

Predictors for Indication to Catheterization after Myocardial Perfusion Gated Spect

Fernanda de Oliveira Mesquita,¹ Larissa Andrade,¹ Lívia Pitta,² Andrea Rocha de Lorenzo,^{1,2} Ronaldo de Souza Leão Lima^{1,2}

Universidade Federal do Rio de Janeiro(UFRJ),¹ Centro de Diagnóstico por Imagem CDPI,² Rio de Janeiro, RJ – Brazil

Abstract

Background: Patients with coronary artery disease with left ventricular dysfunction present higher mortality and are the major beneficiaries of a myocardial revascularization procedure. A previous study showed that left ventricular ejection fraction (LVEF) is a negative determinant for cardiac catheterization (CAT) after myocardial perfusion scintigraphy (MPS).

Objective: To determine clinical and scintigraphic factors associated with cardiac catheterization (CAT) indication in patients undergoing myocardial perfusion SPECT (MPS). Population: Patients consecutively submitted to PMC in the period from March 2008 to December 2012.

Methods: All patients undergoing MPS during the study were recorded in a data bank, where epidemiological, clinical and scintigraphic data (perfusion scores and LVEF) were recorded. Patients or their attending physicians were contacted by phone semiannually for follow-up. For statistical analysis, univariate analyzes were performed and variables were selected for inclusion in a logistic regression model.

Results: 5536 patients were submitted to MPS, of which 643 performed CAT after the examination. This group presents a higher prevalence of males, hypertensive, dyslipidemic and previously revascularized. Patients undergoing CAT have angina more frequently, more extensive ischemia scores and lower LVEF. Only presence of angina (IC 95% 1.2 - 1.7, $p < 0.001$) and extent of ischemia (95% CI 1.2 - 1.3, $p < 0.001$) were independent variables for CAT indication.

Conclusion: The presence of angina and the extent of ischemia were the main predictors for CAT post-MPS indication while lower LVEF was not an independent predictor. (Int J Cardiovasc Sci. 2017;30(6)504-509)

Keywords: Coronary Diseases; Ventricular Dysfunction, Left/mortality; Cardiac Catheterization; Myocardial/diagnostic imaging.

Introduction

Chronic arterial disease (CHD) is a cause of high morbidity and mortality. Studies have shown that patients with lower ejection fraction have an increased risk of annual mortality compared with those who maintain normal LVEF.¹⁻³ Considering the increased risk of cardiac events in these patients, a careful analysis should be done (area of ischemia, LVEF, age, comorbidities, etc.) to assess risk vs. benefit that therapies^{4,5} - cardiac revascularization (surgical, percutaneous) and drug treatment - will bring

to the patients. The subgroup of patients with reduced LVEF and extensive CAD are the major beneficiaries of revascularization.^{4,6,7}

Although physical capacity, age, presence of other comorbidities are factors related to patient survival, the most important prognostic factors are the extent of ischemia and left ventricular function. These are evaluated through myocardial perfusion scintigraphy synchronized with the electrocardiogram (Gated SPECT).

Mailing Address: Ronaldo de Souza Leão Lima

Rua Paissandu, 329 ap. 303 - Flamengo, Postal Code: 22210-085. Rio de Janeiro, RJ – Brazil
Email: ronlima@hotmail.com

The present study aims to determine the main clinical and scintigraphic factors associated with the indication of CAT in patients undergoing MPS.

Methodology

A total of 5536 adult patients who underwent MPS because of clinical indication from March 2008 to December 2012 were evaluated.

All data collected [among them, epidemiological, clinical and scintigraphic data (perfusion scores and LVEF)] were recorded in a database and patients or their physicians were contacted every six months by telephone for follow-up.

This study is in conformity with the ethical guidelines of the Declaration of Helsinki of 1975 and all the participants signed the Term of Free and Informed Consent.

Protocol of the study

A one-day protocol was performed, administering⁵⁻⁶ mCi (185-222 MBq) of Tc-99m Sestamibi in the resting phase and 18-20 mCi (666-740 MBq) in stress. Initially, 24 patients (13 men) were selected for a pilot study in which the total acquisition was made in 6 minutes in the listmode. The images were processed using 1 to 6 minutes of the total time of acquisition and then analyzed by 2 experienced observers who did not know the time interval used for the reconstruction, in turn their analyzes were evaluated resulting in satisfactory agreement. The study protocol, both for the stress phase and for rest in the MPS, was defined in a consensual way by the observers.

All patients underwent the 1-day rest/stress protocol with Tc-99m sestamibi. Ten minutes after intravenous injection of the radiotracer, the images were acquired supine. The second phase of the test was stress, performed with an ergometric or pharmacological test. Immediately after the stress phase the supine and prone images began to be acquired. The CZT camera (Discovery NM 530c, GE Healthcare, Haifa, Israel) was equipped with multiple pinhole collimators and 19 fixed cadmium and zinc telluride detectors and 19 cardiac images were simultaneously displayed. Each detector had 32 x 32 matrix and 5mm thick pixels (2.46 x 2.46 mm). The system structure allows high-definition images of volumes in 3D by all detectors (quality field-of-view), where the patient's heart has to be centered. Once the acquisition was started, there was no movement of the detector or the collimator.

Images Interpretation

All images were interpreted by consensus of two experienced observers. Processing was performed through Evolution for Cardiac® software. The images were reconstructed without attenuation or dispersion correction. The short and long, vertical and horizontal axes, as well as polar maps, were generated and interpreted in a video monitor.

The semiquantitative visual interpretation of perfusion defects was performed using a 17-segment model in accordance with the recommendations of the American Society of Nuclear Cardiology and the American Heart Association.⁸ Each segment of the myocardium was analyzed and scored by consensus of 2 observers, According to the level of radiopharmaceutical uptake on a scale of zero to five points (0 = normal perfusion, 1 = mild defect, 2 = moderate defect, 3 = severe defect, 4 = no uptake). The summed stress score (SSS) was obtained by summing the points of the 17 segments in the stress images. Summated rest score (SRS), obtained by summing the scores of the 17 segments in the resting images and the summed difference score (SDS), by the sum of the differences between the stress and rest scores (SSS - SRS).

Post-stress gated images on the short axis were processed using the gated SPECT software (Cedars-Sinai Medical Center, Los Angeles, California), left ventricular ejection fraction, final systolic and diastolic volume were automatically calculated.

Statistical analysis

Kolmogorov-Smirnov test was used to evaluate the presence of normal distribution of the studied variables. In the univariate analysis the continuous variables were expressed as means and standard deviations. They were compared by the independent Student's t test or ANOVA (those with normal distribution) or the Wilcoxon test (those with non-normal distribution). Categorical variables were expressed as proportions and compared using the chi-square test. Multivariate logistic regression was used to evaluate predictors of cardiac catheterization. The value of $p < 0.05$ was considered statistically significant. Statistical analysis was performed using statistical software SPSS 17.0, Chicago Illinois.

Results

Of the 5536 patients undergoing MPS between March 2008 and December 2012, 643 (11.6%) underwent CAT after myocardial scintigraphy.

The baseline and scintigraphic characteristics of the two groups (without and with post-MPS CAT) are presented in Table 1.

Patients undergoing CAT were more frequently males with angina, hypertension, dyslipidemia, diabetes, previous MI and had been submitted to percutaneous transluminal coronary angioplasty or previous surgical myocardial revascularization.

The analysis of the continuous variables of the two groups reveals that the group that went to the post-MPS catheterization were older, with higher perfusion scores and lower LVEF when compared to group 1. In the multivariate analysis, the presence of typical pain (IC95% 1,2 – 1,7; $p < 0,001$), diabetes, past angioplasty and ischemia extension (95% CI 1.2 - 1.3; $p < 0.001$) were independent variables for CAT indication (Table 2).

Discussion

The studies showed the important role of MPS not only as a diagnostic test for CAD, but as an important role in

risk stratification and therapeutic decision-making.⁹⁻¹¹ According to the latest guideline of the European Society of Cardiology, revascularization is recommended in cases in which the ischemic area of the left ventricle is greater than 10% (Class I, level of evidence B).^{12,13}

Although the percentages of ischemia are more understandable for cardiologists, it should be noted that these are obtained automatically and with recognized limitations to obtain them. The scores obtained with the participation of the specialist express much more accurately the interpretation of the test. That is why we chose to use them.

Bateman et al.⁹ in their study performed 4,162 myocardial scintigraphy in 3,374 patients during 26 consecutive months, 60% of the exams presented some degree of myocardial reversibility. The likelihood of catheterization was increased by eight fold in studies demonstrating reversibility, when it was associated with the high risk criteria (multi-vessel or left anterior descending reversal and abnormal radiotracer uptake in the lungs) the likelihood that these patients were referred

Table 1 – Demographic and scintigraphic characteristics of the groups that performed or did not perform post-MPS CAT

Characteristics	Patients without post CAT n = 4893	Patients with post CAT n = 643	p-value
Age	62.8 ± 12.3	63.8 ± 10.7	< 0.01
Male	2692 (55%)	403 (62.7%)	< 0.05
Asymptomatic	3136 (64.1%)	355 (55.2%)	< 0.05
Typical Pain	172 (3.5%)	68 (10.6%)	< 0.001
Atypical Pain	1585 (32.4%)	220 (34.2%)	= 0.124
Previous AMI	412 (8.4%)	106 (16.5%)	< 0.01
SAH	2977 (60.9%)	442 (69 %)	< 0.05
DM	1029 (21%)	196 (30.5%)	< 0.001
Dyslipidemia	2371 (48.5%)	376 (58.5%)	< 0.01
Previous PTCA	802 (16.4%)	204 (31.7%)	< 0.001
Previous MRV	409 (8.4%)	75 (11.7%)	< 0.01
SSS	2.7 ± 4.7	6.4 ± 6.3	< 0.001
SRS	2.0 ± 3.9	3.2 ± 4.2	< 0.001
SDS	0.6 ± 1.9	3.2 ± 4.2	< 0.001
LVEF	59.2 ± 10.9	54.9 ± 12.1	< 0.001

AMI: acute myocardial infarction; SAH: systemic arterial hypertension; DM: diabetes mellitus; Percutaneous transluminal coronary angioplasty; MRV: myocardial revascularization; SSS: added stress score; SRS: rest score; SDS: sum difference score; LVEF: left ventricular ejection fraction.

Table 2 – Independent predictors of CAT post-MPS

Characteristics	Wald	p-value	Risk Ratio (95% CI)
Age	1,970	0,258	0,9 (0,9 – 1,1)
Typical Pain	22,124	0,000	2,2 (1,2 – 1,7)
Previous AMI	0,479	0,489	0,9 (0,6– 1,1)
SAH	1,787	0,181	0,8 (0,7 – 1,0)
DM	11,907	0,001	1,4 (1,1 – 1,7)
Dyslipidemia	12,742	0,000	1,4 (1,1 – 1,6)
Previous PTCA	25,780	0,000	1,7 (1,4 – 2,2)
Previous MRV	3,649	0,056	1,3 (0,9 – 1,8)
SDS	272,341	0,000	1,3 (1,2 – 1,3)
LVEF	7,915	0,090	0,9 (0,9 – 1,1)

CI: confidence interval; AMI: acute myocardial infarction; SAH: systemic arterial hypertension; DM: diabetes mellitus; Percutaneous transluminal coronary angioplasty; MRV: myocardial revascularization; SDS: sum difference score; LVEF: left ventricular ejection fraction.

for angiography increased 20-fold. The scintigraphic findings were the most important factors at the time of the therapeutic decision, supplanting the clinical characteristics of the patients. In another study¹⁴ the determining factors for post-myocardial scintigraphy catheterization were the extent of ischemia and the significant drop in ejection fraction.

Hachamovitch et al.¹⁵ demonstrated in their study, with 3,369 patients, that the indication for CAT and MRV could be explained by the percentage of myocardial ischemia and the ejection fraction. CAT rates increased with LVEF decline and in the presence or absence of ischemia (mild to moderate). However, in patients with severe ischemia the number of CATs decreased proportionally with the drop of the ejection fraction. In our group, we evaluated 5,536 patients, of whom 643 were taken to CAT. These presented more angina and greater area of ischemia. The left ventricular ejection fraction did not significantly influence the catheterization indication.

Our study provides additional information to demonstrate that the LVEF of the MPS did not contribute significantly in our environment for the decision to indicate the catheterization. Determining the reason for this and the impact on patient survival needs to be established.

Study Limitations

The main limitation is due to the design of the study, since the patients come to perform the examination by medical indication and not by their real distribution in the population, and therefore we cannot extrapolate the results found. In addition, this is a study conducted in a single center, so more studies should be done to confirm their findings.

Conclusions

The presence of angina and the extent of ischemia were the main determinants for indication of catheterization in patients undergoing myocardial perfusion scintigraphy in our setting, while LVEF was not an independent predictor.

Author contributions

Conception and design of the research: Lima RSL. Acquisition of data: Andrade L, Pitta L. Analysis and interpretation of the data: Mesquita FO, Lorenzo AR, Lima RSL. Statistical analysis: Lima RSL. Writing of the manuscript: Mesquita FO. Critical revision of the manuscript for intellectual content: Lorenzo AR, Lima RSL. Supervision / as the major investigator: Lima RSL.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of master submitted by Fernanda de Oliveira Mesquita, from Universidade Federal do Rio de Janeiro.

References

1. Curtis JP, Sokol SJ, Wang Y, Rathore SS, Ko DT, Jadbabaie F, et al. The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure. *J Am Coll Cardiol*. 2003;42:736-42. PMID:2932612.
2. Muhlbaier L.H, Pryor D.B, Rankin J.S, Smith LR, Mark DB, Jones RH, et al. Observational comparison of event-free survival with medical and surgical therapy in patients with coronary artery disease: 20 years of follow-up. *Circulation*. 1992; 86 (Suppl II):II198-204. pp. II198-204. PMID:1424000.
3. Emond M, Mock MB, Davis K.B, Fisher LD, Holmes DR Jr, Chaitman BR, et al. Long-term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. *Circulation*. 1994;90(6):2645-57. PMID: 7994804.
4. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation*. 2003;107(923):2900-7. PMID:12771008.
5. Hachamovitch R, Rozanski A, Hayes SW, Thomson LE, Germano G, Friedman JD, et al. Predicting therapeutic benefit from myocardial revascularization procedures: Are measurements of both resting left ventricular ejection fraction and stress-induced myocardial ischemia necessary? *J Nucl Cardiol*. 2006;13(6):768-78. PMID: 17174808.
6. Yusuf S, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomized trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*. 1994;344(8922):563-70. PMID:7914958.
7. Hachamovitch R, Hayes S, Cohen I, Germano G, Berman DS. Inducible ischemia is superior to EF for identification of short-term survival benefit with revascularization vs. medical therapy (abstract). *Circulation*. 2002;106 (Suppl:II):523.
8. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al; American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation*. 2002;105(4):539-42. PMID:118151.
9. Bateman TM, O'Keefe JH Jr., Dong VM, Barnhart C, Ligon RW. Coronary angiographic rates after stress single-photon emission computed tomographic scintigraphy. *J Nucl Cardiol*. 1995;2(3):217-23. PMID:9420791.
10. 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). *J Am Coll Cardiol*. 2003;42(7):1318-33. PMID:14522503.
11. Ward RP, Al-Mallah MH, Grossman GB, Hansen CL, Hendel RC, Kerwin TC, et al. American Society of Nuclear Cardiology review of the ACCF/ASNC appropriateness criteria for single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI). *J Nucl Cardiol*, 14 (2007), pp. e26-e38.
12. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J*. 2013;34(38):2949-3003. Doi: 10.1093/eurheartj/ehq296.
13. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. *Eur Heart J*. 2010;31(20):2501-55. Doi:10.1093/eurheartj/ehq277.
14. Romero-Farina G, Candell-Riera J, Aguadé-Bruix S, Castell-Conesa J, García-Dorado D. Impact of myocardial perfusion gated-SPECT on the decision to perform coronary angiography in patients with left ventricular dysfunction of ischemic origin. *Rev Esp Med Nucl*. 2011;30(3):141-6. doi:10.1016/j.remnu.2010.12.006.
15. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Kang X, Germano G, et al. Is there a referral bias against catheterization of patients with reduced left ventricular ejection fraction? Influence of ejection fraction and inducible ischemia on post-single-photon emission computed tomography management of patients without a history of coronary artery disease. *J Am Coll Cardiol*. 2003;42(7):1286-94. PMID: 12796141.

