

*Scientific Journal of the Faculty of Medicine in Niš 2013;30(3):129-135*

*Original article* ■

# Myocardial Perfusion Scintigraphy in Detection of Myocardial Ischemia and Therapy Planning in Early Stages of Diabetes Mellitus

Miloš Stević<sup>1</sup>, Marina Vlajković<sup>1</sup>, Goran Koraćević<sup>2</sup>, Radivoj Kocić<sup>3</sup>, Milena Rajić<sup>1</sup>, Slobodan Ilić<sup>1</sup>

<sup>1</sup>Centar of Nuclear Medicine, Clinical Center Niš, Serbia

<sup>2</sup>Clinic of Cardiology and Vascular Diseases, Clinical Center Niš, Serbia

<sup>3</sup>Clinic of Endocrinology, Clinical Center Niš, Serbia

## SUMMARY

**Patients with diabetes mellitus (DM) develop complications including coronary artery disease (CAD), which is the leading cause of mortality in this group of patients. One of the diagnostic modalities for early detection of myocardial ischemia in symptomatic and asymptomatic patients with DM is myocardial perfusion tomography (MPI).**

**The aim of this study was to determine the usefulness of MPI in detection of myocardial ischemia in symptomatic and asymptomatic patients in early stages of DM.**

**Thirty-four patients with DM, aged from 24 to 65 years, nine women and fifteen men were examined. Thirteen patients were CAD symptomatic, and 21 were asymptomatic. MPI was performed through a standard two-day protocol, and findings were categorized as normal perfusion, reversible perfusion defect (ischemia), and fixed perfusion defect (scar). Patients with ischemia were elected for coronary angiography (CAG). MPI and CAG findings were statistically analyzed.**

**Fifteen (44,12%) patients had normal left ventricle perfusion, while 19 (55,88%) patients had perfusion defects. Scar was found in one patient, and ischemia in 18 patients. CAG showed stenosis of coronary artery in 7 (36,84%) of 19 patients with perfusion defects on MPI. Statistical analysis showed no correlation between MPI ischemia and stenosis on CAG.**

**Discrepancy between ischemia on MPI and CAG presentations of epicardial coronary arteries is related to endothelial dysfunction rather than atherosclerosis. These patients benefit more from pharmacological therapy than from revascularization. MPI and CAG should be reserved for individuals with high risk of CAD.**

**Key words:** myocardial perfusion scintigraphy, coronary angiography, diabetes mellitus

Corresponding author:

**Miloš Stević** •

phone: 069 4094029 •

e-mail: mlsstvc@gmail.com •

## INTRODUCTION

Patients with diabetes mellitus over time develop several long-term complications which reduce the quality of life and life expectancy. Coronary artery disease (CAD) is one of the complications with outmost significance. Frequently, CAD is diagnosed several years after the occurrence of complications. On the other side, CAD is the leading cause of morbidity and mortality in patients with DM (1). To be worse, CAD is often in advanced stage when the manifestations begin in patients with DM (2). In the management of these patients, it is important to find which patients can benefit from coronary angioplasty (CAG) and from percutaneous coronary angioplasty (PTCA) if it is needed, whether they are symptomatic or asymptomatic. Patients with DM and early-diagnosed CAD can benefit from early intervention in the manner of increasing of long-term survival (3). Myocardial perfusion imaging (MPI) using single photon emission tomography (SPECT) is reported to be useful in detection of myocardial ischemia in symptomatic and asymptomatic patients with diabetes mellitus (4). Several different reports suggest 37% to 62% abnormal MPI findings in patients with DM (5). Perfusion defects found on MPI usually strongly suggests the existence of myocardial ischemia, or myocardial scar, and correlate with findings of coronary artery stenosis on CAG (6).

## AIM

The aim of this study was to correlate perfusion defects found on MPI with coronary artery stenosis found on CAG in patients who are in early stages of DM.

## PATIENTS AND METHODOLOGY

The total of 34 patients was examined, from January 2011 to December 2011, aged from 24 to 65 years. Nine of them were women and 15 were men. All of the patients were in early stages of type II DM (from six months to three years from the onset of DM). Average level of glucose in the blood in this group of patients was  $11,1 \pm 3,3$  mmol/L. There were 13 patients with symptomatology that can be related to coronary artery disease. All of them suffered from chest pain or discomfort, shortness of breath when exercising or during another vigorous activity, weakness, dizziness, nausea or increased sweating. Regarding CAD, twenty-one patients were symptom-free. All the patients had normal ECG.

MPI studies were done by standard two-day protocol (16). On the first day, radiopharmaceutical was intravenously injected immediately after the treadmill ergo stress testing, and on the second day we performed the rest of the study. Treadmill ergo stress testing was done following the Bruce protocol, with the aim of achieving 85% of the maximal predicted heart rate, or it was symptom-limited (7). Radiopharmaceutical was injected in-

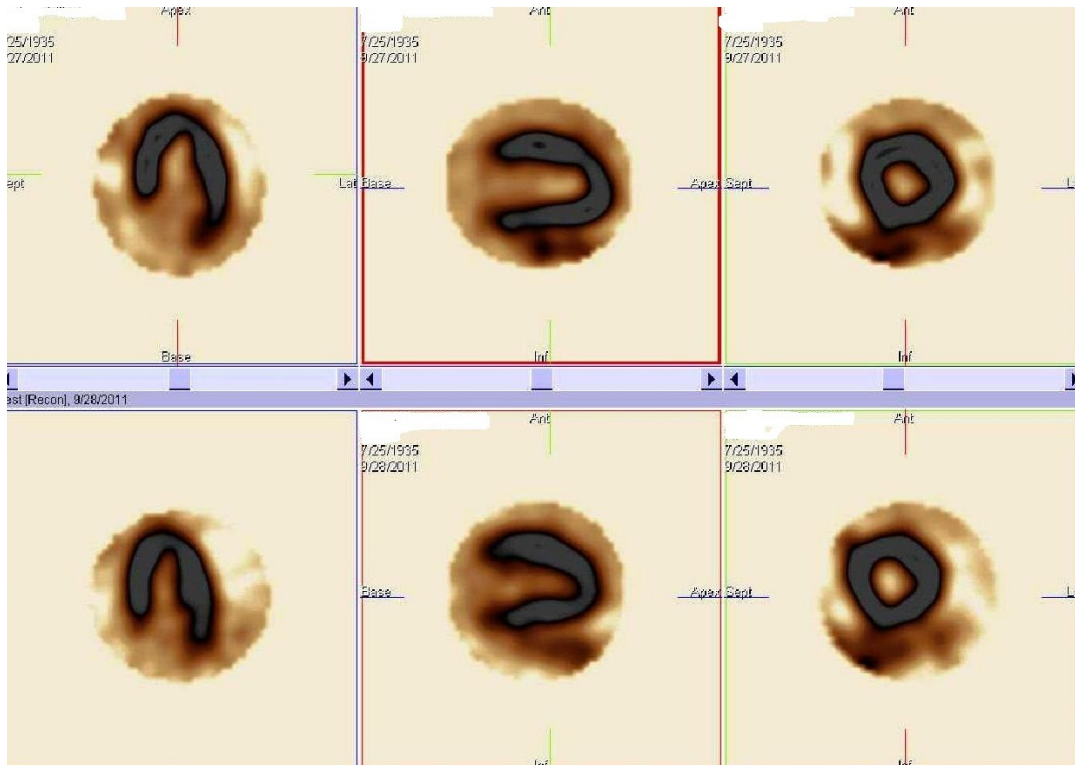
travenously at the peak stress activity of the patient. In all studies, the radiopharmaceutical used was tetrakis (2-metoksiizobutil izonitрил) copper 1 tetrafluoroborat, (STAMICIS, Iba Molecular, France) (8). SPECT MPI images were acquired with double headed gamma camera equipped with high resolution colimators (E-cam, Siemens, Medica Solutions). Detectors of gamma camera were reconfigured in 90 degrees position. Acquisitions were done by 64 projection angles, over a 180 degrees orbit, at 25 seconds duration of each projection. The image data from every projection were recorded in 16 equal time frames gated by ECG. Reconstruction of tomograms from acquired data were done by iterative reconstruction, with 12 iterations and Butterworth prefiltering with cutoff, 0,4 cycle/pixel. Through the reconstruction, for interpretation the available tomograms through long vertical, long horizontal and through short axis of the left heart ventricle myocardium were used. Qualitative analysis of tomograms was performed by nuclear medicine physician, and the findings were categorised as normal perfusion of the left ventricle, reversible perfusion defects, which indicated ischemia, and fixed perfusion defects that indicated myocardial scar (9).

All patients with myocardial perfusion defects were elected for CAG. This method was done by the right femoral artery approach, on Axiom Artis, Siemens, Germany devices. Interpretation of CAG findings was done by cardiologist, with categorisation of stenosis by its localisation and severity. Stenoses were categorised as significant in the manner of existing CAD, if narrowing of the coronary artery lumen were 50% or greater (10).

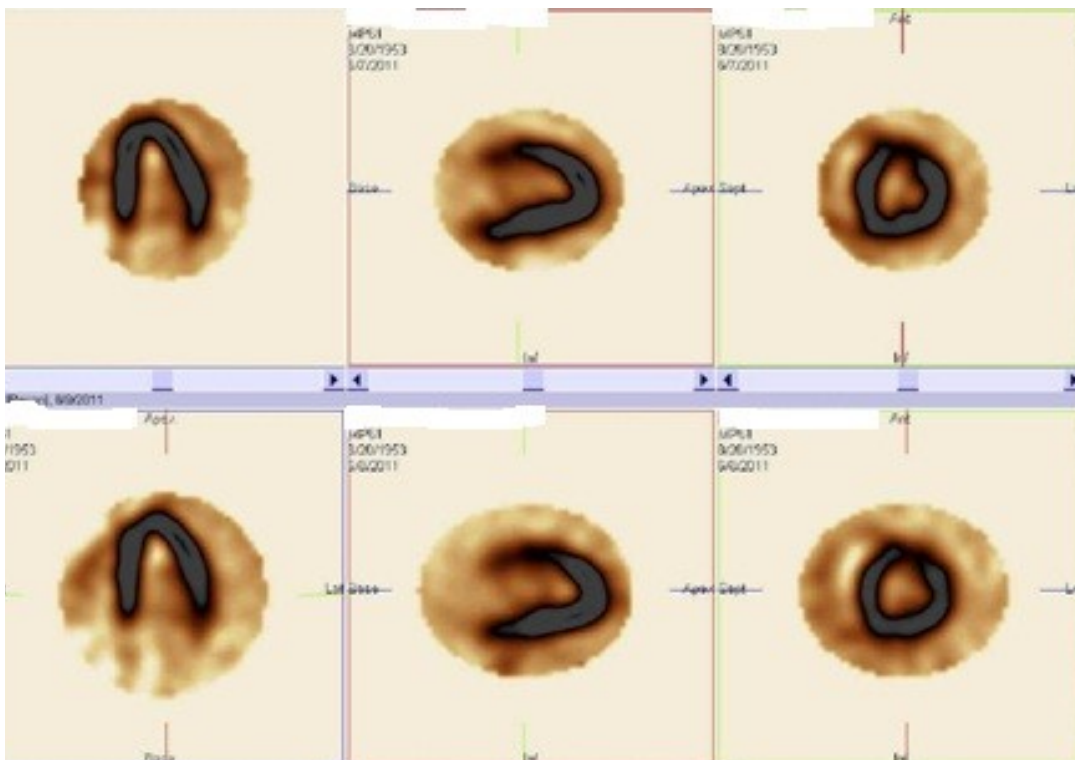
Findings from MPI and CAG were correlated with non-parametric statistical analysis.

## RESULTS

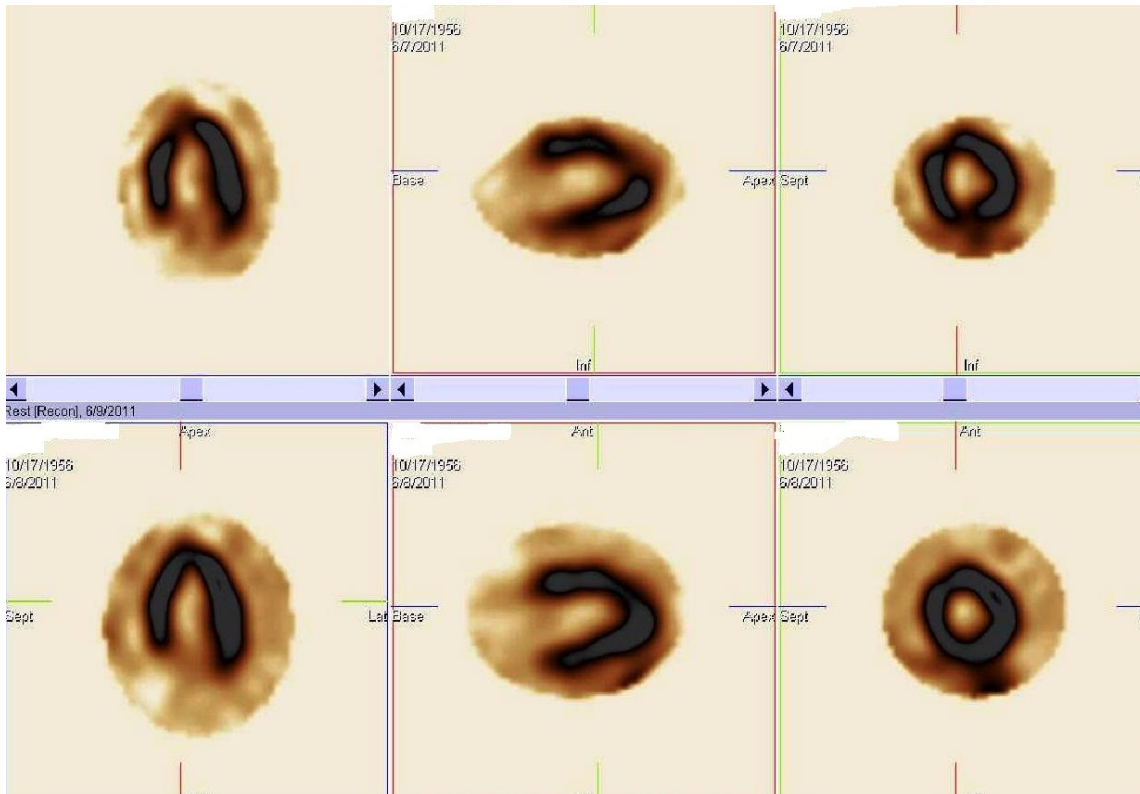
Fifteen (44,12%) of 34 patients had normal left ventricle perfusion (Figure 1). In 19 (55,88%) patients, there were perfusion defects. Fixed defects were found in one patient and reversible defects were found in 18 patients. One patient with fixed perfusion defect was categorized as one who had non-ST elevation myocardial infarction (Figure 2). The other 18 patients with reversible perfusion defects were categorized as patients with silent or apparent ischemia, according to whether they were with or without the CAD-related symptomatology (Figure 3). On CAG, there were 12 (63,16%) patients with normal coronary arteries (Figure 4), 7 (36,84%) with significant coronary artery stenosis (Figure 5). Statistical correlation between the group with perfusion defects on MPI and group with significant stenosis on CAG was done by non-parametric, Related-Samples Wilcoxon Signed Rank Test (Figure 6). The test shows that there was statistically lower detection of ischemia (stenosis) on CAG than on MPI findings (significance 0,01 at significance level 0,05) (Figure 7).



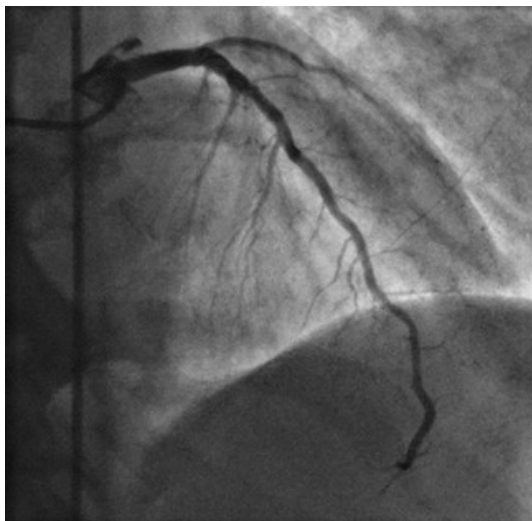
**Figure 1.** Normal perfusion of the left heart ventricle on myocardial perfusion tomography. M.E. asymptomatic, 45 years old, female



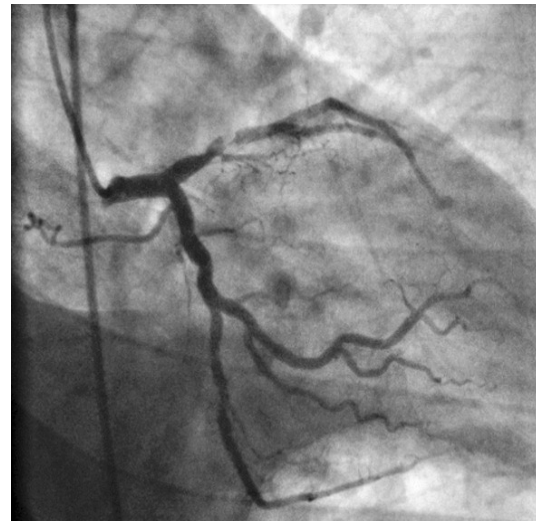
**Figure 2.** Fixed perfusion defect of the anterior wall of the left ventricle (marked with arrows), detecting myocardial scar (Myocardial infarction). N.N. symptomatic, 40 years old, male



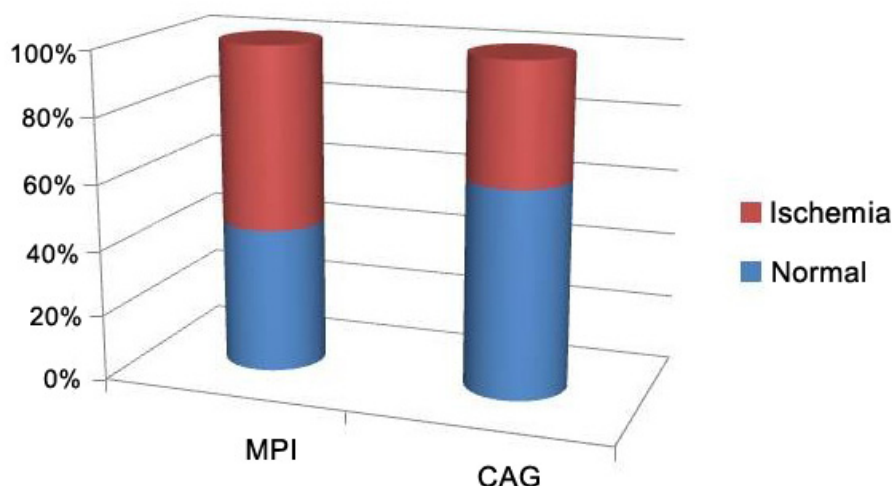
**Figure 3.** Reversible perfusion defect of the anteroseptal region and inferior wall (marked with arrows), detecting myocardial ischemia. T.O. asymptomatic, 52 years old, female



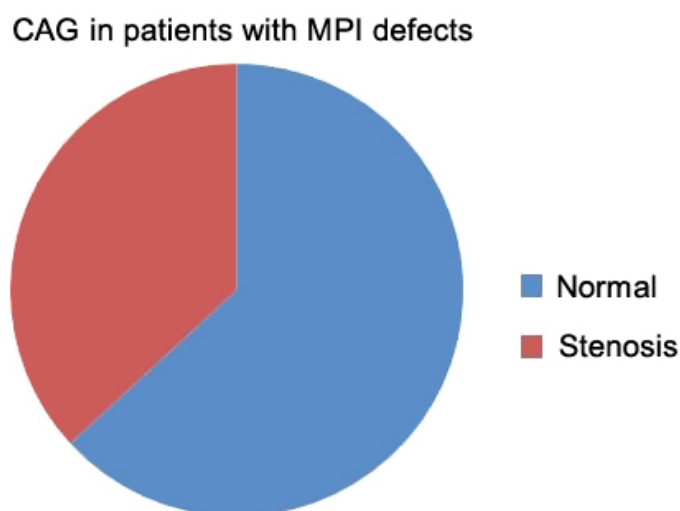
**Figure 4.** Normal finding on coronary angiography. T.O. asymptomatic, 52 years old, female



**Figure 5.** Stenosis of coronary artery on coronary angiography (marked with arrow). N.N. symptomatic, 40 years old, male



**Figure 6.** Ischemia detected on MPI and epicardial coronary artery stenosis on CAG. There were 55,88% cases with ischemia on MPI, and 36,84% on CAG. Significant lower detection of ischemia on CAG by Related-Samples Wilcoxon Signed Rank Test (Significance 0,01 at significance level 0,05)



**Figure 7.** The test shows that there is statistically lower detection of ischemia (stenosis) on CAG than on MPI findings (significance 0,01 at significance level 0,05)

## DISCUSSION

This discrepancy between MPI ischemia positive findings and CAG normal coronary artery presentation can be explained by the fact that in early stages of DM, and especially in asymptomatic patients, there are no extensive atherosclerotic changes in arterial vessels, including coronary arteries (11). Further, in the group of symptomatic patients, even with presentation of several risk factors for CAD, if they are able to successfully exercise, it must exclude high suspicion of CAB. In relatively “healthy” patients with DM, who are able to exercise, there is no likelihood of severe complications as peripheral artery disease and diabetic neuropathy. The-

re is evidence of low coronary artery calcium (CAC) score in DM patients who are able to exercise, and further only patients with high CAC develop severe coronary events (12,13). This is another explanation of discrepancy between ischemia found on MPI and normal CAG presentation of epicardial coronary arteries.

Patients with MPI ischemia findings but without severe complication such as peripheral artery disease and polyneuropathy can benefit more from modification of pharmacologic therapy, than from eventual revascularization (14). Vascular disease in early stages is not treatable with invasive therapy. Reducing ischemia in these cases can be achieved with intensification of therapy with statins, aspirin, and ACE inhibitors (15). Fur-

thermore, more careful follow-up of these patients can result in recognition of asymptomatic ischemia and then refer the patient to further analysis (16). The combination of different diagnostic modalities and protocols can be the solution for election of the DM patients for CAG (17).

## CONCLUSION

There is discrepancy between MPI findings of ischemia and CAG presentation of epicardial coronary arteries. This discrepancy is related to the existence of

endothelial dysfunction rather than atherosclerosis. Patients with perfusion defects on MPI can benefit more from balanced pharmacological and invasive therapy than from revascularization only. MPI evaluation and CAG should be reserved for selected individuals with strong suspicion of high risk CAD.

## References

- Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 23;339(4):229-34.
- The BARI Investigators. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and CAG in patients with multivessel disease: The Bypass Angioplasty Revascularization Investigation (BARI) *Circulation*1997;96:1761-9. <http://dx.doi.org/10.1161/01.CIR.96.6.1761> PMID:9323059
- The BARI Investigators. Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol*2000;35:1122-9. [http://dx.doi.org/10.1016/S0735-1097\(00\)00533-7](http://dx.doi.org/10.1016/S0735-1097(00)00533-7)
- Kang X, Berman DS, Lewin HC, Cohen I, Friedman JD, Germano G, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography in patients with diabetes mellitus. *Am Heart J* 1999;138:1025-32 [http://dx.doi.org/10.1016/S0002-8703\(99\)70066-9](http://dx.doi.org/10.1016/S0002-8703(99)70066-9)
- Giri S, Shaw LJ, Murthy DR, Travin MI, Miller DD, Hachamovitch R, et al. Impact of diabetes on the risk stratification using stress single-photon emission computed tomography myocardial perfusion imaging in patients with symptoms suggestive of coronary artery disease. *Circulation*2002;105:32-40. <http://dx.doi.org/10.1161/hc5001.100528> PMID:11772873
- Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.*Circulation* 2010;122:e584-e636. <http://dx.doi.org/10.1161/CIR.Ob013e3182051b4c> PMID:21098428
- Gerald F. Fletcher, Gary J. Balady, Ezra A. Amsterdam, Bernard Chaitman, Robert Eckel, Jerome Fleg, Victor F. Froelicher, Arthur S. Leon, Ileana L. Piña, Roxanne Rodney, Denise A. Simons-Morton, Mark A. Williams and Terry Bazzarre. Exercise Standards for Testing and Training: A Statement for Healthcare Professionals From the American Heart Association. *Circulation* 2001; 104:1694-740
- Iskander S, Iskandrian AE. Risk assessment using single-photon emission computed tomographic technetium-99m sestamibi imaging. *J Am CollCardiol* 1998; 32(1):57-62 [http://dx.doi.org/10.1016/S0735-1097\(98\)00177-6](http://dx.doi.org/10.1016/S0735-1097(98)00177-6)
- Klocke FJ, Baird MG, Lorell BH, Bateman TM, Messer JV, Berman DS, 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 (11): 1404-18 <http://dx.doi.org/10.1161/01.CIR.0000080946.42225.4D> PMID:12975245
- Scanlon PJ, Faxon DP, Audet AM, Carabello B, Dehmer GJ, Eagle KA. 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 CollCardiol* 1999; 33:1756-824. [http://dx.doi.org/10.1016/S0735-1097\(99\)00126-6](http://dx.doi.org/10.1016/S0735-1097(99)00126-6)
- Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, et al. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: The DIAD study. *Diabetes Care* 2004;27:1954-61. <http://dx.doi.org/10.2337/diacare.27.8.1954> PMID:15277423
- Anand DV, Lim E, Hopkins D, Corder R, Shaw LJ, Sharp P et al. Risk stratification in uncomplicated type 2 diabetes: Prospective evaluation of the combined use of coronary artery calcium imaging and selective myocardial perfusion scintigraphy. *Eur Heart J* 2006; 27: 713-21. <http://dx.doi.org/10.1093/eurheartj/ehi808> PMID:16497686
- Peix A, Cabrera L, Heres F, Rodrigues L, Valdes A, et al. Interrelationship between myocardial perfusion imaging, coronary calcium score and endothelial function

- in asymptomatic diabetics and controls. *J NuclCardiol* 2011; 18(3):398-406  
<http://dx.doi.org/10.1007/s12350-011-9355-2>  
 PMid:21432001
14. Bansal S, Wackers FJ, Inzucchi SE, Chyun DA, Davey JA, Staib LH, et al. Five-year outcomes in high-risk participants in the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study: A post hoc analysis. *Diabetes Care* 2011;34:204-9.  
<http://dx.doi.org/10.2337/dc10-1194>  
 PMid:20929989 PMCid:3005488
15. Wackers FJ, Chyun DA, Young LH, Heller GV, Iskandrian AE, Davey JA, et al. Resolution of asymptomatic myocardial ischemia in patients with type 2 diabetes in the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study. *Diabetes Care* 2007;30:2892-8.  
<http://dx.doi.org/10.2337/dc07-1250>  
 PMid:17682123
16. Rajagopalan N, Miller TD, Hodge DO, Frye RL, Gibbons RJ. Identifying high-risk asymptomatic diabetic patients who are candidates for screening stress single-photon emission computed tomography imaging. *J Am Coll Cardiol* 2005;45:43-9.  
<http://dx.doi.org/10.1016/j.jacc.2004.06.078>  
 PMid:15629371
17. Wackers FJ, Young LH. Lessons learned from the detection of ischemia in asymptomatic diabetics (DIAD) study. *J NuclCardiol* 2009;16:855-9.  
<http://dx.doi.org/10.1007/s12350-009-9138-1>  
 PMid:19685266

## PERFUZIONA SCINTIGRAFIJA MIOKARDA U DETEKCIJI ISHEMIJE MIOKARDA I PLANIRANJU TERAPIJE U RANIM STADIJUMIMA DIJABETES MELITUSA

Miloš Stević<sup>1</sup>, Marina Vlajković<sup>1</sup>, Goran Koraćević<sup>2</sup>, Radivoj Kocić<sup>3</sup>,  
 Milena Rajić<sup>1</sup>, Slobodan Ilić<sup>1</sup>

<sup>1</sup>Centar za nuklearnu medicinu, Klinički centar Niš, Srbija

<sup>2</sup>Klinika za kardiovaskularne bolesti, Klinički centar Niš, Srbija

<sup>3</sup>Klinika za endokrinologiju, Klinički centar Niš, Srbija

### Sažetak

Bolesnici sa dijabetes melitusom (DM) razvijaju komplikacije, uključujući koronarnu bolest, koja predstavlja vodeći uzrok mortaliteta kod njih. Jedan od dijagnostičkih modaliteta za ranu detekciju ishemijske miokarda kod simptomatskih i asimptomatskih bolesnika sa DM je perfuziona scintigrafija miokarda (MPI).

Cilj studije bio je da determiniše korisnost MPI u detekciji ishemijske miokarda kod simptomatskih i asimptomatskih bolesnika sa DM.

Ukupno je pregledano 34 bolesnika, starosti od 24 do 65 godina, 9 žena i 15 muškaraca. Trineastoro bolesnika imalo je simptome CAD, dok je 21 bolesnik bio asimptomatski. MPI je rađen standardnim dvodnevnom protokolom, a rezultati su kategorisani kao normalna perfuzija, reverzibilni perfuzijski defekti (ishemija) i fiksni perfuzijski defekti (ožiljak). Bolesnici sa ishemijskom su upućivani na koronarnu angiografiju (CAG). Rezultati dobijeni na MPI i CAG su statistički obrađeni.

Urednu perfuziju na MPI imalo je petnaestoro bolesnika (44,12%), dok je kod 19 (55,88%) uočeno postojanje perfuzijskih defekata (jedan fiksni i 18 reverzibilnih). CAG je pokazala postojanje stenozе koronarne arterije kod 7 (36,84%) od ukupno 19 bolesnika sa perfuzionim defektima na MPI. Statistička analiza nije pokazala postojanje korelacije između nalaza ishemijske na MPI i stenozе koronarne arterije na CAG.

Neslaganje između ishemijske miokarda utvrđene pomoću MPI i prezentacije epikardnih koronarnih arterija na CAG vezano je za endotelnu disfunkciju a ne za postojanje ateroskleroze. Ovi bolesnici mogu imati veću korist od farmakološke terapije nego od revaskularizacije. MPI i CAG treba da budu rezervisane za bolesnike sa visokim rizikom za postojanje CAD.

**Ključne reči:** perfuziona scintigrafija miokarda, koronarna angiokardiografija, dijabetes melitus

