



Baština Akademije nauka i umjetnosti Bosne i Hercegovine

## **Zbornik radova "Naučni simpozij STEČENE BOLESTI SRCA Svjetski dan srca 2014."**

**Mesihović Dinarević, Senka**

**2015**

Akademija nauka i umjetnosti Bosne i Hercegovine

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## THE IMPORTANCE OF PHARMACOLOGICAL STRESS IN MYOCARDIAL PERFUSION SCINTIGRAPHY

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### Introduction

Myocardial perfusion scintigraphy is a non-invasive diagnostic procedure for assessing coronary flow in the myocardium. It is used for the detection and assessment of the extent of ischaemia and necrosis, the assessment of myocardial viability, and prognosis and risk stratification of coronary disease. The radiopharmaceuticals that are routinely used for this procedure are technetium-labelled monovalent cation complex Tc-sestamibi and Tc-tetrophosmine for SPECT (Single photon emission computed tomography), and Nitrogen-13 ammonium and Rubidium 82 for PET (Positron emission computed tomography).

After the radiopharmaceutical is administered intravenously, it accumulates in myocytes in proportion to the flow through the coronary artery. The two most important factors for uptake in the myocardium are the size of coronary flow and integrity of myocytes. In a healthy coronary artery, myocardium steadily accumulates the radiopharmaceutical, while myocardial segments that supply the stenosed or occluded coronary arteries display reduced or absent uptake. This difference increases significantly during stress to the heart.(1) Myocardial perfusion scintigraphy consists of two parts: stress imaging (applications of radiopharmaceuticals after stress), and rest imaging (applications of radiopharmaceuticals when the heart is at rest).

In normal myocardial perfusion study, there is homogenous radiotracer distribution in both stress and rest images (Figure 1 and 2). If information on the scintigram is defective (or lacking) after stress repairs compared to the scintigram at rest, a reversible defect, or ischemia, is indicated. If the defect on the scintigram after stress persists on the scintigram at rest, this indicates an irreversible defect, occurring as a result of myocardial infarction and caused by the absence of myocytes. (Figure 3 and 4)

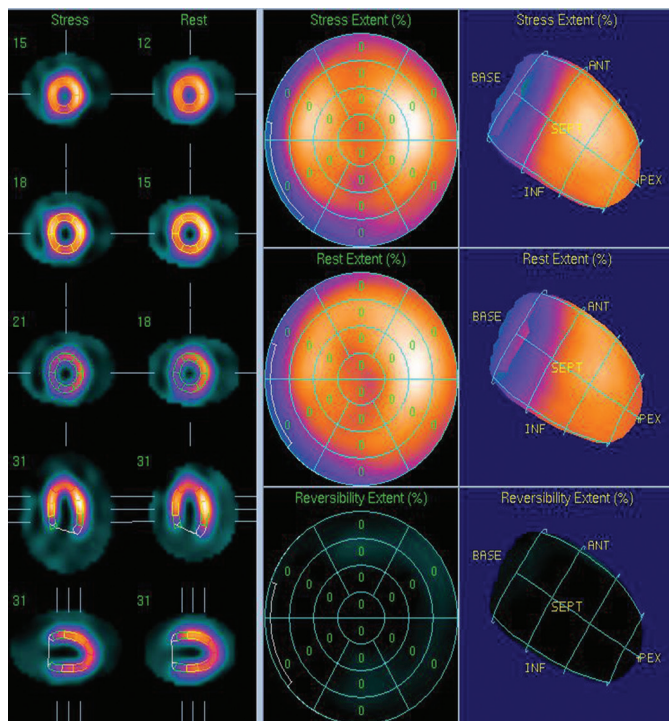
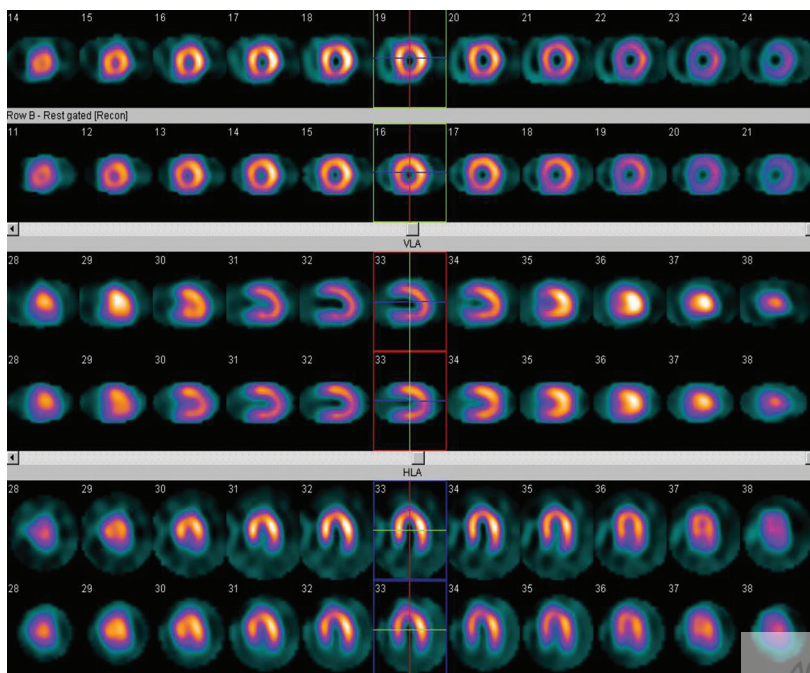


Figure 1 and 2. Normal myocardial perfusion SPECT – homogenous radiotracer distribution in both stress and rest images

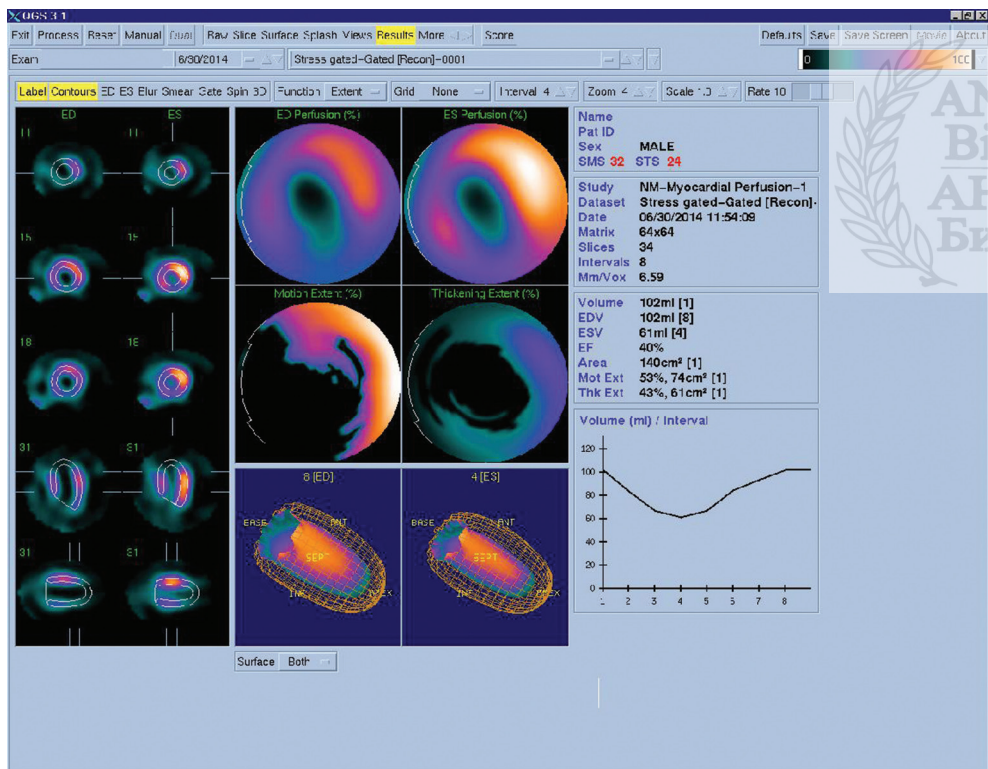
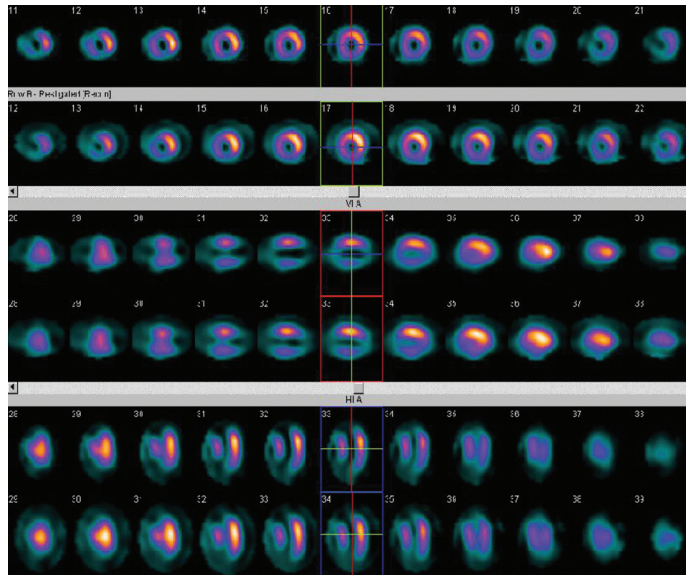


Figure 3. and 4. Abnormal myocardial perfusion SPECT. Stress images show an absence of perfusion in the apex and apical segments of the inferior wall and septum. In the at rest images, defects persist but with a slight improvement to perfusion in the inferior wall and septum. This indicates scarring with surrounding ischaemia

## Single photon emission computed tomography

Single photon emission computed tomography produces images of the heart in three planes: two parallel and one perpendicular to the long axis of the left ventricle. This procedure is performed using a tomographic gamma camera with one or more detectors. The patient lies on his back while the gamma camera rotates around him. To assess the systolic function of the left ventricle, the SPECT recording is synchronised with the patient's ECG.(2)

## Indications for myocardial perfusion scintigraphy

Myocardial perfusion scintigraphy is indicated in: patients with atypical pain in the precordium; asymptomatic patients with risk factors; asymptomatic patients with positive ergometric findings; patients with symptoms but with negative ergometric findings; and patients with existing coronary disease. Before revascularisation, it is essential to: evaluate the extent of ischaemia; distinguish any consequent scarring; evaluate the functional significance of stenosis determined by coronary angiography; and monitor patients after coronary artery bypass or stent implantation. It is indicated in the prognosis of coronary artery disease and assessment of viable myocardium.

## Cardiac stress tests

Stress during myocardial perfusion scintigraphy may be dynamic-ergometric or pharmacological stress.(3)

Exercise testing is a physiological test and most accurately marks the state of the increased metabolic needs of the heart. It can constitute running on a treadmill, or riding a specially provided bike. For patients who cannot adequately perform ergometric stress, pharmacological stress is applied.(4,5) (Table 1.)

*Table 1. Contraindications for adequate ergometric stress*

| <b>Conditions that prevent the proper execution of the acute exercise stress of myocard</b>                      |
|------------------------------------------------------------------------------------------------------------------|
| Peripheral vascular disease                                                                                      |
| Arthritis                                                                                                        |
| cerebrovascular accident                                                                                         |
| Chronic obstructive pulmonary disease                                                                            |
| Poor motivation for dynamic test                                                                                 |
| Application of $\beta$ -blockers, long-acting nitrates, calcium antagonists (alleviate ischemia induced by load) |
| Left bundle branch block                                                                                         |
| The early post-infarction period                                                                                 |

Contraindications for ergometric stress are: uncontrolled unstable angina pectoris; **heart failure**; life-threatening or untreated arrhythmias; uncontrolled hypertension (BP >200/115 mmHg); acute myocardial infarction; myocarditis; pericarditis; acute respiratory infections; severe pulmonary hypertension; pulmonary embolism; and severe aortic stenosis.

## Pharmacological stress test

Pharmacological stress testing involves the use of vasodilators, such as: dipyridamole; adenosine; regadenoson; or the inotropic agent, dobutamine. Dipyridamole and adenosine cause vasodilatation, which occurs in healthy coronary arteries, at an increased flow of 3-5 times compared with that at rest. In a stenosed coronary artery, vasodilatation does not occur after stenosis.

Dobutamine is a  $\beta$ -adrenergic agonist with both positive chronotropic and inotropic effects, resulting in coronary artery dilatation secondary to an increase in myocardial oxygen demand. It is used in patients for whom the use of vasodilators is contraindicated.(6)

Regadenoson is a selective coronary vasodilator (selective A<sub>2A</sub> adenosine receptor agonist) and is used as a pharmacological stress agent in perfusion scintigraphy. Activation of the A<sub>2A</sub> adenosine receptor causes coronary vasodilatation, and a sudden but short-lived increase in coronary blood flow. It is used only for diagnostic purposes. The dose of regadenoson is fixed at 400g (5ml), and administered in a peripheral vein. There is no need to adjust the dose according to body weight, and it is not dependent on renal and hepatic function. Regadenoson is applied in the form of a rapid intravenous injection, making the procedure quicker and easier.(7) Before using regadenoson, patients should avoid the consumption of products containing methylxanthines (e.g. caffeine), as well as any medicine containing theophylline for at least 12 hours before the procedure. If it is possible, dipyridamole should not be taken for at least two days prior to regadenoson administration. Regadenoson causes a sudden increase in heart rate after injection, so patients should remain sitting or lying down and should be monitored until ECG parameters, heart rate and blood pressure readings return to their pre-dosing values. Cardiac frequency returns to baseline within 10 minutes.

### **Contraindications for use of regadenoson are:**

- Hypersensitivity to the active ingredient, or any other components
- Atrioventricular (AV) block, second or third degree, or dysfunctional sinoatrial node, unless the patient does not have a functioning pacemaker (pacemaker)
- Unstable angina that has not been stabilised by drugs
- Severe hypotension
- Heart failure

## Side effects

The most commonly reported side effects during the clinical development of regadenoson were: dyspnoea (29%), headache (27%), redness and heating of the skin (23%), chest pain (19%), changes in the ST segment in the electrocardiogram (18%), discomfort in the gastrointestinal tract (15%), and dizziness (11%). Aminophylline may be used to relieve severe and/or persistent side effects of regadenoson.

Results of the Brinkert, Reyes et al. study demonstrate that regadenoson is well-tolerated, and can be considered safe, with no deaths or severe cardiac complications. Its side effects are slight, and similar to those of adenosine (chest discomfort and dyspnoea), but less expressed, although regadenoson use has more frequent gastrointestinal symptoms.(8) Regadenoson is safe for use in patients with chronic obstructive pulmonary disease, and asthma.(9)

Jager PL et al. performed their research to compare the severity and duration of side effects of regadenoson and adenosine as a medicament for pharmacological cardiac stress. They have shown that regadenoson use has significantly fewer side effects, with shorter durations.(10)

## Conclusion

Myocardial perfusion scintigraphy as a non-invasive diagnostic procedure has a significant place in the algorithm of diagnostic tests in ischaemic heart disease.

Using pharmacological stress agents, this procedure can be performed on patients with a contraindication for ergometry.

With the development of new pharmacologic agents such as regadenoson, these diagnostic procedures have become more efficient, safer, and have fewer side effects.

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