Original article

Appropriate Use of Myocardial Perfusion Scintigraphy Criteria for Assessing Asymptomatic Patients with High Cardiovascular Risk or Known Coronary Disease

Comportamento dos Critérios de Uso Apropriado da Cintilografia de Perfusão Miocárdica na Avaliação de Assintomáticos de Alto Risco Cardiovascular ou com Doença Coronária Conhecida

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Abstract

Background: The use of myocardial perfusion scintigraphy in asymptomatic patients remains restricted to very specific clinical situations, many of which are addressed in the appropriate use criteria (AUC) for myocardial perfusion scintigraphy.

Objective: To critically analyze the application of these criteria in indicating the tests performed in asymptomatic patients of the Dante Pazzanese Institute of Cardiology, a population that is notably at high cardiovascular risk.

Methods: The study selected asymptomatic patients undergoing myocardial perfusion scintigraphy to investigate ischemia. Indications for tests were classified as appropriate, inappropriate, or uncertain. A fixed low uptake, transient low uptake, or transient ischemic dilation were considered changed results. The statistical analysis assessed the correlation between the degree of recommendation of indications and the presence of changed test results.

Results: From an initial selection of 2,999 medical records, 490 were considered asymptomatic and included according to the previously established inclusion criteria. Only 9.8% of the indications were inappropriate, while 61.4% were appropriate and 28.8% were uncertain. Fixed low uptake of the radiopharmaceutical occurred in 43.5% of cases versus transient low uptake in 16.1%. An appropriate or uncertain test request was a predictor of a changed test result in this population.

Conclusion: The use of AUC for myocardial perfusion scintigraphy proved effective at predicting abnormal test results in an asymptomatic population at high cardiovascular risk, especially patients with uncertain indications, which may mean that some of the indications considered uncertain may be appropriate for a population at high cardiovascular risk.

Keywords: Nuclear Medicine; Cardiovascular risk; Diagnosis.

Resumo

Fundamentos: *O papel da cintilografia de perfusão miocárdica em pacientes assintomáticos permanece restrito a situações clínicas muito específicas, muitas delas abordadas nos Critérios de Uso Apropriado (AUC) de Cintilografia de Perfusão Miocárdica.*

Objetivo: *Realizar uma análise crítica da aplicação desses critérios nas indicações de exames realizados em pacientes assintomáticos do Instituto Dante Pazzanese de Cardiologia, cuja população é notadamente de alto risco cardiovascular.*

Métodos: *Foram selecionados pacientes assintomáticos que realizaram cintilografia de perfusão miocárdica para pesquisa de isquemia. As indicações dos exames foram classificadas em apropriadas, inapropriadas ou incertas. Hipocaptação fixa, hipocaptação transitória ou dilatação isquêmica transitória foram consideradas exames alterados. Na análise estatística, buscou-se avaliar a correlação entre o grau de recomendação das indicações e a presença de exames alterados.*

Resultados: *A partir de uma seleção inicial de 2.999 prontuários, 490 foram considerados assintomáticos e incluídos conforme critérios de inclusão estabelecidos previamente. Apenas 9,8% das indicações foram inapropriadas, enquanto que 61,4% foram apropriadas, e 28,8% foram incertas. A hipocaptação fixa do radiofármaco ocorreu em 43,5% dos casos e a hipocaptação transitória, em 16,1%. Solicitar o exame de maneira apropriada ou incerta foi fator preditor de exame com resultado alterado nesta população.*

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Conclusão: *O uso dos critérios de uso apropriado da cintilografia de perfusão miocárdica mostrou-se eficaz em predizer exames alterados em uma população assintomática de alto risco cardiovascular, especialmente no grupo de pacientes com indicação incerta, o que pode significar que algumas das indicações consideradas incertas talvez sejam apropriadas para uma população de alto risco cardiovascular.*

Palavras-chave: *Medicina nuclear; Risco Cardiovascular; Diagnóstico.*

Introduction

Cardiovascular mortality remains the leading cause of death in Brazil, with atherosclerosis and ischemic heart disease playing prominent roles.[1] The high prevalence and mortality rates related to cardiovascular disease in Brazil can be largely attributed to poorly controlled risk factors. Controlling the main cardiovascular risk factors has great impact on reducing cardiovascular death.[2]

Many highly prevalent diseases with high mortality and morbidity rates are often diagnosed only after the first cardiovascular event, which can cause serious sequelae or even death. Considering this scenario, it is essential to establish cardiovascular assessment mechanisms that enable the identification and proper management of patients with cardiovascular disease.

The clinical presentation of patients with ischemic heart disease is quite variable, ranging from acute syndromes to silent ischemia.[3] Symptoms include a late event in the ischemic cascade, and the patient already presents cardiac repercussions and increased risk of events long before their onset.[4] Nuclear medicine is a method with greater sensitivity and power for the earlier detection of myocardial ischemia although with lower specificity.[4]

The active search for disease in the asymptomatic patient begins with a detailed history and physical examination.[3] When a patient is asymptomatic, the assessment of myocardial ischemia proceeds in the form of screening, with the definition of cardiovascular risk occurring through the collection of clinical data and completion of basic complementary tests.[3]

In this context, myocardial perfusion scintigraphy (MPC) is for a method of investigating myocardial ischemia in some subgroups of asymptomatic patients. Some current applications of the test come from the appropriate use criteria (AUC) for myocardial perfusion scintigraphy (MPS) published in 2005 by the American College of Cardiology Foundation and the American Society of Nuclear Cardiology[5] and updated in 2009.[6] This document was an attempt to improve clinical outcomes with the efficient and fair allocation of healthcare resources based on the best available scientific evidence with the aim of improving the cost-effectiveness of medical care without restricting clinical judgment.[5] These criteria were validated in 2013[7] and have been incorporated since then into the latest ischemic heart disease, cardiovascular risk assessment, and nuclear medicine guidelines.

This study aimed to critically analyze the use of these criteria for asymptomatic patients at high cardiovascular risk undergoing MPS.

Methods

This cross-sectional, retrospective, and observational study involved the analysis of patients' medical records. The study was developed at the Nuclear Medicine Department of Dante Pazzanese Institute of Cardiology. The project was registered at Plataforma Brasil and approved by the local ethics committee.

All patients who underwent MPS between December 6, 2017 and July 16, 2018 were selected for medical record analysis.

A total of 2,999 medical records of patients undergoing MPS to investigate ischemia were selected; 2,245 of them were available for analysis at the time of referral. The study included all patients undergoing MPS to investigate ischemia who had no symptoms of myocardial ischemia at the time of referral and the test, i.e., patients not reporting typical or atypical precordial pain, discomfort, or ischemic equivalent.[8]

All patients undergoing pharmacological stress testing were included. Patients with ineffective exercise test results were excluded unless the test result was considered positive for ischemia or presented transient low uptake in the imaging stage. A total of 490 patients met the inclusion criteria and were included in the final statistical analysis.

MPS was performed following the one- or two-day-protocol according to the service routine with or without the suspension of anti-ischemic medications according to the clinician and the standardized recommendations of the nuclear medicine department. The classical known and standardized criteria for myocardial ischemic response to exertion were adopted.[9]

The tests were performed in Millennium VG scintillation chambers (GE Medical Systems, Milwaukee, WI, USA), with two scintillation detectors angled at 90° with high-resolution low-energy parallel-hole collimators. Processing was performed using Xeleris™ workstations and Cedars-Sinai software, with sections in the major and minor vertical plane axes and in the major horizontal plane axis. Rest and stress stage sections were paired for the visual and qualitative analysis of radiopharmaceutical concentrations in the 17 segments of the myocardium and synchronized with the electrocardiography for the analysis of cardiac wall contraction, systolic and diastolic volume indices, and left ventricular ejection fraction.

According to well-established guidelines,[10] the MPS was considered normal when the concentration of the marker was homogeneous in both phases (stress and rest). If the low uptake was reversible after rest, the test result was considered suggestive of ischemia. If the low uptake was fixed in both phases, the test result was considered suggestive of fibrosis. Finally, in case of associated fixed and reversible low uptakes, the test result was considered suggestive of fibrosis and ischemia.

Quantitative variables are described as mean, standard deviation, and minimum and maximum values. Categorical variables are described as frequencies and percentages. Fisher's exact test or the chi-square test was used to assess the association between two categorical variables. Logistic regression models were adjusted for the univariate and multivariate analyses of factors associated with the outcomes of interest (fixed low uptake, transient low uptake, and changed test for at least one of fixed low uptake, transient low uptake, or transient ischemic dilation). The variables for the multivariate models were selected using two approaches: the univariate analysis results and the clinical importance of the variables, followed by stepwise backward regression with a probability of 0.10 for the output of the variables. The Wald test was used to assess the significance of each variable in the models. The estimated measure of association was the odds ratio with 95% confidence interval. P values < 0.05 indicated statistical significance. The data were analyzed using Stata/SE software version 14.1 (StataCorpLP, USA).

Results

Overall, 22.27% of the total number of patients undergoing MPS to assess myocardial ischemia were asymptomatic. The clinical and epidemiological characteristics of the studied population are shown in Table 1.

The rate of tests considered appropriate by the AUC was 61.4%; that of tests considered uncertain was 28.8%; and that of tests considered inappropriate was only 9.8%. The predominant type of stress test requested was pharmacological with dipyridamole (61.4%). Exercise stress testing was performed in 38.4% of cases, all with treadmill exercise test and a predominance of modified Bruce and Bruce protocols.[11]

Analysis of the imaging stage of the test showed a fixed low uptake in 43.5% of cases and a transient low uptake in 16.1%. Changed test results were defined as those with transient low uptake and/or fixed low uptake and/or transient ischemic dilation. The univariate analysis is shown in Table 2.

In the multivariate analysis (Tables 3 and 4), the two models were adjusted according to the selection of the independent variables to be included. One of the models considered the results of the univariate analysis and the clinical relevance of the factors. The other, exclusively technical, considered the stepwise backward model, which makes the selection according to a pre-established criterion regarding statistical significance for the inclusion or exclusion of variables. Figures 1 and 2 present the arrangement of these data in a more visual and graphic format.

Analysis of the association between changed test results and degree of recommendation according to AUC showed a higher prevalence of changed test results in patients with appropriate and uncertain indications, especially in the group with uncertain indications. A similar result occurred when uncertain and appropriate indications were grouped (Table 5).

The AUC criteria found in the study population and used to classify the indications as appropriate, inappropriate, or uncertain are presented in Table 6.

Table 1 - Patients' clinical and epidemiological characteristics.

Variable	Result	Total
Age, years	65.1 ± 10.8 (12-89)	490
Male sex	339 (69.2)	490
Arterial hypertension	400 (81.6)	490
AH under treatment	393 (80.2)	490
SBP, mmHg	134.7 ± 21 (85-250)	489
SBP ≥ 140, mmHg	227 (46.4)	489
Smoking	27 (5.5)	490
Former smoker	205 (41.8)	490
Diabetes	178 (36.3)	490
PAOD	35 (7.1)	490
Carotid disease	75 (15.3)	490
HDL, mg/dL	46.2 ± 13.1 (25-122)	413
LDL, mg/dL	91 ± 35.3 (13-251)	416
≤ 70	124 (29.8)	416
CKD	34 (6.9)	490
Obesity	64 (13.1)	490
FH CAD	28 (5.7)	490
PH CAD	257 (52.4)	490
CVR-SBC		
Low	13 (2.7)	490
Moderate	48 (10)	490
High	420 (87.3)	490
Previous AMI	154 (31.4)	490
Previous MRS	101 (20.6)	490
Previous PCI	103 (21.0)	490
MRS or previous PCI	189 (38.6)	490
Limitation on physical effort	21 (5.1)	413
LVEF*	56.4 ± 13.2 58 (14-81)	430

*Results expressed as mean ± standard deviation (minimum-maximum) or as n (%). *Calculated in the resting phase of myocardial scintigraphy. AH, arterial hypertension; AMI, acute myocardial infarction; BSC, Brazilian Society of Cardiology; CKD, chronic kidney disease; CVR, cardiovascular risk; FH CAD, family history of coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MRS, myocardial revascularization surgery; PAOD, peripheral arterial occlusive disease; PH CAD, personal history of coronary artery disease; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.*

Discussion

The AUC were not applied to the entire population of asymptomatic patients at the service; rather, it was applied respectively to only patients for whom an assessment of ischemia with MPS was previously requested. This characteristic makes the present study an assessment of test requests rather than an overall assessment of its use since it does not have the power to assess the adequacy to the AUC of this segment of an asymptomatic population of patients who did not undergo the test but may have been indicated for it.

Considering that greater care is needed for indications for MPS for asymptomatic patients and that there are already defined criteria for this indication with different degrees of recommendation according to the AUC, there was doubt as to whether these criteria would be adequate for assessing a population at such high cardiovascular risk.

Table 2 - Univariate analysis of factors associated with changed myocardial scintigraphy results*.

Variable	n	Test result*		P value	OR (95% CI)
		Normal	Changed		
Age, years					
< 60	122	62 (50.8)	60 (49.2)		
≤ 60	354	180 (50.9)	174 (49.2)	0.996	1.0 (0.66-1.51)
Sex					
Male	332	147 (44.3)	185 (55.7)		
Female	144	95 (66)	49 (34.0)	< 0.001	2.44 (1.62-3.67)
SAH					
No	87	54 (62.1)	33 (37.9)		
Yes	389	188 (48.3)	201 (51.7)	0.021	1.75 (1.09-2.82)
Diabetes mellitus					
No	301	162 (53.8)	139 (46.2)		
Yes	175	80 (45.7)	95 (54.3)	0.088	1.38 (0.95-2.01)
Dyslipidemia					
No	180	106 (58.9)	74 (41.1)		
Yes	296	136 (46)	160 (54.1)	0.006	1.68 (1.16-2.45)
CKD					
No	443	221 (49.9)	222 (50.1)		
Yes	33	21 (63.6)	12 (36.4)	0.132	0.57 (0.27-1.18)
Obesity					
No	413	208 (50.4)	205 (49.6)		
Yes	63	34 (54)	29 (46)	0.594	0.87 (0.51-1.47)
FH CAD					
No	448	228 (50.9)	220 (49.1)		
Yes	28	14 (50)	14 (50)	0.927	1.04 (0.48-2.22)
PH CAD					
No	225	164 (72.9)	61 (27.1)		
Yes	251	78 (31.1)	173 (68.9)	<0.001	5.96 (4.01-8.87)
Previous AMI					
No	324	217 (67)	107 (33)		
Yes	152	25 (16.5)	127 (83.6)	<0.001	10,3 (6.3-16.8)
Previous MRS					
No	376	219 (58.2)	157 (41.8)		
Yes	100	23 (23)	77 (77)	<0.001	4.67 (2.81-7.77)
Previous PCI					
No	375	212 (56.5)	163 (43.5)		
Yes	101	30 (29.7)	71 (70.3)	<0.001	3.08 (1.92-4.94)
SBP, mmHg					
< 140	254	124 (48.8)	130 (51.2)		
≤ 140	221	117 (52.9)	104 (47.1)	0.37	0.85 (0.59-1.22)
Current/previous smoker					
No	251	141 (56.2)	110 (43.8)		
Yes	225	101 (44.9)	124 (55.1)	0.014	1.57 (1.10-2.26)
Vascular disease					
No	387	196 (50.7)	191 (49.4)		
Yes	89	46 (51.7)	43 (48.3)	0.86	0.96 (0.60-1.52)
HDL, mg/dL					
> 50	115	75 (65.2)	40 (34.8)		
≤ 50	284	130 (45.8)	154 (54.2)	<0.001	2.22 (1.42-3.48)
LDL, mg/dL					
≤ 70	119	50 (42)	69 (58.0)		
> 70	283	158 (55.8)	125 (44.2)	0.012	0.57 (0.37-0.88)
CVR-BSC					
Low/moderate	59	45 (76.3)	14 (23.7)		
High	408	190 (46.6)	218 (53.4)	<0.001	1.92 (1.40-2.63)
Previous revascularization (MRS/PCI)					
Yes	290	191 (65.9)	99 (34.1)		
No	186	51 (27.4)	135 (72.6)	<0.001	5.11 (3.41-7.64)
Previous MPS					
Normal	59	49 (83.1)	10 (17.0)		
Changed	76	16 (21.1)	60 (79.0)	<0.001	18.4 (7.7-44.1)
Stress with exercise					
Positive	62	38 (61.3)	24 (38.7)		
Negative/ inconclusive	114	68 (59.7)	46 (40.4)	0.832	1.07 (0.57-2.02)
Stress with dipyridamole					
Positive	27	11 (40.7)	16 (59.3)		
Negative/ inconclusive	245	119 (48.6)	126 (51.4)	0.441	0.73 (0.32-1.63)
Use of anti-ischemic drug					
No	182	116 (63.7)	66 (36.3)		
Yes	267	119 (44.6)	148 (55.4)	<0.001	2.19 (1.48-3.22)
Stress type					
Exercise test	185	106 (57.3)	79 (42.7)		
Dipyridamole	288	136 (47.2)	152 (52.8)	0.033	1.50 (1.03-2.18)

*Results are expressed as n (%) unless otherwise indicated. *A changed test result included at least one of the following: fixed low uptake, transient low uptake, or transient ischemic dilatation. 95% CI, 95% confidence interval; AMI, acute myocardial infarction; CKD, chronic kidney disease; CVR-BSC, cardiovascular risk calculated by the Brazilian Society of Cardiology; FH CAD, family history of coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MPS, myocardial perfusion scintigraphy; MRS, myocardial revascularization surgery; OR, odds ratio; PCI, percutaneous coronary intervention; PH CAD, personal history of coronary artery disease; SAH, systemic arterial hypertension; SBP, systolic blood pressure.*

The studied population was marked by high cardiovascular risk due to several factors. First, it was composed of patients already screened at other health services and referred due to their greater cardiac complexity, high prevalence of multiple risk factors, and difficultly controlling these risk factors for the most diverse reasons. These characteristics are evident in the results, with 87.3% of the patients in the study being at high cardiovascular risk, more than half already having known coronary artery disease, less than 30% having a low-density lipoprotein (LDL) level within the recommended target for patients at high cardiovascular risk, and almost half having an outpatient blood pressure above the recommended range.[12] Also, this population differed from the one assessed in the study of the validation of the use of the AUC published in 2013.[7]

The rate of inappropriate indications (9.8%) was quite low. Besides the expertise of a reference cardiology teaching center, a likely explanation for this result is that the high cardiovascular risk characteristic of this population is a factor alone that increases the degree of the recommendation in several of the AUC for asymptomatic patients. Another possible contribution to this result may be the usual difficulty in scheduling appointments and tests with ideal deadlines in the Brazilian Unified Health System given the extreme demand, leading to longer than desirable intervals between appointments. Under these circumstances, the test is performed later than it probably

Table 3 - Multivariate analysis of factors associated with changed test results.

Variable	Changed test result	P value* (univariate)	P value* (multivariate)	OR	95% CI
Age, years					
< 60	60 (49.2)				
≤ 60	174 (49.2)	0.996	0.273	0.72	0.4-1.29
Sex					
Female	185 (55.7)				
Male	49 (34.0)	<0.001	0.037	1.79	1.04-3.1
SAH					
No	33 (37.9)				
Yes	201 (51.7)	0.021	0.995	1	0.5-2.02
Diabetes mellitus					
No	139 (46.2)				
Yes	95 (54.3)	0.088	0.423	1.24	0.73-2.1
Dyslipidemia					
No	74 (41.1)				
Yes	160 (54.1)	0.006	0.724	0.9	0.51-1.6
PH CAD					
No	61 (27.1)				
Yes	173 (68.9)	<0.001	0.001	3.23	1.57-6.66
SBP, mmHg					
< 140	130 (51.2)				
≤ 140	104 (47.1)	0.37	0.283	0.77	0.47-1.25
Current and previous smoking					
No	110 (43.8)				
Yes	124 (55.1)	0.014	0.782	0.93	0.56-1.55
HDL, mg/dL					
> 50	40 (34.8)				
≤ 50	154 (54.2)	<0.001	0.236	1.4	0.8-2.45
LDL, mg/dL					
≤ 70	69 (58.0)				
> 70	125 (44.2)	0.012	0.706	0.9	0.52-1.55
Previous revascularization (MRS/PCI)					
No	99 (34.1)				
Yes	135 (72.6)	<0.001	0.071	1.95	0.94-4.02
Using anti-ischemic drug					
No	66 (36.3)				
Yes	148 (55.4)	<0.001	0.044	1.72	1.01-2.9
Stress test type					
Exercise	79 (42.7)				
Dipyridamole	152 (52.8)	0.033	0.023	1.87	1.09-3.21
Test result					
Negative/ inconclusive	171 (47.8)				
Positive	40 (44.9)	0.633	0.288	0.7	0.37-1.35

*Results are expressed as n (%) unless otherwise indicated. *Logistic regression model and Wald test, p<0.05. 95% CI, 95% confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MRS, myocardial revascularization surgery; OR, odds ratio; PCI, percutaneous coronary intervention; PH CAD, personal history of coronary artery disease; SAH, systemic arterial hypertension; SBP, systolic blood pressure.*

Table 4 - Multivariate analysis of factors associated with changed test results using the stepwise backward model.

Variable	Changed test result	P value* (univariate)	P value* (multivariate)	OR	95% CI
Using anti-ischemic drug					
No	66 (36.3)				
Yes	148 (55.4)	< 0.001	0.025	1.65	1.07-2.57
Sex					
Female	185 (55.7)				
Male	49 (34.0)	< 0.001	0.003	2.02	1.27-3.21
PH CAD					
No	61 (27.1)				
Yes	173 (68.9)	< 0.001	< 0.001	5.09	3.33-7.77
Stress test type					
Exercise	79 (42.7)				
Dipyridamole	152 (52.8)	0.033	0.019	1.71	1.09-2.68

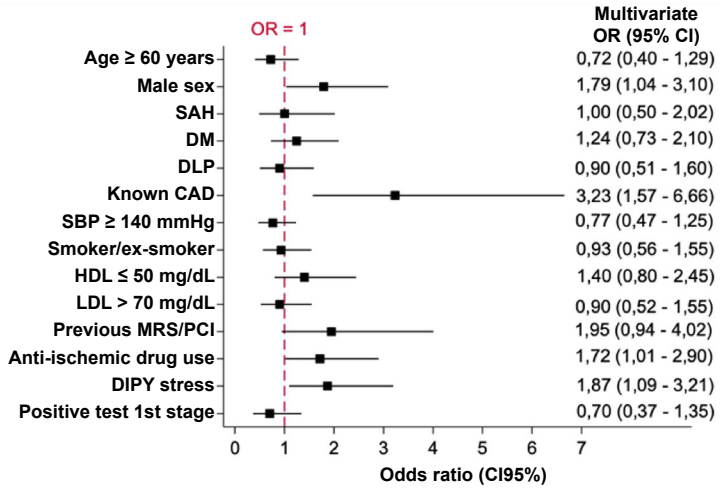
*Results are expressed as n (%) unless otherwise indicated. *Logistic regression model (stepwise backward method, pr 0.10) and Wald test (n = 448). 95% CI, 95% confidence interval; OR, odds ratio; PH CAD, personal history of coronary artery disease.*

would be if the public services were not as saturated, which increases the probability of a properly performed test since, for many criteria, there is a minimum interval for the test not to be considered an inappropriate indication.

Another point to be carefully observed is that, although the ischemia assessment is the reason for the MPS, the division of criteria into appropriate, uncertain, and inappropriate does not necessarily mean that changed test results are expected in appropriate indications versus normal test results in inappropriate indications. This classification also consider the test's ability to provide prognostic information and the usefulness of its result in the clinical context, and not just the exam result alone.

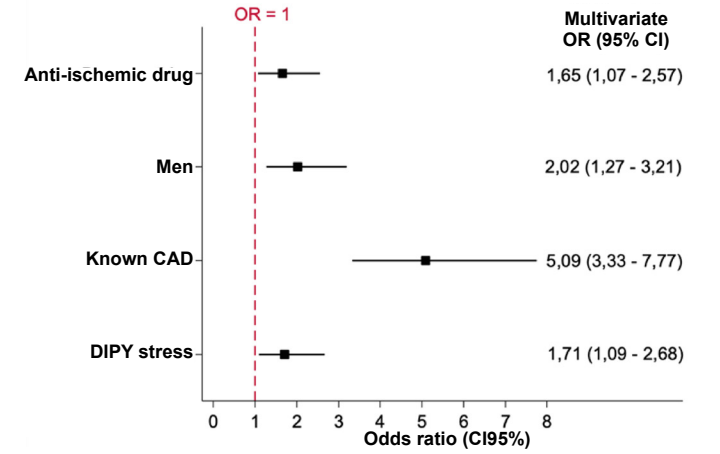
Sometimes it was difficult to find a criterion whose specifications met the patient's exact profile. At other times, more than one criterion fit the patient's profile, raising questions about which one to use. Therefore, doubtful patients were classified according to the criterion that was closest to their clinical situation or, in those with more than one possible criterion, the one referring to the condition of greatest clinical importance in the investigator's opinion was chosen. There is a suggested hierarchy for the AUC; however, it remained difficult to choose the most appropriate criterion in situations with more complex conditions. The degree of recommendation changed a few times when there was doubt; when it did, it generally oscillated between uncertain and appropriate indications, which are degrees of recommendations with good acceptability in the definition of conduct as well as in patient management.

The ischemia assessment revealed that 16.1% of the target population of this study had ischemia, i.e., a rate similar to the one of another study conducted at the same service but that also included patients with atypical symptoms.[13] This study was expected to present a lower rate of ischemia since it excluded patients with atypical symptoms, but this did not



CAD, coronary artery disease; PCI, percutaneous coronary intervention; CI, confidence interval; DIPY, dipyridamole; DLP, dyslipoproteinemia; DM, diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MRS, myocardial revascularization surgery; OR, odds ratio; SAH, systemic arterial hypertension; SBP, systolic blood pressure.

Figure 1 – *Multivariate analysis of test result changes.*



CAD, coronary artery disease; CI, confidence interval; DIPY, dipyridamole; OR, odds ratio

Figure 2 – *Multivariate analysis of changed test results using the stepwise model.*

occur. This could mean that, in such a high-risk population, the prevalence of ischemia would remain similar regardless of the inclusion of patients with atypical symptoms.

Another Brazilian study[14] addressed a specific situation contemplated in some of the AUC, specifically the prognostic value and clinical use of MPS in asymptomatic patients after percutaneous coronary intervention (PCI). MPS was suggested to play an important role in asymptomatic patients after they underwent angioplasty regardless of the time the test was performed after the procedure, i.e., the two-year milestone recommended of the guidelines could not separate patients with more severe outcomes. However, that study reported the important role of suspected incomplete revascularization in the indication of most of these tests. Considering the AUC published in 2009, which has specific criteria for suspected incomplete revascularization in addition to the criteria related to the time to perform the test after PCI, patients with suspected incomplete revascularization should not be evaluated with other asymptomatic patients in the post-PCI setting, as the role of MPS in suspected incomplete revascularization is well established.

The correlation between tests performed with appropriate or uncertain degree of recommendation and changed test results showed the good ability of the AUC to predict changed results.

The univariate analysis showed a correlation between classic risk factors and perfusion changes. The association between the use of anti-ischemic drugs and a changed test result is probably the result of a more aggressive clinical treatment in more severe patients. The same reasoning can be

Table 5 - Association between changed myocardial perfusion scintigraphy and degree of indication according to the appropriate use criteria.

Indications	n	MPS		P value*
		Normal	Changed	
Inappropriate	46	34 (73.9)	12 (26.1)	
Appropriate	294	153 (52.0)	141 (48.0)	< 0.001
Uncertain	136	55 (40.4)	81 (59.6)	
Inappropriate	46	34 (73.9)	12 (26.1)	0.001
Appropriate/uncertain	430	208 (48.4)	222 (51.6)	

*Results are expressed as n (%) unless otherwise indicated. *Chi-square test or Fisher's exact test, p < 0.05.*

used to analyze that lower, not higher, LDL levels are correlated with a higher rate of changed test results.

In the multivariate analysis, when the variables involved were analyzed together, a personal history of CAD was the factor most associated with changed test results. MPC with pharmacological stress maintained a statistically significant association in the multivariate analysis as well, a result that has been demonstrated in other studies.[15-17] The possible explanation that has been suggested is that patients undergoing pharmacological stress testing would have more comorbidities and higher cardiovascular risk than those undergoing exercise stress testing, therefore increasing the association between changed test results and worse clinical outcomes.[18]

If, on the one hand, the study has limitations of being cross-sectional, observational, retrospective, and subject to the degree of quality of the notes taken in medical records; on the other hand, it approaches a realistic view of the current functioning of this service. Calculating cardiovascular risk with the calculator proposed by the Dyslipidemia Division of the Brazilian Society of Cardiology[19] differs from what is proposed in the AUC, which used the ATP III score;[20] however, it is currently the most used commonly used form in this service and the one that best reflects how a patient's cardiovascular risk has been calculated.

In addition, for the purpose of grouping into criteria, some patients were allocated to criteria that do not exactly represent their clinical situation, but this limitation was already described in the AUC publication.[6] The authors did not exclude or create a category for unclassified patients who did not exactly fit into any of the criteria since this tool should be used to guide rather than restrict medical care. Thus, the results must be analyzed from the perspective of the power of such criteria to guide the search process for the correct use of the test. Additionally, the classification of indications as adequate or inappropriate is the result of an individual interpretation of the AUC by the investigator.

Table 6 - Distribution by criteria used in the classification of indications*.

Criterion - scenario covered by the criterion†	Classification/n (%)‡
15 - Detection of CAD at high cardiovascular risk	A/73 (14.9)
28 - Changed angiography or changed functional test (≥ 2 years)	UC/72 (14.7)
58 - 5 years or more after MRS	A/44 (9)
29 - Doubtful prior non-invasive assessment	A/38 (7.8)
19 - Ventricular tachycardia with moderate or high cardiovascular risk	A/32 (6.5)
38 - Moderate risk Duke score	A/32 (6.5)
60 - 2 years or more after PCI	IC/31 (6.3)
32 - Coronary stenosis of uncertain meaning	A/24 (4.9)
16 - HFrEF of recent diagnosis	A/18 (3.7)
56 - Suspected incomplete revascularization	A/18 (3,7)
26 - Moderate or high cardiovascular risk with normal functional test (≥ 2 years)	IC/15 (3.1)
21 - Moderate or high cardiovascular risk with syncope	A/13 (2.7)
45 - Preoperative of vascular surgery with good functional capacity	I/13 (2.7)
57 - Less than 5 years of MRS	IC/12 (2.4)
13 - Intermediate cardiovascular risk with interpretable ECG	I/10 (2)
14 - Intermediate cardiovascular risk with uninterpretable ECG	UC/8 (1.6)
59 - Less than 2 years of PCI	I/8 (1.6)
27 - Changed angiography or changed functional test (< 2 years)	I/6 (1.2)
12 - Low cardiovascular risk	I/4 (0.8)
17 - AF	UC/4 (0.8)
18 - Ventricular tachycardia with low cardiovascular risk	A/4 (0.8)
52 - ACS evaluation occurred up to 3 months before, without coronary angiography	A/3 (0,6)
24 - Moderate or high cardiovascular risk with normal functional test (< 2 years)	I/2 (0,4)
41 - General preoperative with good functional capacity	I/2 (0,4)
43 - General preoperative with at least one clinical risk factor and low functional capacity	A/2 (0,4)
37 - Low risk Duke score	I/1 (0,2)
39 - High Risk Duke Score	A/1 (0,2)
42 - General preoperative without clinical risk factor	I/1 (0,2)
46 - Preoperative of vascular surgery without clinical risk factor	I/1 (0,2)
47 - Preoperative of vascular surgery with at least one clinical risk factor and low functional capacity	A/1 (0,2)

**In descending order of frequency; †according to the appropriate use criteria;[6] ‡percentages of total cases (N = 490). A, appropriate; ACS, acute coronary syndrome; AF, atrial fibrillation; CAD, coronary artery disease; ECG, electrocardiogram; HFrEF, heart failure with reduced ejection fraction; MRS, myocardial revascularization surgery; PCI, percutaneous coronary intervention; UC, uncertain; I: inapropriate.*

Conclusion

With the purpose of critically analyzing the role of the AUC in asymptomatic patients within a population, this study demonstrated that their retrospective application to guide the referral for MPS could predict that the adequate indication of the exam (appropriate and uncertain indications) is correlated with changed test results, especially in the subgroup of patients classified as having uncertain indications. Perhaps, in a population with a high cardiovascular risk as the one in this study, some indications considered uncertain might actually be appropriate.

Finally, considering these results, further studies are needed to identify whether certain clinical situations classified as

uncertain in the AUC would be subject to changes in the degree of recommendation when the test is used in an asymptomatic population with high cardiovascular risk.

Authors' contributions

Research conception and design: VSFA and PEPS; data collection: VSFA; data analysis and interpretation: VSFA and PEPS; statistical analysis: VSFA; funding: VSFA; manuscript writing: VSFA; critical review of the manuscript for important intellectual content: VSFA and PEPS.

Conflict of interest

The authors have declared that they have no conflict of interest.

References

1. Mansur AP, Favarato D. Mortalidade por doenças cardiovasculares no Brasil e na região metropolitana de São Paulo: atualização 2011. Arq Bras Cardiol. 2012;99(2):755-61. doi: https://doi.org/10.1590/S0066-782X2012005000061

2. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med. 7;356(23):2388-98. doi: https://doi.org/10.1056/NEJMsa053935

3. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al.; American College of Cardiology Foundation/American Heart Association Task Force. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2012;126(25):e354-471. doi: https://doi.org/10.1161/CIR.0b013e318277d6a0. Erratum in: Circulation. 2014;129(16):e463.

4. Schinkel A. Noninvasive evaluation of ischaemic heart disease: myocardial perfusion imaging or stress echocardiography? Eur Heart J. 2003;24(9):789-800. doi: https://doi.org/10.1016/s0195-668x(02)00634-6

5. Brindis RG, Douglas PS, Hendel RC, Peterson ED, Wolk MJ, Allen JM, et al.; American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group; American Society of Nuclear Cardiology; American Heart Association. ACCF/ASNC appropriateness criteria for single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI): a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group and the American Society of Nuclear Cardiology endorsed by the American Heart Association. J Am Coll Cardiol. 2005;46(8):1587-605. doi: https://doi.org/10.1016/j.jacc.2005.08.029. Erratum in: J Am Coll Cardiol. 2005;46(11):2148-50.

6. ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/SNM 2009 appropriate use criteria for cardiac radionuclide imaging. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. Circulation. 2009 [cited 2021 Jul 11];119(22):e561-87. Available from: https://www.asnc.org/files/AUC%20for%20Cardiac%20Radionuclide%20Imaging.pdf

7. Doukky R, Hayes K, Frogge N, Balakrishnan G, Dontaraju VS, Rangel MO, et al. Impact of appropriate use on the prognostic value of single-photon emission computed tomography myocardial perfusion imaging. Circulation. 2013;128(15):1634-43. doi: https://doi.org/10.1161/CIRCULATIONAHA.113.002744

8. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37(3):267-315. doi: https://doi.org/10.1093/eurheartj/ehv320

9. Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al.; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Nutrition, Physical Activity and Metabolism, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention. Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation.;128(8):873-934. doi: https://doi.org/10.1161/CIR.0b013e31829b5b44

10. Dorbala S, Ananthasubramaniam K, Armstrong IS, Chareonthaitawee P, DePuey EG, Einstein AJ, et al. Single photon emission computed tomography (SPECT) myocardial perfusion imaging guidelines: instrumentation, acquisition, processing, and interpretation. J Nucl Cardiol. 2018;25(5):1784-1846. doi: https://doi.org/10.1007/s12350-018-1283-y

11. Meneghelo RS, Araújo CG, Stein R, Mastrocolla LE, Albuquerque PF, Serra SM. III Diretrizes da Sociedade Brasileira de Cardiologia sobre teste ergométrico. Arq Bras Cardiol. 2010;95(5):1-26. doi: https://doi.org/10.1590/S0066-782X2010000800001

12. Malachias MV, Souza WK, Plavnik FL, Rodrigues CI, Brandão AA, Neves MF, et al. 7a Diretriz Brasileira de Hipertensão Arterial. Arq Bras Cardiol. 2016 [citado 2021 Jul 11];107(3). Disponível em: http://publicacoes.cardiol.br/2014/diretrizes/2016/05_HIPERTENSAO_ARTERIAL.pdf

13. Smanio PE, Silva JH, Holtz JV, Ueda L, Abreu M, Marques C, Machado L. Myocardial scintigraphy in the evaluation of cardiac events in patients without typical symptoms. Arq Bras Cardiol. 2015;105(2):112-22. doi: https://doi.org/10.5935/abc.20150074

14. Andrade LF, Souza AC, Peclat T, Bartholo C, Pavanelo T, Lima RS. The prognostic value and clinical use of myocardial perfusion scintigraphy in asymptomatic patients after percutaneous coronary intervention. Arq Bras Cardiol. 2018;111(6). doi: https://doi.org/10.5935/abc.20180199

15. Heller GV, Herman SD, Travin MI, Baron JI, Santos-Ocampo C, McClellan JR. Independent prognostic value of intravenous dipyridamole with technetium-99m sestamibi tomographic imaging in predicting cardiac events and cardiac-related hospital admissions. J Am Coll Cardiol. 1995;26(5):1202-8. doi: https://doi.org/10.1016/0735-1097(95)00329-0

16. Calnon DA, McGrath PD, Doss AL, Harrell FE Jr, Watson DD, Beller GA. Prognostic value of dobutamine stress technetium-99m-sestamibi single-photon emission computed tomography myocardial perfusion imaging: stratification of a high-risk population. J Am Coll Cardiol. 2001;38(5):1511-7. doi: https://doi.org/10.1016/s0735-1097(01)01565-0

17. Hachamovitch R, Hayes S, Friedman JD, Cohen I, Shaw LJ, Germano G, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: what is the warranty period of a normal scan? J Am Coll Cardiol. 2003 Apr 16;41(8):1329-40. doi: https://doi.org/10.1016/s0735-1097(03)00125-6.

18. Hachamovitch R, Berman DS. The use of nuclear cardiology in clinical decision making. Semin Nucl Med. 2005;35(1):62-72. doi: https://doi.org/10.1053/j.semnuclmed.2004.09.005

19. Faludi A, Izar M, Saraiva J, Chacra A, Bianco H, Afiune Neto A, et al. Atualização da diretriz brasileira de dislipidemias e prevenção da aterosclerose - 2017. Arq Bras Cardiol. 2017 [citado 2021 Jul 11];109(1). Disponível em: http://www.gnresearch.org/doi/10.5935/abc.20170121

20. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106(25):3143-421.