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DETERMINATION OF CULPRIT LESION IN PATIENTS UNDERGOING ELECTIVE PERCUTANEOUS CORONARY INTERVENTION BY MYOCARDIAL PERFUSION IMAGING

Baskot B.,[1] Obradovic S.,[2] Rafajlovski S.,[2] Jankovic Z.,[1] Rusovic S.,[3] OrozovicV.,[2] Gligic B.,[2] Ratkovic N.,[2] Jung R.,[4] Ivanovic V.,[4] Bikicki M.[4]

[1]Nuclear Medicine Institute, Military Medical Academy, Belgrade, Serbia
[2]Urgent Medicine Clinic, Military Medical Academy, Belgrade, Serbia
[3]Institute for Radiology, Military Medical Academy, Belgrade, Serbia
[4]Cardiovascular Disease Institute, Sremska Kamenica, Serbia

A b s t r a c t: The aim of this study was to determine and localize culprit lesion by myocardial perfusion imaging (MPI) in cases of angiographically detected coronary narrowing ≥ 75% of at least one coronary artery.

Material and Methods: One hundred and thirty-two (132) patients with angiographically detected significant coronary narrowing (≥ 75% luminal stenosis of at least one major coronary artery) were studied. All the patients submitted MPI ^{99m}Tc-MIBI, with pharmacologic dipyridamole stress protocol with concomitant low level bicycle exercise 50W **(**DipyEX**)**. We measured relative uptake ^{99m}Tc-MIBI for each myocardial segment using short-axis myocardial tomogram study. A 5-point scoring system was used to assess the difference between uptake degree in stress and rest studies for the same segments, and we created two indices: Sum reversibility score (SRS), Index of sum reversibility score (ISRS).

Results: A total of 396 vascular territories (2244 segments) were analyzed before elective percutaneous coronary intervention (ePCI). Overall sensitivity, specificity and accuracy using SRS were 90.2%, 87.5%, and 89.4%, with a positive predictive value of 94.1%. Overall sensitivity, specificity, and accuracy using ISRS were 94.4%, 90.6%, 93.2% and the positive predictive value was 95.7%.

Conclusion: DipyEX MPI with the two indices created, SRS and ISRS, significantly improves sensitivity, specificity and accuracy in the determination and localization of culprit lesions in patients undergoing elective PCI.

Key words: MPI, Coronary Angiography, Culprit lesion, elective PCI

Introduction

One of the most powerful uses of MPI is the evaluation of the risk of future events in patients with suspected or known CAD. Over the years, MPI has evolved as an essential tool in the evaluation and assessment of patients prior to coronary revascularization [1, 2, 3, 4]. It has a dual role. Prior to coronary angiography, MPI is extremely useful in documenting ischaemia and determining the functional impact of single or multiple lesions identified subsequently, after the coronary anatomy is known, and despite some limitations in the setting of multivessel disease, MPI remains the test of choice for identifying the lesion responsible for the ischaemic symptoms, or so-called culprit lesion [4, 5, 6, 8, 9]. This is extremely useful for further management decisions with respect to percutaneous interventions. In contrast, the absence of reversible ischaemia in patients with known CAD is an excellent prognostic marker and predicts a low annual event rate [9, 11, 12, 13]. The current definition of culprit lesion: *zone of ischaemia under the coronary artery stenoses is not quite right,* because that does not define two pathophysiologic aspects of ischemia; severity and extent. The primary objective of the study was to determine and localize culprit lesion by introducing new parameters SRS (*summary reversible score*) and ISRS (*index of summary reversible score*), where there is angiographically detected coronary narrowing ≥ 75% for the least one coronary artery [11, 17].

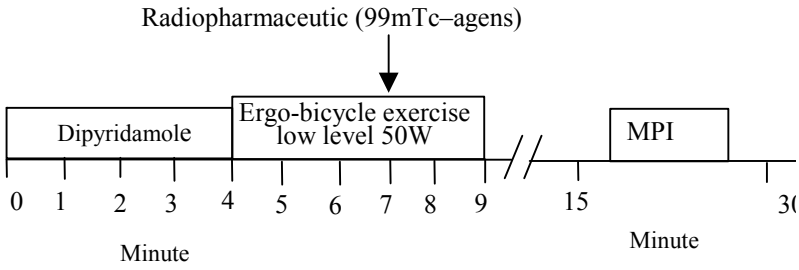
Methods

One hundred and thirty-two patients (78 male and 54 female, with a mean age of 52, 12 ± 8.26, yrs. ranging from 35 to 63) with angiographically detected significant coronary narrowing (≥ 75% luminal stenosis of at least one major coronary artery) were studied. They had angina pectoris with no clinically evident myocardial infarction.

Exercise protocol: We used DipyEX protocol;

Dipyridamole was administered by IV. Infusion (0, 56 mg/kg/min) for 4 min, after that we followed with the low level exercise 50W Bruce protocol by ergo bicycle for the next five minutes [7, 10, 17]. Radiopharmaceutical ^{99m}Tc-MIBI (the first dose) was administered during the 3rd minute of ergo bicycle exercise (Fig 1).

All patients were submitted to 2 IV injections of ^{99m}Tc-MIBI, one during the DipyEX protocol in the third minute (dose 740 MBq) of ergo bicycle exercise, and the other dose of tracer (370 MBq) 3 hours later. Imaging started 15 minutes after the DipyEX protocol finished and 30 minutes after second dose application.



0, 56 mg/kg/min IV.

Figure 1 – DipyEX protocol
Слика 1 – DipyEX протокол

Image Analysis

Images of the heart were taken 15 min after injections for the stress studies, and 30 minutes after injections for the rest study, using an Orbiter Siemens gamma camera, which was fitted with a low energy, all-purpose collimator, and connected to a dedicated Microdelta computer system. Briefly, 32 projections were obtained over a semicircular 180^0 arc which extended from the anterior 0^0 to the left posterior position 180^0. In each patient, we used the *Stirner program* (Euro menu) modified and standardized myocardial segmentation and nomenclature for topographic imaging of the heart analyzed SPECT. Quantification regional ^{99m}Tc-MIBI uptake was performed using short-axis myocardial tomography that was divided into 16 segments + apex for each study (17 segments overall) [2].

Left anterior descendent (LAD) vascular territory including: basal anterior, basal anteroseptal, mid anterior, mid anteroseptal, apical anterior, apical septal, and apex; Left circumflex artery (ACx); basal inferolateral, basal anterolateral, mid inferolateral, mid anterolateral, apical lateral; Right coronary artery (RCA); basal inferoseptal, basal inferior, mid inferoseptal, mid inferior, apical inferior (Fig 2).

We measured relative uptake, in the area of individual coronary artery vascular territory, from each segment and compared with the segment with the best uptake, and in the *DipyEX study* we established**:** Normal relative uptake (> 85%); Probably normal (75%–85%); Equivocal (65%–75%); Probably abnormal (50%–65%); Abnormal (< 50%). *Rest study:* Normal relative uptake (> 90%); probably normal (80%–90%); equivocal (70%–80%); probably abnormal (55%–75%); abnormal (< 55%). The difference between the relative uptake of

each segment was scored using a 5-point scoring system to assess the difference between uptake degree in stress and rest studies for the same segments (1 = normal, 2 = mild ischaemia, 3 = moderate ischemia, 4 = reversibility, 5 = severe reversibility).

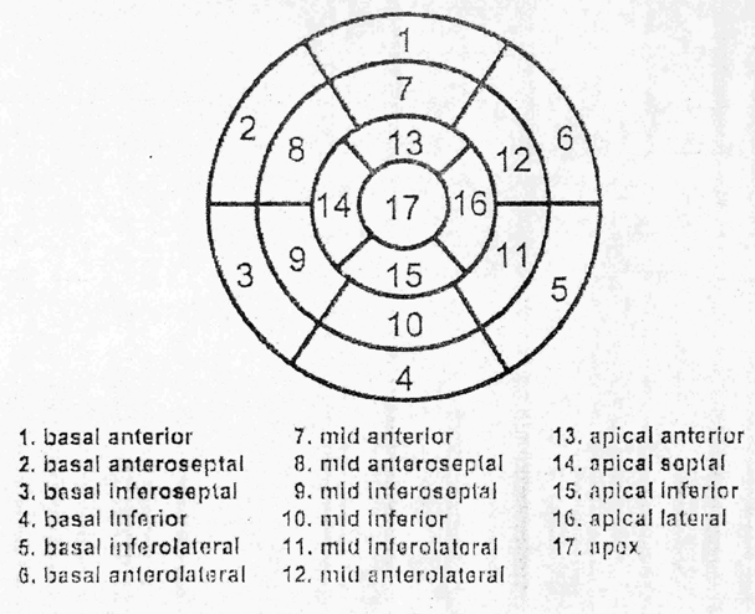


Figure 2 – Left Ventricular Segmentation
Слика 2 – Поделба на сегменти на левата комора

We introduced two new index scores to determine culprit lesion. *Summary reversible score (SRS)* ≥ 3 in the territory of the stenotic coronary artery was determined culprit lesion. At least two segments with a score of *5 (index of summary reversible score – ISRS)* in the territory of the stenotic coronary artery was determined culprit lesion.

Statistical analysis: We measured the Accuracy of Diagnostic Procedures by the *2 × 2 Table Method* [18].

Results

During the DipyEX protocols we followed these procedures: Recorded blood pressures (BP); heart rate (BPM) ECG on the monitor, recorded occurrence of symptoms (chest pain, nausea, dyspnea etc.); marked clock time of the injection of radiotracer relative to the start and end of ergo bicycle; after

injection of radiotracer, the ergo bicycle exercise continued for the next 2 minutes. We were monitoring BP, BPM and ECG for the next 5 minutes after completion of infusion, continuing clinical monitoring if chest pain or significant ECG changes persisted.

Coronary angiography finding

All 132 patients underwent coronary angiography. Coronary angiography showed significant ≥ 75% stenosis in at least one major coronary artery in all patients.

Fig. 3 of the 396 coronary territories, we found 207 (52.3%) ≥ 50% stenotic vessels. Individual vessel analysis showed moderate luminal stenosis (≥ 50% to < 75%) of the coronary artery in 64 (31%), and severe stenosis ≥ 75% in 143 (69%).

For LAD stenoses: overall 86 (≥ 75% = 63, < 75% = 23), ACx: overall 55 (≥ 75% = 38, < 75% = 17), and RCA: overall 66 (≥ 75% = 42, < 75% = 24).

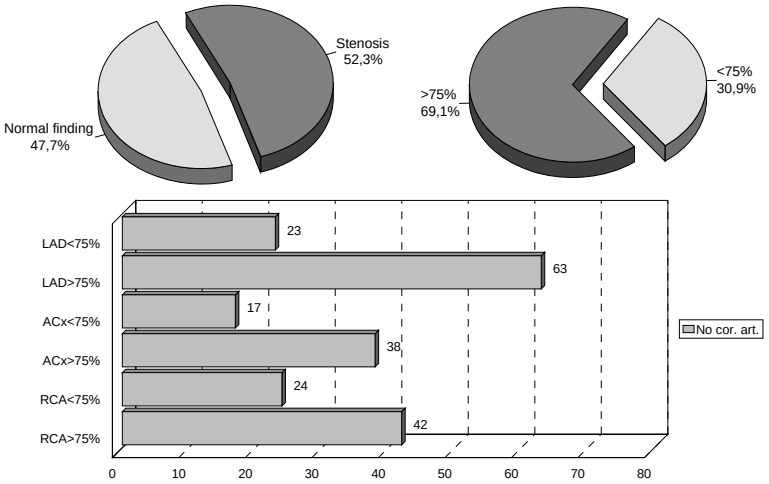


Figure 3 – 396 coronary territories, we founded 207 (52, 3%) ≥ 50% stenosed vessel. Individual vessel analysis showed moderate luminal stenosis (≥ 50% to < 75%) in the 64 coronary artery (31%), and 143 (69%) severe stenosis ≥ 75%. For LAD stenoses; overall 86 (≥ 75% = 63, < 75% = 23), ACx; overall 55 (≥ 75% = 38, < 75% = 17), and RCA; overall 66 (≥ 75% = 42, < 75% = 24)

Слика 3 – Од 396 коронарни територии, најдовме во 207 (52,3%) стеносирани садови (≥ 50%). Посебната садовна анализа прикажа умерена стеноза (≥ 50%, ≤ 75%) во 64 територии (31%) и 143 (69%) тешка стеноза ≥ 75%. Стенозата на ЛАД присутна кај 86 (≥ 75%= 63, < 75% = 23), АСх кај 55 (≥ 75% = 38, < 75% = 17) и RCA кај 66 (≥ 75% = 42, < 75% = 24)

Fig 4 shows 2244 examined segments, scoring with a 5-point scoring system to assess the difference between uptake degree in stress and rest studies for the same segments (1= normal, 2 = mild ischaemia, 3 = moderate ischaemia, 4 = reversibility, 5 = severe reversibility. We found overall 496 segments (22, 1%) with a score of 5 which determined culprit lesion – at least two segments with a score of 5 in the territory of the stenosed coronary artery.

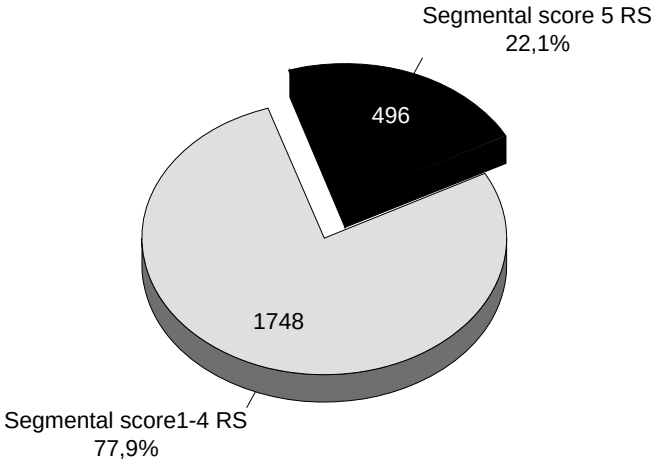


Figure 4 – Overall 2244 examined segments, scoring with a 5-point scoring system. We founded an overall of 496 segments (22, 1%) with scoring 5 where culprit lesion was determined – at least two segments with score 5 in the territory of stenoses coronary artery

Слика 4 – 2244 анализирани садови со 5-бодовен (scoring) сисшем. Најдовме 496 сегменши (22,1%) со "score" 5 каде шшо е и йрисушна "culprit" лезија.

^{99m}Tc-MIBI imaging: in all the patients image quality was excellent in both DipyEX and rest studies. On visual analysis, all patients with significant stenosis of at least one major coronary artery showed an abnormal finding. In the 132 subjects included in this study, a total of 2244 myocardial segments were quantitatively analyzed.

On the basis of analyses using SRS ≥ 3 which determine culprit lesion overall sensitivity, specificity, accuracy, PPV, and NPV was (90.1%, 87.1%, 89.4%, 95.78% and 73%) Fig 5.

In the detection of culprit lesion of individual stenosed vessel by SRS sensitivity, specificity, accuracy, PPV, and NPV for LAD was (95.2%, 88.9%, 94.1%, 97%, and 80%); ACx (82%, 83.3%, 82.3%, 90%, and 71.5%); and RCA (89.2%, 90%, 89.4%, 97%, and 69.2%) Fig 6.

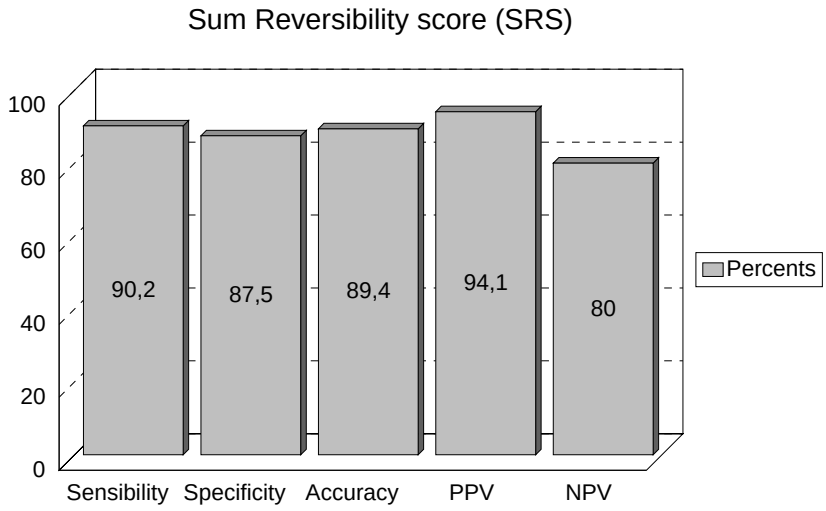
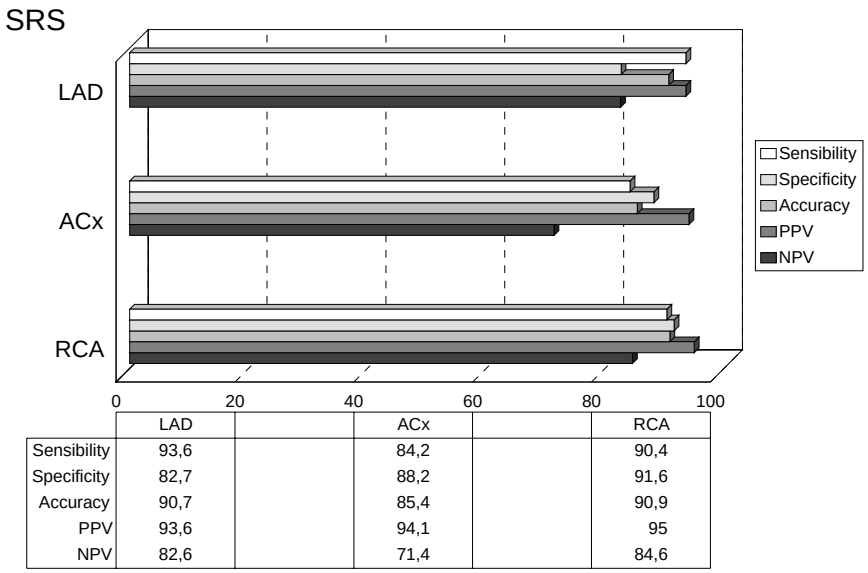


Figure 5 – Analyses used SRS ≥ 3 for determining culprit lesion

Слика 5 – Анализата користеше вредност на SRS ≥ 3 за одредување на "culprit" лезија



	LAD		ACx		RCA
Sensibility	93,6		84,2		90,4
Specificity	82,7		88,2		91,6
Accuracy	90,7		85,4		90,9
PPV	93,6		94,1		95
NPV	82,6		71,4		84,6

Figure 6 – Detection culprit lesion of individual stenosed vessel by SRS ≥ 3 which determine culprit lesion

Слика 6 – Одредувањето на "culprit" лезија на поединечната стеноза со вредност на SRS ≥ 3

On the basis of the analyses used ISRS in the identification of culprit lesion (at least two segments with score *5* in the territory of stenosed coronary artery) overall sensitivity, specificity, accuracy, PPV, and NPV was (94.1%, 93.3%, 94%, 98%, and 82.3%) Fig 7.

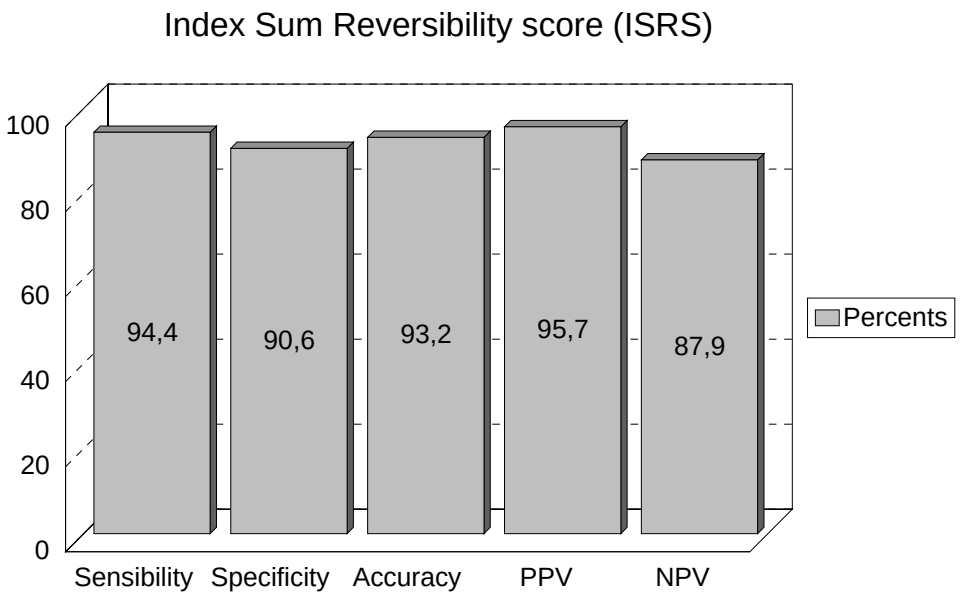


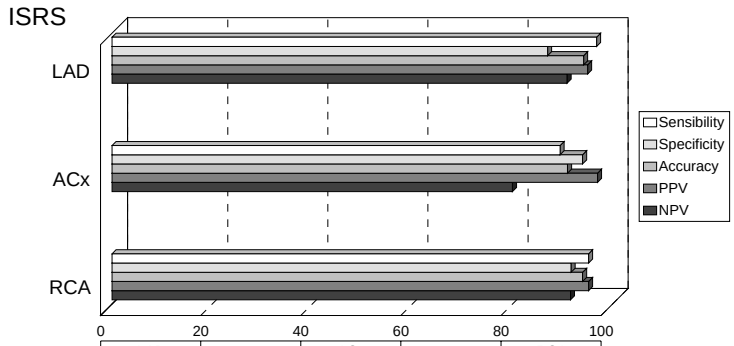
Figure 7 – Analyses used ISRS in the identification of culprit lesion (at least two segments with score 5 in the territory of stenoses coronary artery)

Слика 7 –Анализата користеше ISRS за препознавање на "culprit" лезија (најмалку два сегменти со "score" 5 во територијата на стенозата на коронарната артерија)

In the detection of culprit lesion of individual stenosed coronary artery by ISRS sensitivity, specificity, accuracy, PPV, and NPV for LAD was (97.7%, 100%, 98%, 100%, and 90%); ACx (87%, 90.1%, 88.3%, 95.2%, and 77%); RCA (94.6%, 91.6%, 93.6%, 97.2%, and 81.8%) Fig 8.

Sensitivity, specificity and accuracy in the determined culprit lesion was very good, but it was significantly higher when we used the index of sum reversibility score (ISRS) in quantitative analyses.

Figs 9, 10, and 11 show one representative example: *culprit lesion* (in the lateral, inferolateral, and inferior region) on the DipyEX cardiac tomography imaging which indicated angiography and invasive revascularization. After ePCI with stent implantation myocardial perfusion imaging showed normal findings.



	LAD		ACx		RCA
Sensibility	96,8		89,5		95,2
Specificity	87		94		91,7
Accuracy	94,2		91		94
PPV	95		97		95,2
NPV	90,9		80		91,6

Figure 8 – Detection culprit lesion of individual stenosed coronary artery by ISRS

Слика 8 – Одредување на "culprit" лезија на посебната стеноза на коронарната артерија со ISRS

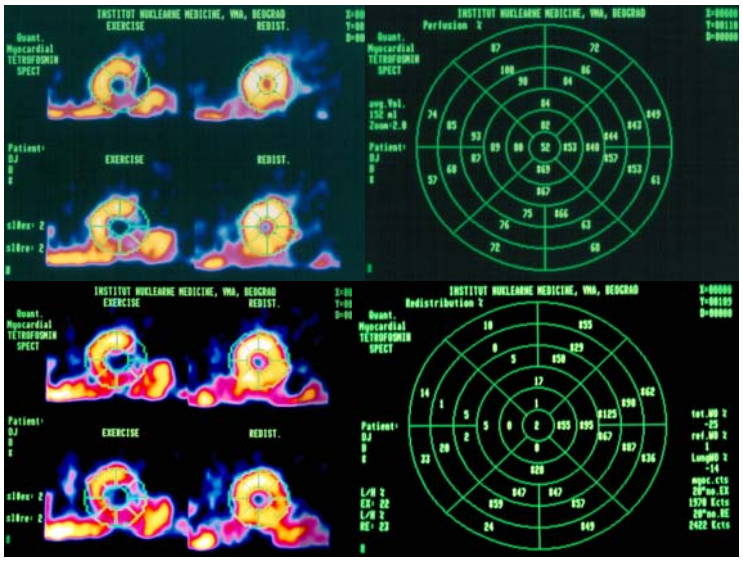


Figure 9 – Figure showed culprit lesion on the short axis after DipyEX protocol. In the rest of the study (right) we will see normal finding in the same area. We indicated coronary angiography

Слика 9 – Сликата прикажува "culprit" лезија на кратката оска по DipyEX протокол. Во рест студијата (десно) се гледа уреден наод во самата регија. Индицираме коронарна ангиографија

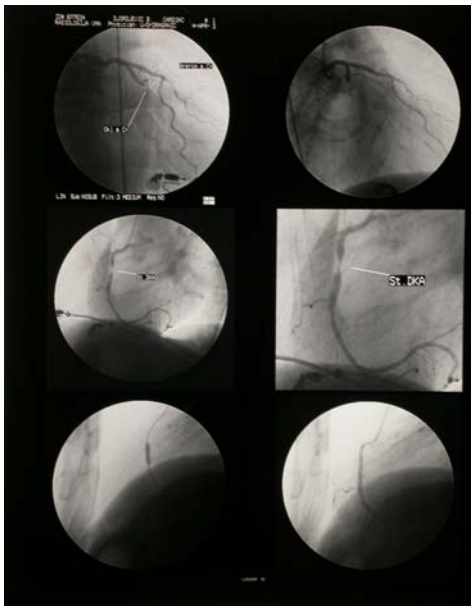


Figure 10 – Figure showed coronary angiography finding was occlusion ACx, and subtotal stenosis RCA. In the same acts we performed PCI with stent implantation. The final result (below) showed absolutely success

Слика 10 – Сликата прикажува коронарна ангиографија со оклузија на ACx и суптотална стеноза на RCA. Во истиот акт изведовме PCI со имплантација на стент. Крајниот резултат прикажува целосен успех

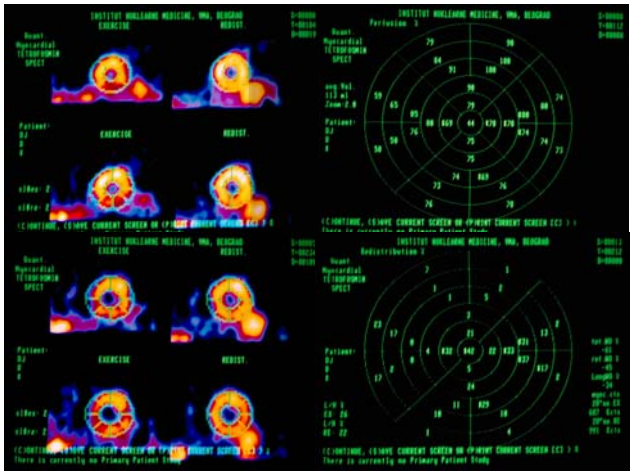


Figure 11 – Myocardial perfusion imaging performed two week after ePCI, in the same condition showed normal finding

Слика 11 – Миокардна перфузиона сцинтиграфија изведена две недели по ePCI, во истата состојба покажа нормални наоди

Discussion

In this recent work the author [11] defined culprit lesion using two physiological aspects: severity of ischaemia and extension zone of ischaemia. With quantification of these two parameters of culprit lesion, the author determined patients who underwent PCI with stent implantation, and who had the best therapy effects with PCI therapy. Conversely, we considered patients with mild ischaemia with good exercise tolerance as candidates for intense medical therapy [11]. Published data from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluations (COURAGE) trial indicate that many ischaemic defects may markedly improve with aggressive lowering of abnormal lipids and other pharmacological interventions [14, 15, 16]. Hachamovitch and colleagues reported that patients with a mildly abnormal scan had a 0.8% annual cardiac death rate compared with 0.9% for those who underwent revascularization. The death rate in medically treated patients who had moderately abnormal scans was 2.3% versus 1.1% for such patients undergoing revascularization. Finally, patients with a severely abnormal scan treated medically had an annual cardiac death rate of 4.6% versus 1.3% for such patients who were revascularized. In the second study, these investigators showed that medically treated patients who had greater than 20% of the total myocardium rendered ischaemic had a higher annual cardiac death rate (6.7%) compared with 2.0% for patients with this degree of extensive ischaemia who underwent revascularization. For patients with 10% or less of the total myocardium rendered ischaemic, there was no difference in outcome between medical therapy and revascularization [14, 15, 16].

Exercise myocardial perfusion imaging is a valuable adjunct for separating high to low risk patients who present symptoms consistent with stable CAD, or in patients who have known disease and in whom further prognostication is warranted. Multiple high-risk nuclear imaging variables can be identified, and the greater the extent of exercise/induced ischaemia, the greater the risk of cardiac events. Adjunctive variables, such as transient ischaemic cavity dilatation and functional assessment with evaluation of regional wall thickening or wall motion and left ventricular ejection fraction greatly assist in the risk stratification process [7, 8, 11].

Recent evidence in large patient cohorts has revealed that factors estimating the extent of left ventricular dysfunction (left ventricular ejection fraction, extent of infarcted myocardium, transient ischaemic dilatation of the left ventricle and increasing lung uptake) are excellent predictors of cardiac mortality [14, 15, 16]. However, measurements of inducible ischaemia are the best predictors of the development of acute coronary syndromes. Several reports have shown that nuclear testing yields incremental prognostic value over clinical information with respect to cardiac death, or the combination of cardiac death and nonfatal myocardial infarction as isolated endpoints [3, 4, 6, 11, 14].

Now it is possible to tailor the therapeutic decision-making for an individual patient based on a combination of clinical factors and nuclear scan results. Patients with severe perfusion abnormalities on their stress image may have a five- to ten-fold higher likelihood of cardiac death versus patients with a normal myocardial perfusion SPECT. If the defects perfusion is determined as a culprit lesion, invasive therapy (PCI) is an optimized outcome for that patient [11, 14, 15, 17].

Conclusion

DipyEX MPI with the two created indices SRS and ISRS significantly improves sensitivity, specificity, and accuracy for determination and localization of culprit lesions in patients undergoing elective PCI.

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Резиме

ОДРЕДУВАЊЕ НА "CULPRIT" ЛЕЗИИ СО МИОКАРДНА ПЕРФУЗИОНА СЦИНТИГРАФИЈА КАЈ ПАЦИЕНТИ КОИ СЕ ПОДЛОЖУВААТ НА ЕЛЕКТИВНА ПЕРКУТАНА КОРОНАРНА ИНТЕРВЕНЦИЈА

Башкот Б.,[1] Обрадовиќ С.,[2] Рафајловски С.,[2] Јанковиќ З.,[1] Русовиќ С.,[3] Орозовиќ В.,[2] Глигиќ Б.,[2] Ратковиќ Н.,[2] Јунг Р.,[4] Ивановиќ В.,[4] Бикички М.[4]

[1]Институт за нуклеарна медицина, Воена медицинска академија, Белград, Србија
[2]Ургентна медицинска клиника, Воена медицинска академија, Белград, Србија
[3]Институт за радиологија, Воена медицинска академија, Белград, Србија
[4]Институт за кардиоваскуларни болести, Сремска Каменица, Србија

Апстракт: Целта на студијата беше да се одреди и локализира "culprit" лезија so миокардна перфузиона сцинтиграфија (МПС) кај стеснување на коронарна артерија (> 75%) ангиографски докажана.

Материјал и методи: Беа испитувани 132 пациенти со коронарна артериска болест. Кај сите пациенти најдовме стеснување на најмалку една коронарна артерија од ≥ 75% и изведовме МПС со ^{99m}Tc-MIBI, со фармаколошки дипиридамолски стрес тест и ниско ниво на оптоварување со велосипед на 50W. Измеривме релативна задршка на ^{99m}Tc-MIBI за секој миокарден сегмент со користење на томограма со кратка оска. Пет бодовен "scoring" систем беше користен за одредување на разликата на задршката на изотопот во рест и стрес студијата за секој сегмент, и беа одредувани индексите: Sum reversibility score (SRS), Index of sum reversibility score (ISRS).

Резултати: Вкупно 396 васкуларни територии (2 244 сегменти) беа анализирани пред изведувањето на елективната перкутана коронарна интервенција. Беше добиена сензитивност, специфичност и точност 90,2%, 87,5% и 89,4%, кога беше користен SRS, и позитивна предиктивна вредност од 94,1%. Сензитивиноста, специфичноста и точноста беше: 94,4%, 90,6%, 93,2%, а позитивната предикативна вредност 95,7%, кога се користеше ISRS.

Клучни зборови: MPI, коронарна ангиографија, "Culprit" лезии, елективна перкутана коронарна интервенција.

Corresponding Author:

Branislav Baskot
Nuclear Medicine Institute
Military Medical Academy
Belgrade, Serbia

E-mail: baskotbranislav@yahoo.com