Kada je uključena stenoza od 30% do 69%, dobijene vrednosti dijagnostičkih pokazatelja pouzdanosti SPECT MPI-ja bile su sledeće: SE 91%, SP 100%, PPV 100%, NPV 50% i ACC 91%.

**Zaključak.** Samo korišćenjem CA nije moguće dokazati postojanje hemodinamskog značaja stenozа koronarnih arterija od 30% do 69%, što predstavlja opseg za razvoj ishemije. SPECT MPI pokazuje visoke SE, SP, PPV i ACC u otkrivanju postojanja poremećaja perfuzije miokarda leve komore sa stenozama koronarnih arterija sa anatomski značajnim vrednostima ili bez njih.

**Ključne reči:** perfuziona scintigrafija miokarda, koronarna bolest, hemodinamika stenozе koronarne arterije, anatomska signifikantnost koronarne stenozе