MYOCARDIAL PERFUSION SCINTIGRAPHY USING A STRESS-ONLY PROTOCOL IS SAFE IN PATIENTS WITH LOW PRE-TEST PROBABILITY OF CORONARY ARTERY DISEASE AND REDUCES RADIATION EXPOSURE

CINTILOGRAFIA DE PERFUSÃO MIOCÁRDICA UTILIZANDO APENAS ESTRESSE É SEGURO EM PACIENTES DE BAIXA PROBABILIDADE PRÉ-TESTE DE DOENÇA ARTERIAL CORONÁRIA E REDUZ EXPOSIÇÃO À RADIAÇÃO

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ABSTRACT

Introduction: A normal Myocardial Perfusion Imaging (MPI) provides a prognosis and current guidelines recommending to perform the exam under the standard resting / stress (R / S) protocol to confirm that a MPI is normal. **Purpose:** To evaluate the prognosis of MPI using the protocol of only stress in selected population of low risk. **Methods:** It was prospectively studied 46 consecutive patients through a MPI. The patients whom meeting the following admission criteria performed the stress phase first: 1. Low pretest probability (<50%) of significant CAD based on Diamond and Forrester criteria; 2. Capacity to perform stress in treadmill; 3. Do not have a previous diagnosis of Coronary Artery Disease (CAD); 4. Have interpretable rest ECG. The MPI indication was an abnormal prior exercise test due to ST changes in 63% and atypical angina in 22%. The mean pre-test probability of CAD was 11.25% (4-46%). The mean age was 40 years (30 - 49), 60% were female. The patients underwent the stress phase, under the Bruce protocol; the mean heart rate (HR) achieved was 92.9% of the predicted maximum HR for age. All Patients achieved a workload ≥ 6 METS (average 9.4 METs). If the stress image was normal unambiguously, the examination was finished. Any suspicion of artifacts and / or presence of perfusion defects on stress, the patients were submetted to the resting phase and were excluded from the study. **Results:** Stress ECG revealed changes in ST segment in 30% of the patients, with an ascending pattern in 35%, horizontal in 7% and descending in 57%. No patients reported angina in the stress phase. The mean duration of the examination was 115 min (standard protocol R / S 240 min). The dose of the radiopharmaceutical (Tc99m-MIBI) injected was significantly lower than that predicted for the standard protocol (9.2 mCi, vs 33.9 mCi-p <0.00001) with a reduction in radiation exposure of 77% (2.5 mSv vs 11.4 mSv). Follow-up was obtained on all patients with an average of 19.9 months (ranging from 6 to 34 months). No hard events (death, fatal or non-fatal MI) or myocardial revascularization occurred during the follow-up period. **Conclusion:** The normal MPI using the stress-only protocol in low-probability pre-test of CAD, gives a good prognosis, and there were no hard events and / or revascularization in a follow-up of 19.9 months, with a significant reducing exposure to radiation, and with a shorter protocol.

Keywords: *Coronary disease. Radionuclide imaging. Abnormalities. Radiation-Induced.*

RESUMO

Introdução: Para estabelecimento de prognósticos a partir da cintilografia de perfusão miocárdica (CPM), as diretrizes atuais recomendam sua realização sob o protocolo padrão de repouso/estresse. **Objetivo:** Avaliar o prognóstico da CPM utilizando apenas o protocolo de estresse em população de baixo risco. **Métodos:** Estudo prospectivo com 46 pacientes consecutivos após CPM. Realizaram primeiro a fase de estresse aqueles que preencheram os seguintes critérios na admissão: 1. baixa probabilidade pré-teste (<50%) de doença arterial coronária (DAC) significativa baseada nos critérios de Diamond e Forrester; 2. capacidade de realizar estresse em esteira ergométrica; 3. não possuir diagnóstico prévio de DAC; e 4. possuir eletrocardiograma

de repouso interpretável. A indicação da CPM foi teste ergométrico prévio anormal por alterações de ST em 63% e angina atípica em 22%. A probabilidade média pré-teste de DAC foi de 11,3% (4% a 46%). A média das idades foi de 40 anos (30 a 49), 60% era do sexo feminino. Os incluídos foram submetidos à fase de estresse sob o protocolo de Bruce; a frequência cardíaca média alcançada foi 92,9% da máxima prevista para a idade. Todos os envolvidos alcançaram carga de trabalho ≥ 6 METS (média de 9,4 MET). Se a imagem de estresse fosse inequivocamente normal, o exame era finalizado. Diante de qualquer suspeita de artefatos e/ou presença de defeitos perfusionais no estresse, os participantes realizavam o exame em repouso e eram excluídos do estudo. **Resultados:** O eletrocardiograma de estresse revelou alterações do segmento ST em 30% dos participantes, com padrão ascendente em 35%, horizontal em 7% e descendente em 57%. Nenhum referiu angina na fase de estresse. A duração média do exame foi de 115 min (protocolo padrão repouso/estresse 240 min). A dose injetada do radiofármaco (Tc99m-MIBI) foi significantemente menor do que a prevista para o protocolo padrão (9,2 mCi, *vs* 33,9 mCi – p < 0,00001), com redução de 77% (2,5 mSv *vs* 11,4mSv) da exposição à radiação. O seguimento foi obtido em todos os participantes com média de 19,9 meses (variando de 6 a 34). Nenhum evento mórbido (óbito, infarto do miocárdio fatal ou não fatal) ou revascularização do miocárdio ocorreu durante o período de seguimento. **Conclusão:** A CPM normal, utilizando o protocolo de estresse, em indivíduos de baixa probabilidade pré-teste de DAC confere bom prognóstico, não tendo ocorrido eventos fatais e/ou revascularização em um seguimento de 19,9 meses, com importante redução da exposição à radiação e com protocolo de realização mais curto.

Palavras-chave: Doença das coronárias; Cintilografia; Anormalidades induzidas por radiação

INTRODUCTION

Myocardial perfusion scintigraphy (MPS) using single-photon emission computed tomography (SPECT) detects ischemia in patients with coronary artery disease (CAD) with high accuracy and incremental prognostic value[1]. The increased use of ionizing radiation for diagnostic purposes prompted professionals to search for methods to reduce radiation exposure[2]. Three critical questions need to be addressed regarding radiation exposure and MPS performance: "Is the MPS test appropriate and necessary in this patient?"; "How can the MPS protocol be optimized to provide the lowest radiation dose and maintain diagnostic accuracy?"; and "How new technologies could be utilized to minimize radiation dose and preserve diagnostic accuracy?"[3]

The *American Society of Nuclear Cardiology* (ASNC) established goals to reduce radiation exposure and provide continuing medical education as components of this strategy. The *American College of Cardiology Foundation* (ACCF) and ASNC jointly published guidelines for MPS indications, classifying them as appropriate, inappropriate, and uncertain. Correct examination indications favor strategies to reduce radiation exposure[4], such as performing the stress-only protocol[5].

According to the ASNC guidelines, MPS follows a standard protocol with two *sets* of images, rest-stress or vice versa, with a radiopharmaceutical injected in each phase to acquire myocardial perfusion images. The examination is performed using one- or two-day protocols. In a one-day protocol, the first phase has a lower radiopharmaceutical dose based on patient weight, and the second has a threefold higher dose. Most nuclear cardiology services employ a rest-stress one-day protocol with a two-hour interval, resulting in a total examination time of three to four hours. Patients receive a rest injection followed by rest perfusion imaging after one hour. Two hours after initial injection, stress (physical or pharmacological) is followed by a new perfusion image series. After, stress perfusion analysis is compared with resting images. The two *sets* of images are used to differentiate ischemia (a reversible abnormality) from scar (a fixed abnormality), recognize artifacts, and evaluate non-perfusion variables, such as transient left ventricular dilatation[6].

Laboratories have a significant number of examinations and resting images performed for comparison with stress images. Resting provides minimal diagnostic and prognostic value with normal stress, commonly observed in patients with a low pre-test probability of CAD. According to Bayes' theorem, the probability of a disease occurring depends on its prevalence in the population being studied[7]. Therefore, patients with a low pre-test probability of CAD, based on age, sex, and symptom characteristics, have a high chance of normal examinations. A stress-only imaging strategy proves most useful in low- or low-to-intermediate-risk populations, which

are expected to have normal stress studies. ASNC emphasizes that this strategy requires highly experienced physicians capable of determining who would benefit from rest imaging[8].

Services have used stress-only protocols non-systematically for years, with careful initial selection. Patients with low pre-test probability of CAD may begin with stress examination, and low ventricular function and severe obesity should be avoided to ensure normal and artifact-free examinations. Literature validation demonstrates that normal stress determines the end of the examination and elimination of rest phase. Examination time is reduced to two hours and radiation dosimetry is decreased by 60 to 80%[9-11].

Brazilian services barely use this protocol. Implementation requires a pre-test evaluation that considers all the aforementioned variables. Most patients are young women and men with atypical angina or asymptomatic with inconclusive exercise testing. Normal examinations guarantee a good prognosis with a frequency of morbid events (death, fatal or non-fatal MI) below 1% annually[12].

This study aimed to evaluate MPS prognosis using a stress-only protocol in a selected low-risk population.

METHODS

This descriptive and prospective study was conducted at the Nuclear Cardiology Laboratory of the Hospital Santa Joana Recife, in Recife, Pernambuco, Brazil. Patients were prospectively evaluated between December 2015 and June 2017 using the stress-only protocol in a selected population with low pre-test probability of CAD.

The inclusion criteria were low pre-test probability of CAD based on Diamond and Forrester criteria, considering age, sex, and precordial pain characteristics; ability to perform treadmill stress testing; absence of previous CAD diagnosis (myocardial infarction or myocardial revascularization); and an interpretable resting electrocardiogram regarding the ST segment for defining stress-induced ischemia. Patients with an indication for pharmacological stress, older age, and comorbidities had a higher probability of significant CAD and were excluded.

The radiopharmaceutical used was the Tc99m-MIBI, administered with weight-adjusted doses according to ASNC guidelines for the rest phase of the rest-stress protocol. Images were acquired using a Siemens ECAN SPECT gamma camera with two detectors, with 60 stops of 18 seconds each, and synchronized heartbeats to obtain GSPECT images of global and segmental contractility. After acquisition, images were pre-processed for axis definition and reconstruction in conventional short-axis and vertical and horizontal long-axis cuts. Additionally, Wackers-Liu (Yale University) software was used for quantitative analysis to obtain circumferential profiles of stress images and to compare them with asymptomatic patients from a database with a low pre-test probability of CAD. Rotational images were examined to identify artifacts (e.g., diaphragmatic and breast attenuation) and normal images. Patients with suspected artifacts or perfusion defects were referred to the rest phase and excluded from the study. Patients were followed using telephone contact or a questionnaire sent to their mailing address.

Qualitative variables were expressed as absolute and relative frequencies.

RESULTS

A total of 46 patients were evaluated, with 60% female, mean age of 40 years (ranging from 30 to 49 years), 34% were hypertensive, 2% diabetic, 50% dyslipidemic, and 2% smokers. MPS indication was patients with previous abnormal exercise test due to ST segment changes (63%) and atypical angina (22%). Mean pre-test probability of CAD was 11.25% (ranging from 4% to 46%). Patients underwent the stress phase under the Bruce protocol; the mean heart rate was 92.9% of the maximum predicted for their age. All patients performed a workload greater than or equal to six metabolic equivalent of task (MET), with a mean of 9.4 MET. The stress electrocardiogram showed ST segment changes compatible with myocardial ischemic response in 30% of patients. The upsloping ST depression, measured at 80 ms from the J point, was observed in 35% of patients, horizontal ST depression at the J point in 7%, and downsloping ST depression at the J point in 57%. Patients did not report angina during the stress phase. The mean examination duration was 115 minutes, compared to the expected 240 minutes for the rest-stress protocol. The mean radiopharmaceutical dose for stress was 9.2 mCi, compared to 39.9 mCi expected for the rest-stress protocol, resulting in a 77% reduction in radiation exposure (2.5 mSv vs 11.4 mSv). Follow-up was obtained from all patients with a mean time of 19.9 months (ranging from 6

to 34 months). During follow-up, morbid events (death, fatal or non-fatal MI) or revascularization did not occur.

DISCUSSION

This study evaluated the safety of the stress-only protocol in 46 patients with normal MPI using assessment for morbid events and myocardial revascularization during 19.9 months of follow-up. The event rate was zero in this sample; previous studies using this technique have shown a low frequency (< 1% per year), similar to stress-rest protocols[3], regardless of patient age, sex, clinical risk factors, CAD history, and stress modality used with MPI.

The sample assessed represented a fraction of the total patients undergoing MPI in the service, indicating careful patient selection. Patients receiving stress-only imaging had a 77% reduction in radiopharmaceutical dose compared with the standard protocol. Additional rest imaging was unnecessary in patients with normal stress MPI. Selecting appropriate candidates for stress-only imaging reduces examination costs by eliminating unnecessary imaging time and radiopharmaceutical doses. Thereby, improving laboratory performance and reducing radiation exposure. Technical advances, including global and segmental contractile function evaluation, attenuation correction, and perfusion image quantification, increase confidence in interpreting studies as normal using only stress images[3, 10, 12].

Examinations were considered normal with homogeneous perfusion in the LV wall, normal cavity size, ejection fraction ≥ 50% with normal regional contractility, and quantitative analysis with circumferential profiles within normal limits of two standard deviations compared with CAD-free patients from a normal database[12].

This stress-only sample demonstrated the absence of morbid events and the need for revascularization. Larger samples may validate this interpretation algorithm, as few studies address the feasibility and clinical outcomes of stress-only imaging. Evaluation of 652 patients with low-to-intermediate CAD probability undergoing stress-only MPI with a 22.3-month mean follow-up showed that 93% of patients underwent treadmill stress, and the remaining 7% received pharmacological stress with dipyridamole. Thirty-seven percent of the images required rest and were considered normal after attenuation correction. Overall, the cardiac event rate was 0.6%, without cardiac deaths and one non-fatal myocardial infarction. Similarly, 116 patients followed after normal stress-only MPI showed a 0.9% annual mortality rate. Normal MPI generally defines groups with an annual risk of less than 1% for cardiac death and 0.5% for non-fatal myocardial infarction.

CONCLUSION

Patients with normal MPI-SPECT based on stress-only imaging had low mortality rates similar to those with normal examinations using the standard stress-rest protocol. The stress-only protocol in populations with low pre-test probability of CAD resulted in normal studies and proved viable for implementation. Moreover, the protocol reduced radiation exposure and examination time, requiring strict initial screening and rigorous quality control in image interpretation.

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