Anais da Faculdade de Medicina de Olinda
Annals of Olinda Medical School

afmo.emnuvens.com.br ISSN: 2674-8487 Original Article

Relationship between myocardial perfusion scintigraphy and workload for identifying patients at high risk for myocardial ischemia

Relação entre cintilografia de perfusão miocárdica e carga de trabalho na identificação de pacientes com alto risco para isquemia miocárdica

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Abstract

The stress and rest myocardial perfusion scintigraphy (MPS) measures the workload achieved using metabolic equivalents (METs) and verifies the presence of ischemic changes in electrocardiographic exams. Thus, this study aimed to evaluate these variables and identify which ones would be useful in identifying patients with severe myocardial ischemia. This cross-sectional retrospective study analyzed 2,388 medical records of patients who had been referred for MPS; they were recruited using non-probabilistic convenience sampling. The patients were divided into two groups according to the METs achieved, and the prevalence of severe ischemia was measured using the Wackers-Liu software. A total of 506 patients achieved 10 METs without electrocardiographic changes in the ST segment during stress; they were classified as group B. Of these, 0.4% presented severe myocardial ischemia. Patients from group A did not reach 10 METs (n = 515 patients) and presented ischemic electrocardiographic changes in the ST segment; 3.6% of them presented severe myocardial ischemia, which was significantly different ($p < 0.0002$). These findings highlight that patients presenting ischemic electrocardiographic changes in the stress phase with a workload <10 METs were 9-fold more likely to have severe myocardial ischemia than those who achieved ≥10 METs without ischemic electrocardiographic

How to cite: Marins **GSSG**, Pacífico **FA**, Lages **DB**, Farias **MA**, Couto **MC**, Santos **LS** et al. Relationship between myocardial perfusion scintigraphy and workload for identifying patients at high risk for myocardial ischemia. An Fac Med Olinda 2024; 1(11):26 doi: https://doi.org/10.56102/afmo.2024.307

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E-mail: giovannasherly@outlook.com
Funding: none.
Ethics approval: CAAE nº 65605922.1.0000.8033
Received: 06/20/2023
Approved: 11/14/2023

changes. Therefore, a workload that reaches ≥10 METs without electrocardiographic changes compatible with ischemia may be a good predictor for the absence of severe myocardial ischemia in MPS.

Keywords: Coronary artery disease, Ischemia, Metabolic equivalent, Radionuclide imaging.

Resumo

Durante a realização da cintilografia de perfusão miocárdica (CPM) de estresse e repouso, é medida a carga de trabalho alcançada, definida pelos equivalentes metabólicos (METs), e verificada a presença de alterações isquêmicas nos exames eletrocardiográficos. O objetivo deste estudo foi avaliar essas variáveis e identificar quais seriam úteis na identificação dos pacientes com isquemia miocárdica severa. Para tanto, foi realizado um estudo do tipo transversal, observacional e retrospectivo, com amostragem do tipo não probabilístico por conveniência, feito por meio da análise de 2.388 prontuários cujos pacientes haviam sido encaminhados para realização de CPM. Os pacientes foram divididos em dois grupos de acordo com os METs alcançados, e foram comparadas as prevalências de isquemia severa aferida pelo software Wackers-Liu. Dos 2.388 prontuários, 506 atingiram 10 METs sem alterações eletrocardiográficas do segmento ST no estresse, os quais foram enquadrados no grupo B; desses, 0,4% (2/506) apresentou isquemia severa. Os 515 pacientes do grupo A não alcançaram 10 METs e apresentaram, simultaneamente, alterações eletrocardiográficas isquêmicas do segmento ST; 3,6% (19/515) deles evidenciaram isquemia severa, diferença estatisticamente significante (p < 0,0002). Com base nesses achados, conclui-se que, na presença de alterações eletrocardiográficas isquêmicas na fase de estresse com carga de trabalho < 10 METs, a probabilidade de isquemia miocárdica severa é nove vezes maior em comparação aos que alcançaram ≥ 10 METs sem alterações eletrocardiográficas isquêmicas. Desse modo, uma carga de trabalho que alcança ≥ 10 METs sem alterações eletrocardiográficas compatíveis com isquemia pode ser um bom preditor para ausência de isquemia severa na CPM.

Palavras-chave: Cintilografia; Equivalente metabólico; Isquemia; Doença da artéria coronariana.

INTRODUCTION

Myocardial perfusion scintigraphy (MPS) is a noninvasive test that can demonstrate abnormalities in myocardial perfusion. Thus, this test is important to assess the cardiovascular function of patients with suspected coronary artery disease (CAD).[1]

During cardiopulmonary exercise testing, metabolic equivalents (METs) measure the capacity of the heart to cope with physical effort.[2] This capacity, also known as exercise capacity, is one of the most important measures obtained in an exercise test. One MET is the amount of oxygen consumption needed at rest and is equivalent to 3.5 ml of oxygen per kilogram of body weight per minute for a young adult.[3] The measurement of METs is a practical and easily understandable procedure that is included in the final report of an exercise test.[4] Moreover, this variable

is considered a powerful predictor of cardiovascular events in the general population, with better results observed in patients who achieve high workloads

An accurate risk stratification is crucial in patients with known or suspected CAD for proper management and to improve prognosis.[5] Exercise electrocardiogram (ECG) and stress echocardiography are widely used tools for risk stratification in stable CAD. Additionally, exercise capacity, which can be assessed during stress echocardiography, is an established predictor of mortality.[5]

Therefore, the present study aimed to analyze the relationship between workload achieved in METs during MPS and the risk of developing severe myocardial ischemia.

METHODS

This cross-sectional and retrospective study with non-probabilistic convenience sampling was conducted from March to April 2023, using the database of the nuclear medicine laboratory of a hospital in the metropolitan region of Recife, Pernambuco. A total of 2.388 medical records were analyzed, considering random patients with or without known CAD treated from 2006 to 2007 who underwent MPS with technetium sestamibi 99mTc.

Inclusion criteria comprised patients aged between 20 and 85 years who achieved more than 85% of their maximum predicted heart rate for their age. Those unable to perform a physical stress test and underwent pharmacological stress testing, who did not reach 85% of their maximum predicted heart rate for their age, or who were below 20 or over 85 years were excluded.

The patients were divided into two groups (A or B) according to the intensity of workload (in METs) achieved during the ergometric test and by the electrocardiographic changes found in the ST segment. Group A included patients who achieved a workload < 10 METs and presented electrocardiographic changes, while group B included those who achieved a workload ≥ 10 METs and did not present electrocardiographic changes. The Bruce protocol was used in the ergometric test to evaluate the workload.[2]

Patients who achieved a workload < 10 METs and did not present electrocardiographic changes or those who achieved a workload ≥ 10 METs and presented electrocardiographic changes were not included in the analysis.

The Wackers-Liu software for quantitative analysis of myocardial perfusion assessed the prevalence of ischemia, which was considered severe when it presented an ischemic area larger than 10% of the affected left ventricle.

Data were tabulated and processed by the Predictive Analytics Software for Microcomputers (PASW® Statistics; version 17.0). Initially, a descriptive analysis was performed, and the results were presented as absolute frequency, expected frequencies, total percentage, and adjusted residual. The Chi-Square test of independence was applied to verify the association between variables. The established precision level was 5%, the confidence level was 95%, and the

maximum variability was 0.5.

RESULTS

The mean age of the patients was 58 years (20 to 85 years) for both groups. Considering sex, the mean age was 59 (22 to 84 years) for women and 57 years (23 to 84 years) for men. The distribution by sex was 43.29% women (N = 1,034) and 56.71% men (N = 1,354).

Considering patients who reached 10 METs, 285 were excluded due to ST segment electrocardiographic changes, and the remaining 506 were included in group B for analysis; 0.4% of them presented severe myocardial ischemia. Among those who did not reach 10 METs, 1,082 were excluded because they did not present ST segment electrocardiographic changes, resulting in 515 patients included in group A; 3.6% of them presented severe myocardial ischemia, which was a value 9-fold higher than the group B (Table 1).

Table 1. Distribution of the risk of developing severe myocardial ischemia according to the workload achieved (METs) in the cardiopulmonary exercise testing and electrocardiographic changes

Workload achieved and ECG changes	**Severe myocardial ischemia**		Total
	Absence	Presence	
METs < 10 with ECG changes			
Absolute frequency	496	19	515
Expected frequency	504.4	10.6	515
Total percentage	48,6%	1,9%	50.4%
Adjusted residue	-3.7	3.7	
METs ≥ 10 without ECG changes			
Absolute frequency	504	2	506
Expected frequency	495.6	10.4	506
Total percentage	49.4%	0.2%	49.6%
Adjusted residue	3.7	-3.7	
Total			
Absolute frequency	1000	21	1021
Expected frequency	1000	21	1021
Adjusted residue	97.9%	2.1%	100.0%

Metabolic equivalents (METs), electrocardiogram (ECG) Chi-Square test value = 13.748, $p < 0.001$.

A table was constructed with data on the presence of severe myocardial ischemia according to workload achieved to assess the association between the workload and the risk of developing severe myocardial ischemia. Then, the Chi-square test was used to evaluate whether the distributions were significantly different.

The assumptions of the test were met, including that the expected frequency in each cell of the table should be greater than five. The calculated value for the Chi-square test of independence was 13.748 ($p < 0.001$), suggesting that the risk of developing severe myocardial ischemia was significantly higher among patients from group A than those from group B. The Chi-square test of independence revealed an association between the workload achieved and the risk of developing severe myocardial ischemia [$X2(2) = 13.748$; $p < 0.001$)].

DISCUSSION

The Brazilian guideline for cardiovascular rehabilitation suggests the stratification of patients clinical risk, considering clinical decompensation, intervention or cardiovascular event, exercise capacity (METs), signs and symptoms of myocardial ischemia defined as an ischemic threshold, symptomatology, and other clinical characteristics.[6] Patients who achieved functional capacity < 5 METs were classified as high clinical risk (functional classes III and IV); those who achieved 5 to 7 METs were of intermediate clinical risk (functional classes I and II); and low-risk patients achieved > 7 METs without any symptomatology.[6]

Patients who achieved 10 METs have demonstrated an excellent prognosis with low rates of cardiovascular events and low prevalence of severe left ventricular ischemia, regardless of peak exercise heart rate.[5] Although the exercise load and heart rate are directly correlated, the maximum achievable heart rate decreases with age and varies among individuals of the same age.[7] On the other hand, patients who did not achieve 10 METs may be more likely to be classified as high risk, as they would initially fall into the high clinical risk category and often require drug adjustments, reevaluations, and possible interventions (revascularizations or other procedures).[6]

Exercise stress testing verifies the ST segment depression and also provides valuable diagnostic and prognostic information[4], including exercise capacity, chronotropic response, heart rate recovery, and blood pressure response.[4] Still, one of the most important parameters is the exercise capacity assessed in METs.[4]

Studies showed that besides the presence of electrocardiographic changes on the ECG, the time these changes take to return to baseline levels may influence the prognosis.[8] Patients who showed a quick return of the ST segment had fewer high-risk findings than those with a longer return time.[8]

In the face of all stratification, diagnosis, and prognosis alternatives, protocols have been created to improve the selection of patients for MPS, protecting them from unnecessary radiation exposure and reducing costs.[5] Therefore, a stepwise diagnostic method may be cost-effective. No further testing will be needed when the symptom-limited exercise ECG (step 1) is normal[7], as patients with intermediate to high clinical risk for arterial disease achieving ≥ 10 METs without ischemic changes in the ECG are less likely to develop severe ischemia.[9] However, when the

exercise ECG is positive, an MPS (step 2) is required to address the issue of a false-positive exercise ECG.[7] With this modification, a substantial number of low-probability patients will not require MPS.[7]

CONCLUSION

In the presence of ischemic electrocardiographic changes during stress with a workload <10 METs, the probability of severe myocardial ischemia was 9-fold higher than those who achieved ≥ 10 METs without ischemic electrocardiographic changes. Therefore, a workload ≥10 METs without electrocardiographic changes (ST segment) may be a good predictor for the absence of severe myocardial. The use of METs in performing cardiac perfusion imaging in randomly selected patients, regardless of the presence of CAD, sex, and age, was a good predictor of severe myocardial ischemia.

The study may allow for a better understanding of how the exercise capacity of the heart is related to myocardial perfusion. Also, the results evidenced the importance of a well-performed exercise test in cardiovascular risk stratification. This test spares patients from undergoing further testing, reducing costs and exposure to radiation in other exams that are routinely requested in healthcare services.

Last, prognostic information is important for more effective patient management. Moreover, the ergometric test is a cheap, feasible, reproducible, and accurate test for risk stratification and for assessing the relationship between workload and ischemic changes in the electrocardiogram.

CONFLICT OF INTERESTS

Nothing to declare

AUTHOR CONTRIBUTIONS

GSSGM: Writing - original writing, Writing - review and editing; **FAP**: Data curation, Formal Analysis, Methodology, Supervision, Writing - original writing, Writing - revision and editing; **DBL**: Writing - original writing, Writing - review and editing; **MAF**: Writing - original writing, Writing - review and editing; **MCC**: Writing - original writing, Writing - revision and editing; **LSS**: Writing - original writing, Writing - revision and editing; **ELP**: Conceptualization, Data curation, Investigation, Methodology, Project management, Resources, Supervision, Original writing, Writing – revision and editing.

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