

Preliminary Data on the Prognostic Value of a New Protocol of Ultra-fast Myocardial Scintigraphy with Less Radiation in CZT Gamma Camera

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Abstract

Background: Myocardial perfusion scintigraphy (MPS) is one of the most used imaging methods for the evaluation of patients for coronary artery disease (CAD) due to its diagnostic and prognostic value. Two of its main limitations are radiation use and scan duration. However, CZT cameras (CZT-C) have allowed tracer dose and scan time reductions. However, the prognostic value of these new protocols is not known.

Objective: To determine the prognostic value of a new, ultrafast, low dose protocol in a CZT-C. Population: Patients with suspect CAD undergoing MPS from 11/2011 to 6/2012 were studied.

Methods: They had a 1-day Tc-99m sestamibi protocol starting with rest study (5 mCi dose) followed by stress (15 mCi). Acquisition times were 6 and 3 minutes respectively. MPS studied were classified as normal or abnormal and perfusion scores (SSS, SRS and SDS) were calculated. Patients were accompanied by 6-month phone calls. Events were defined as death, nonfatal myocardial infarction and late revascularization (> 60 days after MPS) and analyzed with the Cox method.

Results: 792 patients were followed for 21.3 ± 3.7 months. Age was 65.2 ± 12.7 years, 50.3% were male and body mass index was 26.9 ± 4.7 . Hypertension was the most frequent risk factor (59.5%), followed by hypercholesterolemia (51.9%) and diabetes (23.3%). Exercise was used in 438 (55.3%); 618 (78%) MPS studies were normal. Mean dosimetry was 6 mSv and mean scan time, 48 ± 11 minutes. During follow-up, there were 12 deaths, 4 nonfatal infarctions, 42 angioplasties and 5 coronary artery bypass surgeries. Annual hard event rate was higher in patients with abnormal MPS (3.0% vs. 0.7%, $p < 0.01$), as well as the frequency of patients undergoing late revascularization (10.8% vs 1.9%, $p < 0.001$). SSS and SDS were higher in patients with hard events compared to those without events (7.8 ± 8.8 vs 2.9 ± 5.7 ; 3.3 ± 5.7 vs 0.7 ± 2.2 , $p < 0.01$) and among revascularized patients compared to non-revascularized (7.1 ± 7.9 vs 2.7 ± 5.6 ; 3.1 ± 4.4 vs 0.6 ± 2.1 , $p < 0.001$).

Conclusion: A new MPS protocol in a CZT-C allowed faster, lower radiation studies without compromising the prognostic ability of this imaging method. (Arq Bras Cardiol: Imagem cardiovasc. 2016;29(1):11-16)

Keywords: Coronary Disease; Radiation Exposure Control, Prognosis; Myocardial Perfusion Imaging; Radiopharmaceuticals; Gamma Cameras; Cadmium; Zinc; Tellurium.

Introduction

MPS is one of the methods most used to evaluate patients with suspected coronary artery disease (CAD), and its value in the risk stratification of patients with CAD is well established.¹⁻⁵ However, MPS has some limitations, two of which are prolonged duration of the test and the need to employ radiation.

New gamma cameras (GC) using semiconductors to increase sensitivity for detection of photons and increased spatial and energetic resolution have been recently developed. Most of these devices use a Cadmium-zinc-tellurium (CZT) alloy for the detection of photon.⁶ These semiconductors produce electric current directly in response to the photon, combining the functions of the crystal and photomultipliers. Studies have

demonstrated that Discovery 530 increases up to five times the sensitivity to photon, has a 2.5 times higher spatial resolution and double energetic resolution than conventional SPECT.⁷

A recent study has shown that these advances allow reduced testing time and especially of radiation doses with increased sensitivity⁸ and accuracy for diagnosis of obstructive coronary disease.⁹ The prognostic value of the tests performed with these devices has not been established yet.

Objective

To determine the prognostic value of MPS held in a CZT-GC in patients with known or suspected CAD, employing an ultra-fast acquisition protocol with lower radiation doses.

Methods

Population

The study included 830 consecutive patients with suspected CAD who underwent MPS at Clínica de Diagnóstico por Imagem in Rio de Janeiro in Rio de Janeiro from November

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Manuscript received June 26, 2015; revised manuscript August 10, 2015;
accepted September 11, 2015.

2011 to June 2012. Patients with myocardial infarction or previous CABG were not included. From the initial population, 38 patients (4.6%) did not complete the follow-up, resulting in a final population of 792 patients. The Research Ethics Committee from Hospital Universitário Clementino Fraga Filho of Universidade Federal do Rio de Janeiro approved this study and all participants signed an informed consent form. Before the MPS, a team of cardiologists collected clinical data and risk factors such as hypertension, diabetes, hypercholesterolemia, smoking and family history of early CAD, history of prior myocardial infarction, angioplasty and CABG.

Protocol of images

Patients were submitted to a same-day protocol beginning with a resting phase after injection of ^{99m}Tc sestamibi (6 mCi) and acquisition of MPS with duration of 6 minutes after ingestion of 3 - 4 glasses of water. Immediately after that, the patients were subjected to the stress phase. The physical or pharmacological stress protocols were performed as described in a previous study.⁴ The acquisition of post-stress images was carried out after five minutes with duration of three minutes. Images were acquired in prone position of all male patients and lasted 90 seconds. Images were acquired in a gamma camera with CZT detectors (Discovery 530, GE Healthcare, Waukesha, WI, USA). The tests were processed using the Evolution for cardiac computer program (GE Healthcare, Waukesha, WI, USA). Cardiac contours were evaluated by a physician experienced in MPS assessment and manual correction was carried out when necessary.

Effective dose of the patients was estimated from the following formula: 0.0079 mSv/MBq for the stress phase and 0.009 mSv/MBq for the resting phase.¹⁰

A visual semiquantification was performed by two experienced cardiologists who were unaware of the clinical data using tomographic sections of the short axis and long vertical axis divided into 17 segments.¹¹ The quantification of the ^{99m}Tc sestamibi uptake was evaluated in each segment, graded on a scale of 0 to 4: 0 = normal uptake; 1 = error; 2 = moderate; 3 = severe; 4 = none. Summed stress score (SSS) was used with the following classification: SSS < 4 = normal; 4 - 8 = slightly abnormal; 9 - 13 = moderately abnormal; > 13 = severely abnormal. The summed rest score (SRS) was obtained in a similar way with the resting images. Then we calculated the difference between the two scores (SSS - SRS) to obtain the summed difference score (SDS).¹¹ Ejection fraction and diastolic and systolic left ventricular volumes were measured automatically using the QGS software; (Cedars-Sinai Medical Center, Los Angeles, CA, USA).

Follow-up

Follow-up was conducted by contacting the patients every six months after the MPS through a standardized questionnaire, by medical students. Occurrences of death from all causes, myocardial infarction or CABG (angioplasty or surgery) were recorded. Events were confirmed through contacts with the assistant physicians or hospital records. Hard events were defined by the presence of death or heart attack, and total events, by hard events plus CABG.

Statistical Analysis

All statistical calculations were performed using the SPSS statistical package (version 17). The categorical variables were expressed as frequencies and the continuous variables were expressed as mean \pm standard deviation. The variables were compared using the Chi-square test for categorical variables and Student's *t* test for continuous variables. The annual event rate was calculated by dividing the number of events by the number of people-years and was compared between the groups using the log-rank test. Kaplan-Meier curves were generated to visually evaluate the survival in different groups. The Cox proportional hazards analysis was performed to assess predictors of hard events and total events using $p < 0.05$ in the univariate analysis. In this analysis, we test SSS, SRS and SDS (as described above), as both dichotomous and categorical variables. LVEF was analyzed as a dichotomous variable in the Cox analysis with a 40% cut.

Results

During the study, 792 patients were followed for 21.3 ± 3.7 months. The mean age was 65.2 ± 12.7 years, 50.3% were male and the mean body mass index was 26.9 ± 4.7 . Hypertension was the most common risk factor (55.3%) followed by hypercholesterolemia (49.1%) and diabetes (21.1%). Physical stress was used in 438 patients (55.3%). MPS were normal in 78% of cases. Average dosimetry was 6 mSv and the MPS mean duration was 50 ± 11 minutes. The general characteristics of the study population are found in Table 1.

During follow-up, there were 12 deaths, 4 non-fatal infarctions, 42 angioplasties and 5 coronary artery bypass grafting surgeries. The annual rate of hard events was higher in patients with abnormal MPS (3.0% vs. 0.7%, $p < 0.01$), as well as the

Table 1 – Demographic data of the study population

Demographic Data	N (%) or Mean \pm SD
Male sex	398 (50%)
Age	65 \pm 12
Chest pain	356 (45%)
Dyspnea	103 (13%)
Hypertension	438 (55%)
Dyslipidemia	389 (49%)
Weight (kg)	77 \pm 16
BMI	26 \pm 4
Diabetes mellitus	167 (21%)
Family history	291 (30%)
Smoking	63 (8%)
Type of stress employed	
Physical stress	438 (55%)
Dipyridamole	341 (43%)
Dobutamine	13 (1.6%)

BMI: body mass index.

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frequency of patients who underwent late CABG (10.8% vs. 1.9%, $P < 0.001$). The SSS and SDS scores were higher in patients with hard events compared to those without events (7.8 ± 8.8 vs. 2.9 ± 5.7 , 2.9 ± 5.7 vs. 0.7 ± 2.2 , $P < 0.01$) and among CABG patients compared to non-

CABG patients (7.1 ± 7.9 vs. 2.7 ± 5.6 , 3.1 ± 4.4 vs. 0.6 ± 2.1 , $p < 0.001$). Kaplan-Meier curves of hard event-free survival and total events comparing patients with normal and abnormal scans and comparing different SDS groups are shown in Figures 1 and 2.

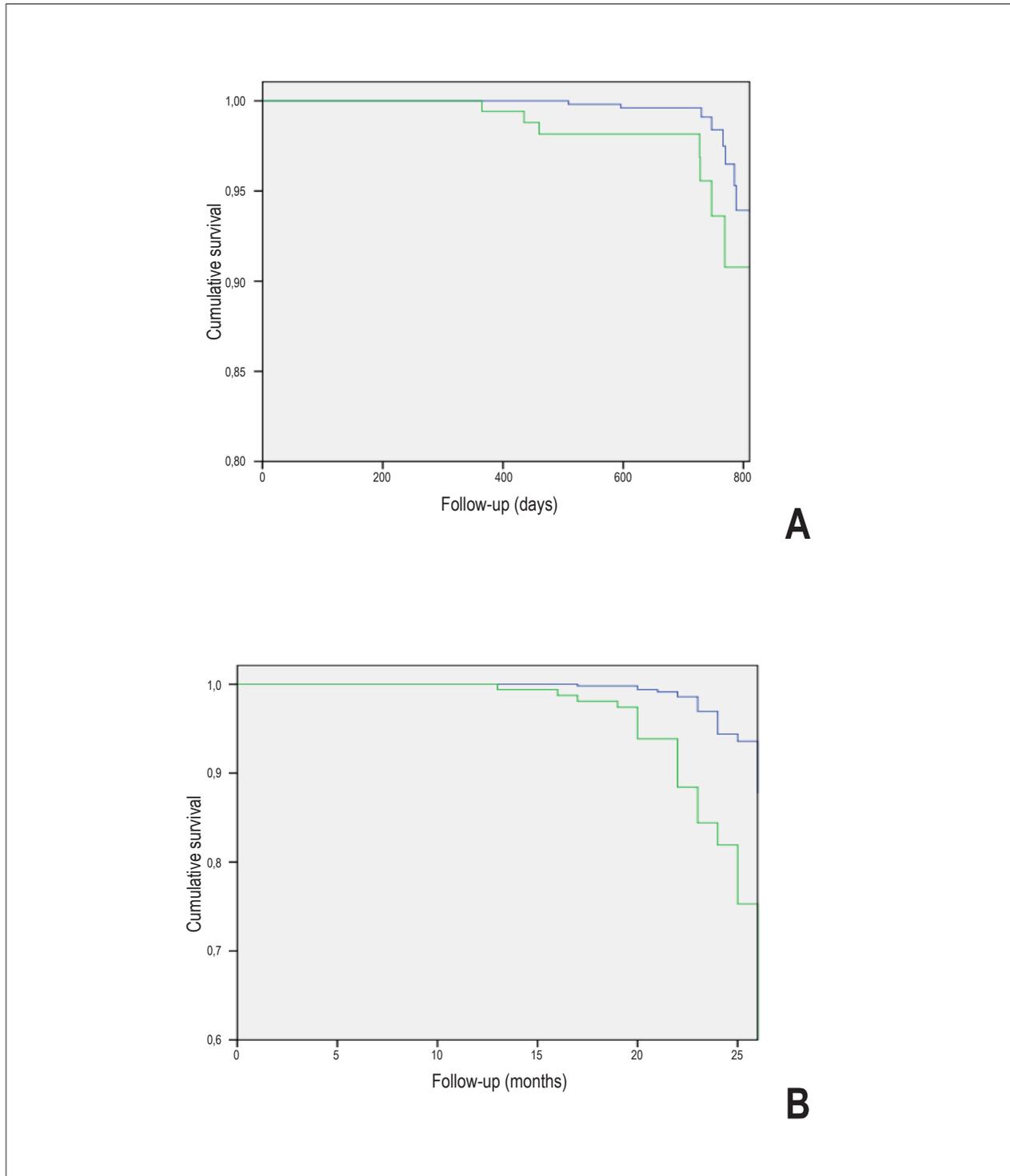


Figure 1 – A: Survival curve without hard events; B: Survival curve without total events; Blue line: normal scintigraphy; Green line: abnormal scintigraphy.

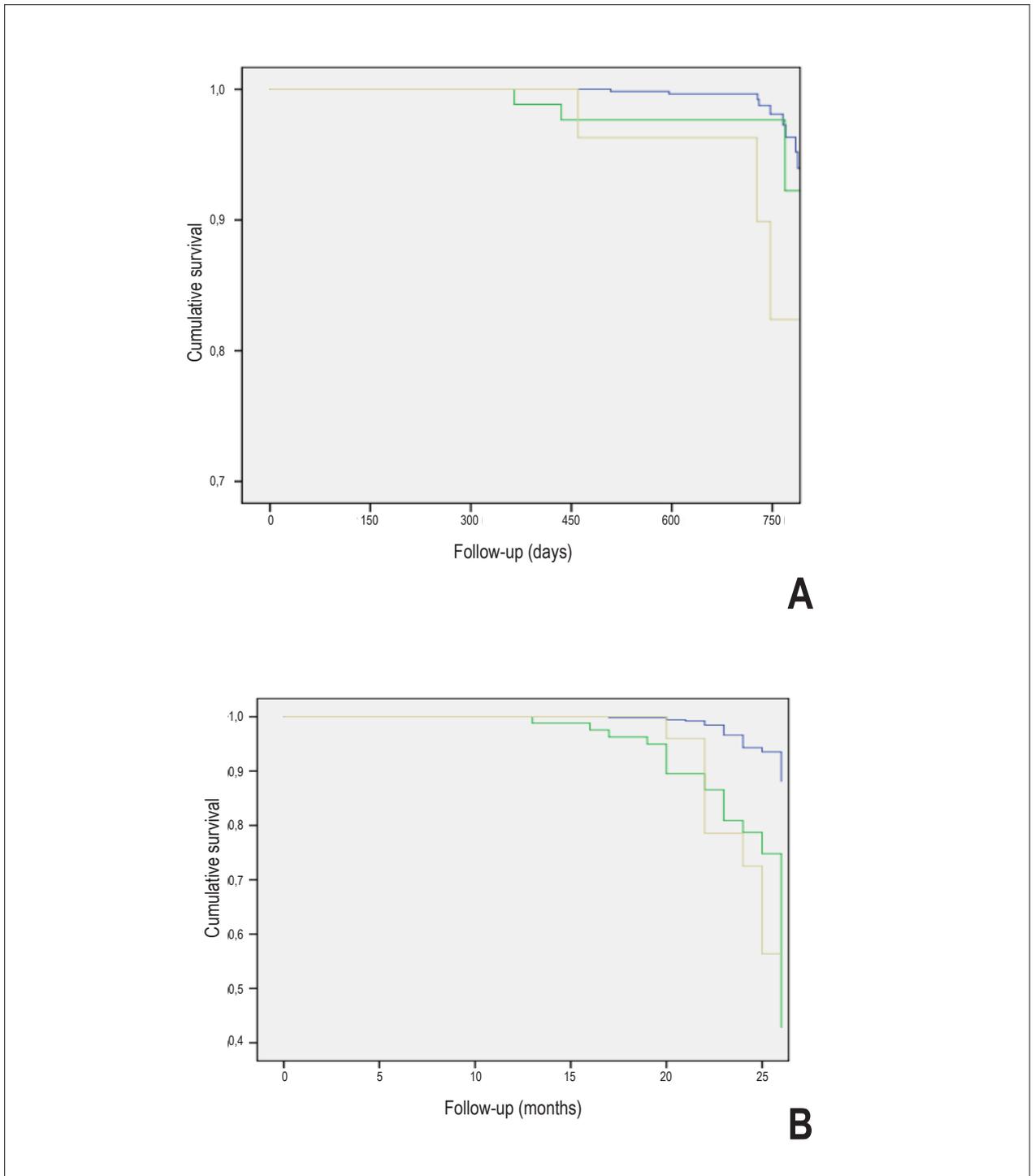


Figure 2 – A: Survival curve without hard events; B: Survival curve without total events; Blue line: SDS 0; Green line: SDS 1-5; Beige Line: >5. SDS is the summed difference score.

Discussion

MPS is a well-established methodology to determine the prognosis of patients with known or suspected CAD. However, exposure to radiation and the duration of prolonged test are two important limitations.

New CG using CZT detectors allow fast scanning at lower doses of radiotracers. Nakazato et al.¹² have recently shown that the prognostic value of MPS using CZT-GC was comparable to that using conventional SPECT scans. However, in this study, a number of different protocols were employed associating Thallium-201 to sestamibi, both in the stress and

in the rest phase. In our study, we used a standard protocol making the results more reproducible.

Chowdhury et al.¹³ evaluated the accuracy and the prognostic value in CZT-GC and its negative predictive value was similar to that found in our study. These authors used protocols very similar to traditional protocols, making stress and rest on different days with much higher doses.

This study has major limitations. The most significant ones are the lack of a control group of patients who underwent MPS in a conventional GC and the limited number of events found. The problem of the lack of a control group can be minimized because the prognostic data in conventional GC have been widely published, even by our research group, serving as a comparison parameter.¹⁴ The continuation of this evaluation with the increase in population over the next two years will make it possible to solve the issue of number of events. The authors did not perform intra and interobserver variability analysis in this study because the researchers had already published those data.¹⁵

Conclusion

Preliminary data presented in this paper suggest that a new ultrafast MPS protocol held in CZT-GC with much lower radiation doses than the conventional ones maintains

its accuracy in terms of risk stratification in CAD patients or patients with suspected CAD.

Authors' contributions

Research creation and design: Lima R; Data collection: Peclat T, Amaral AC, Nakamoto A, Lavagnoli D, Oliveira F; Data analysis and interpretation: Lima R, Peclat T, Amaral AC, De Lorenzo A; Statistical analysis: Lima R; Manuscript drafting: Lima R, De Lorenzo A; Critical revision of the manuscript for important intellectual content: Lima R.

Potential Conflicts of Interest

There are no relevant potential conflicts of interest.

Sources of Funding

This study had no external funding sources.

Academic Association

This study is not associated with any graduate program.

References

1. Berman D, Kang X, Van Train K, Lewin H, Cohen I, Areeda J, et al. Comparative prognostic value of automatic quantitative analysis versus semiquantitative visual analysis of exercise myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol*. 1998;32(7):1987-95.
2. Leslie WD, Tully SA, Yogendran MS, Ward LM, Nour KA, Metge CJ. Prognostic value of automated vs visual analysis for adenosine stress myocardial perfusion imaging. *J Nucl Med*. 2005;46(2):204-11.
3. Xu Y, Nakazato R, Hayes S, Hachamovitch R, Cheng VY, Gransar H, et al. Prognostic value of automated vs visual analysis for adenosine stress myocardial perfusion SPECT in patients without prior coronary artery disease: a case-control study. *J Nucl Cardiol*. 2011;18(6):1003-9.
4. Lima RS, De Lorenzo A, Pantoja MR, Siqueira A. Incremental prognostic value of myocardial perfusion 99m-technetium-sestamibi SPECT in the elderly. *Int J Cardiol*. 2004;93(2-3):137-43.
5. De Lorenzo A, Lima RS, Siqueira-Filho AG, Pantoja MR. Prevalence and prognostic value of perfusion defects detected by stress technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography in asymptomatic patients with diabetes mellitus and no known coronary artery disease. *Am J Cardiol*. 2002;90(8):827-32.
6. Garcia EV, Faber TL, Esteves FP. Cardiac dedicated ultrafast SPECT cameras: new designs and clinical implications. *J Nucl Med*. 2011;52(2):210-7.
7. Esteves FP, Raggi P, Folks RD, Keidar Z, Askew JW, Rispler S, et al. Novel solid-state-detector dedicated cardiac camera for fast myocardial perfusion imaging: multicenter comparison with standard dual detector cameras. *J Nucl Cardiol*. 2009;16(6):927-34.
8. Duvall WL, Croft LB, Ginsberg ES, Einstein AJ, Guma KA, George T, et al. Reduced isotope dose and imaging time with a high-efficiency CZT SPECT camera. *J Nucl Cardiol*. 2011;18(5):847-57.
9. Gimelli A, Bottai M, Genovesi D, Giorgetti A, Di Martino F, Marzullo P, et al. High diagnostic accuracy of low-dose gated-SPECT with solid-state ultrafast detectors: preliminary clinical results. *Eur J Nucl Med Mol Imaging*. 2011; 39(1):83-90.
10. ICRP, 2008. Radiation dose to patients from radiopharmaceuticals Addendum 3 to ICRP Publication 53. ICRP Publication 106. *Ann ICRP*. 2008;38(1-2)
11. Hendel RC, Budoff MJ, Cardella JF, Chambers CE, Dent JM, Fitzgerald DM, et al. AHA/ACR/ASE/ASNC/HRS/NASCI/RSNA/SAIP/SCAI/SCCT/SCMR/SIR 2008 Key Data Elements and Definitions for Cardiac Imaging A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Clinical Data Standards for Cardiac Imaging). *J Am Coll Cardiol*. 2009;53(1):91-124.
12. Nakazato R, Berman DS, Gransar H, Hyun M, Peats R, Kite F, et al. Prognostic value of quantitative high-speed myocardial perfusion imaging. *J Nucl Cardiol*. 2012;19(6):1113-23.
13. Chowdhury F, Vaidyanathan S, Bould M, Marsh J, Trickett C, Dodds K, Clark TP, Sapsford RJ, Dickinson CJ, Patel CN, Thorley PJ. Rapid-acquisition myocardial perfusion scintigraphy (MPS) on a novel gamma camera using multipinhole collimation and miniaturized cadmium-zinc-telluride (CZT) detectors: prognostic value and diagnostic accuracy in a 'real-world' nuclear cardiology service. *Eur Heart J Cardiovasc Imaging*. 2014;15(3):275-83.
14. Lima RS, De Lorenzo A, Camargo G, Oliveira, Reis T, Peclat T, Rothstein T, et al. Prognostic value of myocardium perfusion imaging with a new reconstruction algorithm. *J Nucl Cardiol* 2014;21(1):149-57.
15. De Lorenzo A, Fonseca L, Landesmann MC, Lima RS. Comparison between short-acquisition myocardial perfusion SPECT reconstructed with a new algorithm and conventional acquisition with filtered back projection processing. *Nucl Med Commun*. 2010;31(6):552-7.

