Article published online: 2022-05-23

Original article

# Nuclear Scan Strategy and Outcomes in Chest Pain Patients Value of Stress Testing with Dipyridamole or Adenosine

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## Abstract

**Objective:** To update the prognostic value of scan strategy with pharmacological stress agent in chest pain (CP) patients presenting with normal electrocardiography (ECG) and troponin. **Methods:** Two consecutive nonrandomized series of patients with CP and negative first-line workup inclusive of serial ECG, serial troponin, and echocardiography underwent myocardial perfusion imaging single photon emission computed tomography (SPECT) in the emergency department. Of 170 patients enrolled, 52 patients underwent dipyridamole-SPECT and 118 adenosine-SPECT. Patients with perfusion defects underwent angiography, whereas the remaining patients were discharged and followed-up. Primary endpoint was the composite of nonfatal myocardial infarction, unstable angina, revascularization, and cardiovascular death at follow-up or the presence of coronary stenosis > 50% at angiography. **Results:** At multivariate analysis, the presence of perfusion defects or hypertension was independent predictor of the primary endpoint. Sensitivity and negative predictive value were higher in patients subjected to adenosine-SPECT (95% and 99%, respectively) versus dipyridamole-SPECT (56% and 89%; yield 70% and 11%, respectively; $P < 0.03$). Of note, sensitivity, negative, and positive predictive values were high in patients with hypertension (100%, 93%, and 60%, respectively) or nonischemic echocardiography alterations (100%, 100%, and 100%, respectively). **Conclusions:** In CP patients, presenting with normal ECG and troponin, adenosine-SPECT adds incremental prognostic values to dipyridamole-SPECT. Costly scan strategy is more appropriate and avoids unnecessary angiograms in patients with hypertension or nonischemic echocardiography alterations.

**Keywords:** Chest pain, emergency medicine, myocardial ischemia, myocardial perfusion imaging, nuclear medicine, prognosis, risk assessment

## Introduction

The management of patients who present to the emergency department with the chest pain (CP) as the main complaint remains a critical problem.[1] Electrocardiography (ECG) and cardiac troponin currently form the diagnostic cornerstones of evaluation on presentation.[2-4] Some patients show ECG changes of acute coronary syndrome; however, the majority of patients do not have either ECG changes or abnormal plasma level of troponin, and will require further costly workup to rule out acute cardiac ischemia or coronary stenosis.[1,5,6] Indeed, low-risk CP patients with normal ECG and normal troponin have been recognized as having up to 20% coronary disease diagnosis.[1,6-9] Exercise testing in CP centers has shown safety and diagnostic efficacy; however, in patients unable to exercise, pharmacological stress echocardiography or myocardial perfusion imaging (MPI) should be considered.[10-12] MPI single photon emission computed tomography (SPECT) showed higher sensitivity and higher negative predictive value (NPV) as compared with clinical, lab, and ECG data in recognizing patients at very low-risk of coronary event.[9,13] Predictive values in stress-SPECT and stress-echocardiography were found

Access this article online

Quick Response Code:

Website: www.wjnm.org

DOI: 10.4103/1450-1147.139138

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to be comparable; however, stress-SPECT should be considered in the absence of good acoustic window.[11,14]

Adenosine and dipyridamole are the most widely available pharmacologic agents used in stress testing in patients unable to perform the standard exercise stress test.[15,16] They dilate coronary vessels, and cause increased blood velocity and flow rate in normal vessels; conversely, the response in stenotic vessels is poor. This difference in response leads to a steal of flow, and perfusion defects appear in cardiac nuclear scans or as ST-segment changes in ECG. Adenosine is a direct coronary vasodilator, while dipyridamole is an indirect vasodilator that works by increasing intravascular adenosine levels. The increase in coronary blood flow induced by dipyridamole is considered to be less predictable than that of adenosine. Thus, the aim of this study was to update the role of the pharmacological stress agent adenosine as compared with dipyridamole in scan strategy for diagnosis of myocardial ischemia and coronary stenosis in CP patients presenting normal ECG and normal troponin

# Methods

## Patient selection

All consecutive patients with CP lasting ≤ 24 h who presented between 2007 and 2011 years to the emergency department of the tertiary care teaching Careggi-Hospital, in Florence, Italy, were considered for enrollment. All patients underwent a first-line 6-h workup with clinical evaluation, serial ECGs, and serial troponins.[1,5,17] The inclusion criteria were the presence of CP lasting ≤ 24 h, normal ECGs and normal troponins. The exclusion criteria were represented by age < 18 years, hemodynamic instability, severe comorbidity, and eventually patients considered at high-risk of coronary events, including those with ECG alterations diagnostic of acute coronary syndrome.[3] Furthermore, patients with atypical CP inclusive of pleuritic CP or pulmonary conditions or musculoskeletal disease or pericardial disease associated with nondiagnostic ECG and normal serial troponins were excluded from the study. Thus, the remaining patients complaining of typical CP or chest discomfort presenting nondiagnostic ECGs and troponins were considered as being at low-risk of a coronary event and were enrolled in the study for the second-line evaluation by scan strategy. Each patient gave informed consent to participate in the study and the publication of data. This study was performed in accordance with good clinical practice and principles of the Declaration of Helsinki, which are morally binding on physicians and respect for the individual right to self-determination regarding participation in research. The institutional review board approved the protocol. Departmental sources supported the work and no contributorship or competing interest existed. Thus, authors declare that they have no conflict of interest.

## Management of patients and study protocol

Enrolled CP patients were characterized by the presence of major coronary risk factors such as hypertension, diabetes mellitus, high blood cholesterol, and current smoking. The diagnosis of hypertension consisted of a history of systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg. The diagnosis of diabetes was based on a history or the presence of fasting glucose >125 mg/dL in at least two measurements or current hypoglycemic drug therapy. On the basis of self-reported cholesterol levels, mean total blood cholesterol levels of 200 mg/dl or higher were considered abnormal. Nonsmoker were considered those patients who had stopped smoking cigarette for >6 months. Baseline clinical data were collected from the clinical history obtained from patients, relatives, caregivers, or events analyzed by reviewing previous hospital or laboratory data available on the hospital network. To avoid overestimation of the coronary risk profile, when information regarding some risk factors was unavailable, we assumed that the patient did not have that risk factor.

## Basal nonischemic electrocardiography and basal nonischemic echocardiography alterations

Resting echocardiography was performed in all patients. Positive echocardiography was defined by the detection of segment kinetic alterations as hypokinesia and dyssynergia. Conversely, mild-to-moderate left ventricular hypertrophy, mild-to-moderate dilated left ventricle without hypokinesia and dyssynergia or dyssinergia related to left bundle-branch block, electrical atrial and ventricle pacing, and mild-to-moderate hypokinesia in only one segment were considered basal nondiagnostic echocardiography alterations.[11]

Resting serial ECGs were performed during the First line six-hour workup. Abnormal nondiagnostic ECG alterations were considered in the presence of ST-segment depression <0.05 mm, asymmetrical T-wave inversion <0.20 mm, Q waves <0.03 seconds (s) in two contiguous leads, complete bundle-branch block, and paced rhythm.[10,17,18]

## Stress testing

Patients unable to exercise underwent early in-hospital pharmacological stress with adenosine or dipyridamole. No food or coffee, tea, or chocolate during 12-24 h before test. Adenosine was given intravenously at a dose of 140 mcg $min^{-1}$ $kg^{-1}$ for a period of 6 min and the tracer (technetium-99m-sestamibi, 740 MBq) was injected

at the 3rd min of infusion. Dipyridamole was given intravenously at the dose of 0.56 mg/kg body weight, in 4 min, and the tracer was injected after three more minutes. Image acquisition began 20 min after tracer injection; SPECT was carried out using a three-head gamma-camera (Picker–3000XP; Philips, Cleveland, Ohio, USA) equipped with a low-energy collimator. 120 projections (31/step) were acquired on a 64 × 64 matrix through a 360 elliptical orbit. The acquisition time was 20 s/frame. Short axis, horizontal long axis, and vertical long axis images were reconstructed. No attenuation or scatter correction was performed. Images were analyzed by a dedicated nuclear cardiology investigator. A 17-segment model was used for perfusion analysis according to guidelines for segmentation in cardiac imaging.[12,19]

## Analysis of perfusion defects

Classification of perfusion defects were derived from the Consensus of the American College of Cardiology/American Heart Association/American Society of Nuclear Cardiology Task Force on Practice Guidelines (ACC/AHA/ASNC Guidelines for the clinical use of cardiac radionuclide imaging).[12,19]

Visual perfusion defect interpretation of SPECT MPI was carried out using the Food and Drug Administration (FDA) Guidance, and the 17-segment, 5-point scoring system (0 = normal, 1 = slight, 2 = moderate, 3 = severe, and 4 = absent tracer uptake) by two independent expert readers, with adjudication of discordant segments by a third expert, and percent abnormal myocardium was derived from normalized summed scores. However, we simplified the classification of perfusion imaging into the following groups: normal, hypoperfused, and equivocal. In our series, the normal group included patients showing normal MPI in all myocardial segments (defined as Class 0, with normal perfusion, in ACC/AHA/ASNC Guidelines). The group with hypoperfused imaging included patients showing severe hypoperfused segment defects, or at least patients showing segment with no myocardial perfusion (defined as Class 3, with severe hypoperfusion, and Class 4, with no perfusion, respectively, in ACC/AHA/ASNC Guidelines). The intermediate group with equivocal imaging included patients showing slight-to-moderate segment perfusion defects (defined as Class 1, with slight perfusion, and Class 2, with moderate perfusion, respectively, in ACC/AHA/ASNC Guidelines). Patients of this study were further studied by means of gated analysis, and special attention was paid to those patients categorized as equivocal and showing slight-to-moderate segment perfusion defects. These patients were finally reassigned to the normal or hypoperfused group as follows: patients with suspected diaphragmatic or breast attenuation artifacts or slight-to-moderate perfusion abnormalities associated with normal wall motion were finally considered "normal"; patients with slight-to-moderate perfusion defects associated with abnormal wall motion (hypokinesia, akinesia) or abnormal thickening were considered 'hypoperfused.[9,12,13,19] Thus, our analysis showed only two groups of patients: patients with normal imaging and patients with hypoperfused imaging. The outcome evaluation based on dichotomy (normal/abnormal tests) and the need of subjecting patients to coronary angiography may be a limitation of any screening workup, but in the emergency setting, especially in patients presenting CP, physicians need to choose to incorporate the nuclear scan technology into daily clinical care.

## Positive testing and coronary artery disease diagnosis

Patients with positive testing were considered as having a high-risk coronary event and were referred for coronary angiography. When the culprit vessel showed angiographic stenosis ≥50%, coronary disease was established. Conversely, patients with negative testing were discharged from the hospital and followed-up at 12 months. Those patients with established coronary events (e.g. adverse coronary events, including cardiac death, acute myocardial infarction, unstable angina, and revascularization) were considered as having coronary disease.

Diagnoses of cardiac death, unstable angina, or acute myocardial infarction were defined according to international guidelines.[2,3,18]

## Endpoint

Primary endpoint was the composite of nonfatal myocardial infarction, unstable angina, revascularization, and cardiovascular death at follow-up or the presence of coronary stenosis ≥ 50% at angiography.

## Follow-up

Follow-up was performed by reviewing the emergency department access archives or by phone after 12 months in patients discharged with a negative clinical evaluation or negative stress testing. Adverse events of suspected myocardial ischemia were analyzed and assessed after clinical charts, ECGs, and lab tests' review.

## Statistical analysis

Summary data are expressed as mean ± standard deviation statistical comparisons of demographic and clinical parameters between the two groups of patients enrolled in the study were performed using the $\chi^2$ test and the Pearson exact test for categorical variables, while the Student's *t*-test was used for continuous variables. Hazard ratios were used to illustrate the probabilities of adverse events. The incidence at 1 year follow-up of the composite endpoint was adjusted for all the established

risk factors of cardiovascular disease. In addition, sensitivity analyses using backward logistic regression were performed. Univariate analysis was performed for all the clinical variables and comorbidity considered in the study. The clinical variables which were found as having a $P < 0.05$ from two-sided tests entered the model for the multivariate backward logistic regression analysis, which was used to define the independent predictors of adverse events. $P$ values are two-sided. $P < 0.05$ was considered to be statistically significant. Calculations were performed with the use of version 17, SPSS statistical package (SPSS Inc., Chicago, IL) for all analyses.

## Results

Baseline clinical characteristics of enrolled patients are shown in Table 1. The two series of patients did not show any significant clinical differences. One-half of patients presented hypertension; 19% had diabetes or high blood cholesterol. The mean age was 69 years, 58% of patients were female and 13% presented with basal nonischemic ECG or basal nonischemic echocardiography alterations. The flow diagram of CP patients to the emergency department between 2007 and 2011 years is shown in Figure 1. Of 170 patients enrolled, 52 underwent stress dipyridamole-SPECT and the remaining 118 underwent stress adenosine-SPECT. Results of SPECT and outcomes are shown in Figure 2. The presence of perfusion defects or the presence of hypertension or basal nonischemic echocardiography alterations were predictor of the composite endpoint at univariate analysis; however, at multivariate regression analysis by backward stepwise only the presence of perfusion defects or the presence of hypertension were independent predictors of the composite endpoint [Table 2].

**Table 1: Basal clinical characteristics of chest pain patients with serial nondiagnostic ECG and troponin enrolled in the study ($n$=170)**

| Basal clinical characteristic | Total SPECT $n$=170 | Dipyridamole-SPECT $n$=52 | Adenosine-SPECT $n$=118 | $P$ value |
|---|---|---|---|---|
| Mean age | 69.0±10.9 | 68.8±10.8 | 69.3±11.0 | 0.78 |
| Female gender | 93 (58%) | 25 (53%) | 68 (58%) | 0.32 |
| Diabetes mellitus | 34 (20%) | 9 (19%) | 24 (21%) | 0.83 |
| Hypertension | 84 (49%) | 25 (53%) | 57 (48%) | 1.0 |
| High blood cholesterol | 36 (21%) | 9 (19%) | 25 (22%) | 0.67 |
| Active smoker | 15 (9%) | 8 (17%) | 10 (9%) | 0.65 |
| Metabolic syndrome | 29( 17%) | 7 (15%) | 20 (17%) | 0.65 |
| Familial history of ischemic heart disease | 39 (23%) | 10 (21%) | 19 (16%) | 0.66 |
| Known ischemic heart disease | 27 (16%) | 9 (19%) | 17 (14%) | 0.65 |
| Nonischemic ECG and echocardiogrphy alterations | 25 (15%) | 7 (15%) | 15 (13%) | 1.0 |

SPECT: Single photon emission computed tomography, ECG: Electrocardiography

### Pharmacological stress myocardial perfusion imaging

Of 52 patients submitted to dipyridamole-SPECT, 15 (29%) showed perfusion defects and 5 (33%) reached the primary endpoint. Dipyridamole-SPECT was negative in 37 (71%) patients and 4 (11%) of these had coronary events at follow-up. Conversely, Of 118 patients submitted to adenosine-SPECT, 35 (30%) showed perfusion defects and 18 (51%) reached the endpoint. Adenosine-SPECT was negative in 83 (70%) patients and 1 patient (1%) reached the endpoint. Sensitivity and NPV were significantly higher in patients subjected to adenosine-SPECT versus dipyridamole-SPECT [Figure 3]. Indeed, sensitivity was 95% versus 56%, respectively, and the yield was found to be up to 70%. NPV was 99% versus 89%, respectively, and the yield up to 11% [Table 3].

### Single photon emission computed tomography in special populations

Results of SPECT in patients with hypertension or basal nonischemic echocardiography alterations showed optimal predictive values although without any statistical difference when compared with all patients enrolled in the study. However, in the same subsets of patients, differences in positive predictive value (PPV) were very high in patients submitted to dipyridamole-SPECT versus adenosine-SPECT [Table 4].

## Discussion

This study shows that nuclear scan strategy is a valuable tool for risk stratification of CP patients, and pharmacological stress adenosine-SPECT adds incremental prognostic value to dipyridamole-SPECT. Indeed, sensitivity and NPV of adenosine-SPECT were significantly higher than dipyridamole-SPECT. The yield in sensitivity was found to be up to 70% and the yield in NPV up to 11% ($P < 0.05$ for both). However, the health care community needs to understand how and why to incorporate costly SPECT technology into daily clinical practice, and when to choose adenosine rather than dipyridamole. Efforts could be represented by applying testing to selective patients unable to exercise and with poor acoustic window. In addition, predictive values of nuclear scan strategy may be improved if the results are integrated into a clinical risk assessment eventually based upon the presence of high likelihood of adverse cardiac events (as in patients with hypertension or with nondiagnostic echocardiography alterations). Indeed, in our series, the yield in PPV in hypertensive patients subjected to adenosine versus dipyridamole rise to a maximum of 3-fold, and to a maximum of 50% in patients with echocardiography alterations, avoiding a substantial amount of unnecessary diagnostic angiograms.

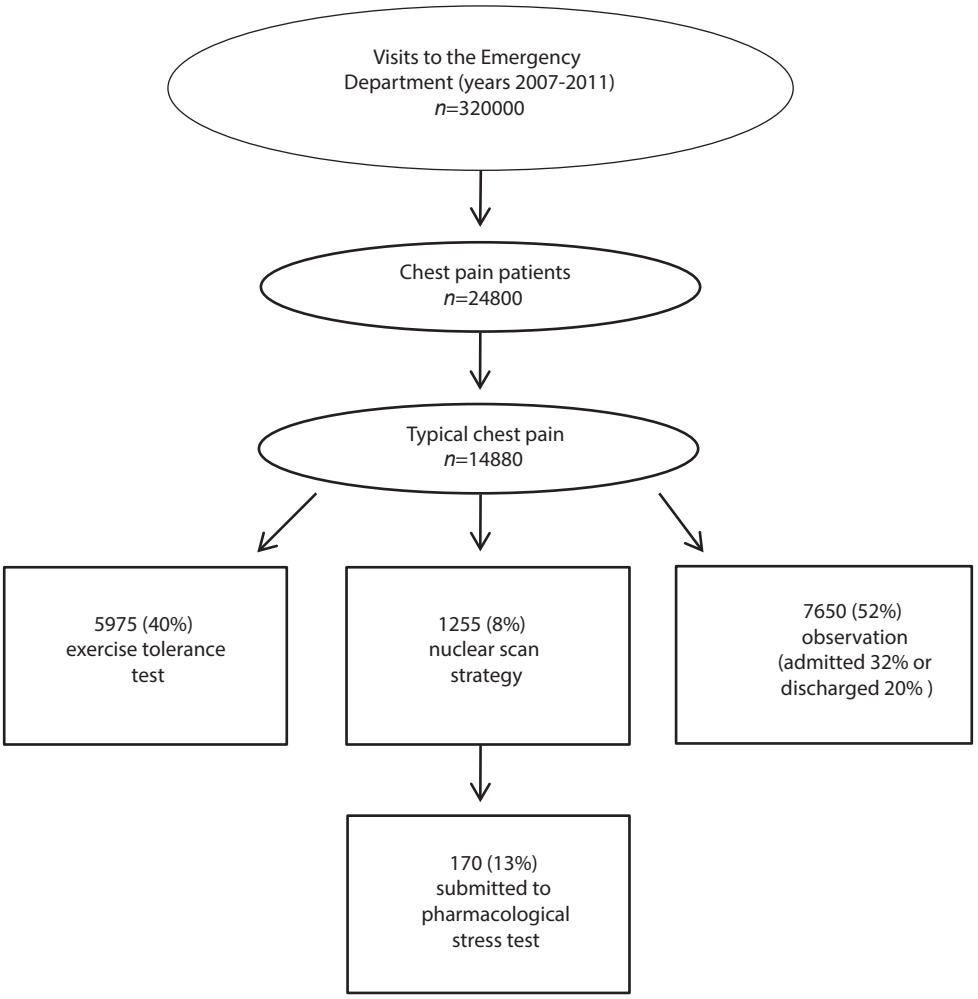


**Figure 1:** Flow diagram of chest pain patients to the Emergency Department between 2007 and 2011

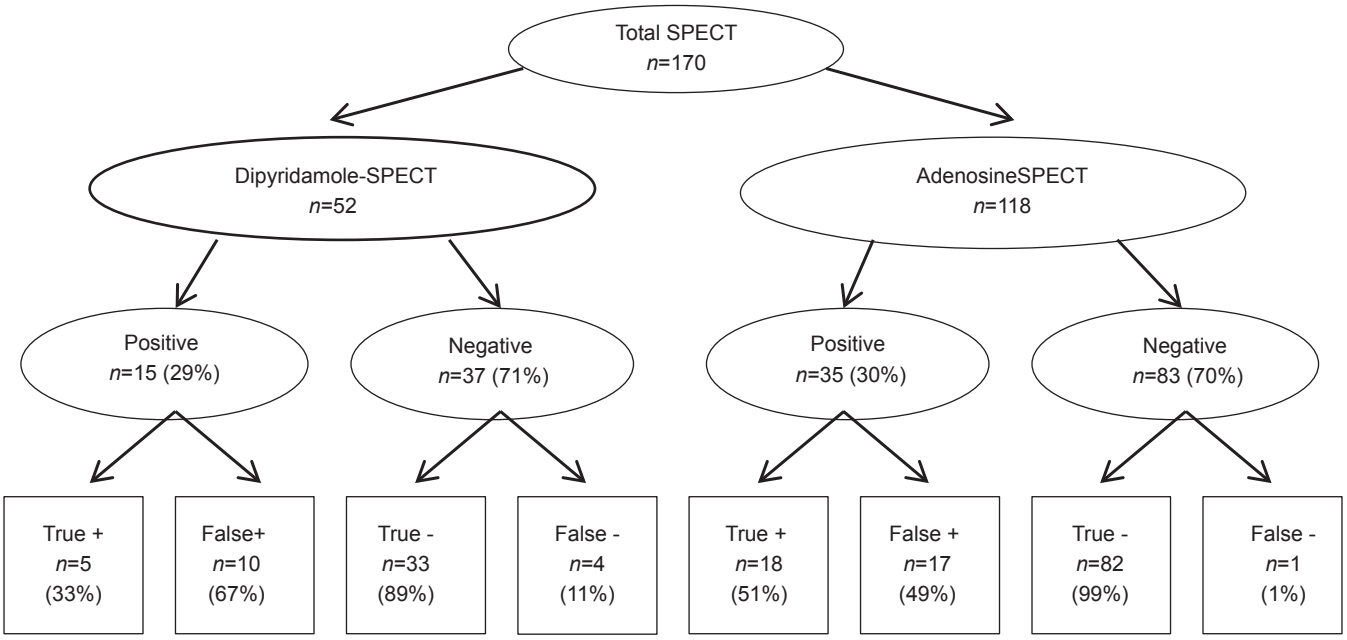


**Figure 2:** Patients enrolled in the study and submitted to Dipyridamole-SPECT or Adenosine-SPECT and outcomes. SPECT, Single Photon Emission Computed Tomography

**Table 2: Predictive parameters of primary endpoint at univariate analysis and multivariate logistic regression analysis by backward stepwise**

| Parameters | OR | Univariate analysis Confidence interval 95% | P | OR | Multivariate analysis Confidence interval 95% | P |
|---|---|---|---|---|---|---|
| Positive SPECT | 19.6 | 6.8-56.2 | <0.0001 | 13.3 | 4.1-42.8 | <0.001 |
| Hypertension | 4.6 | 1.0-21.2 | 0.048 | 6.4 | 1.3-32.4 | 0.025 |
| Nonischemic echocardiogrphy alterations | 7.7 | 1.6-36.7 | 0.010 | | | |
| Nonischemic ECG alterations | 1.7 | 0.6-5.1 | 0.337 | | | |
| Metabolic syndrome | 2.3 | 0.9-5.9 | 0.082 | | | |
| Diabetes mellitus | 1.8 | 0.7-4.5 | 0.219 | | | |
| Active smoker | 1.4 | 0.4-4.8 | 0.564 | | | |
| Familiarity | 0.8 | 0.2-3.0 | 0.819 | | | |
| Male gender | 0.64 | 0.27-1.52 | 0.307 | | | |
| High blood cholesterol | 0.61 | 0.2-1.9 | 0.437 | | | |

SPECT: Single photon emission computed tomography, OR: Odds ratio, ECG: Electrocardiography

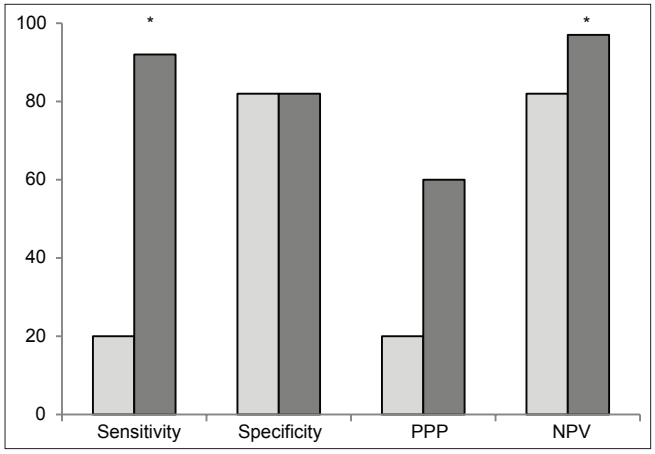


**Figure 3:** Predictive values (%) in patients submitted to Dipyridamole-SPECT or Adenosine-SPECT. SPECT, Single Photon Emission Computed Tomography. Light bars, Dipyridamole-SPECT; dark bars, Adenosine-SPECT; PPV, Positive Predictive Value; NPV, Negative Predictive Value; $^{*}P < 0.05$

**Table 3: Comparison of predictive values (%) in patients submitted to Dipyridamole-SPECT or Adenosine-SPECT and yield**

| | Dipyridamole-SPECT (*n*=52) | Adenosine-SPECT (*n*=118) | P | Yield (%) |
|---|---|---|---|---|
| Sensitivity, % | 56 | 95 | 0.026 | +70 |
| Specificity, % | 77 | 83 | 0.486 | +8 |
| Positive predictive value, % | 33 | 51 | 0.355 | +55 |
| Negative predictive value, % | 89 | 99 | 0.031 | +11 |

SPECT: Single photon emission computed tomography

**Table 4: Predictive values (%) in patients with hypertension or with nonischaemic echocardiography alterations submitted to dipyridamole-SPECT or adenosine-SPECT**

| SPECT | Patients with hypertension | | | Echocardiography alterations | | |
|---|---|---|---|---|---|---|
| | Sensitivity | PPV | NPV | Sensitivity | PPV | NPV |
| Dipyridamole | 20 | 20 | 82 | 50 | 75 | 75 |
| Adenosine | 92* | 60 | 97 | 100 | 100 | 100 |

*$P$<0.01, SPECT: Single photon emission computed tomography, PPV: Positive predictive value, NPV: Negative predictive value

Adenosine and dipyridamole are widely available pharmacologic agents for stress testing. Regadenoson, an adenosine analog, has a longer half-life than adenosine, and therefore a bolus versus continuous administration must be performed. However, regadenoson is not available worldwide. These drugs dilate coronary vessels, which causes increased blood velocity and flow rate in normal vessels and less of a response in stenotic vessels. This difference in response leads to a steal of flow, and perfusion defects appear in cardiac nuclear scans or as ST-segment changes. The mechanisms by which adenosine is produced intracellularly are the S- adenosyl homocysteine and the adenosine triphosphate pathways; the latter plays a role during ischemia. Adenosine activates the $A_1$ and $A_2$ cell surface receptors. In the vascular smooth muscles, adenosine primarily acts by activation of the $A_2$ receptor, which stimulates adenylate cyclase, leading to an increase in cyclic adenosine monophosphate (cAMP) production. Increased cAMP levels inhibit calcium uptake by the sarcolemma, causing smooth muscle relaxation and vasodilation. Activation of the vascular $A_1$ receptor also occurs, which stimulates guanylate cyclase, inducing cyclic guanosine monophosphate production, leading to vasodilation. In arteriosclerotic coronary arteries, a reduced coronary flow reserve exists and coronary arteries cannot further dilate in response to adenosine. A decrease in coronary blood flow may occur, and this regional flow abnormality also induces a perfusion defect during radionuclide imaging. Dipyridamole is an indirect coronary vasodilator that works by increasing intravascular adenosine levels. This occurs by the inhibition of intracellular reuptake and deamination of adenosine. The mechanism of inducing a perfusion abnormality is similar to that of adenosine except the fact that true coronary steal occurs more frequently. Regadenoson is a new pharmacologic stress agent approved by the FDA in 2008 as an additional agent for

use in stress testing for patients unable to perform the standard exercise stress test. Coronary vasodilation and an increase in coronary blood flow results from activation of the $A_{2A}$ adenosine receptor by regadenoson.

Several authors demonstrated nuclear scan strategy should allow effective separation of high-risk patients who need admission from very low-risk patients who can be safely discharged, and added prognostic value to results of clinical observation and exercise ECG.[6,9,13,20] In addition, results of stress-SPECT improve when they are subjected to gated analysis, and the final analysis refers to only two groups of patients with any hypoperfused segment associated with wall motion abnormality.[12,19] In our series, stress-SPECT likely demonstrated high sensitivity and high NPV according to the best of literature data.[6,9,13] The sensitivity and specificity of stress-SPECT for obstructive coronary disease have been reported to be up to 87% and 73%, respectively, both in outpatient clinics and in CP units.[12,19] Although, this high sensitivity is an advantage, it could also results in the detection of coronary disease in the absence of acute coronary syndrome more frequently than with exercise-ECG. This fact could lead to hospitalization of patients with stable disease. The relatively low specificity in our series, in our opinion, is related to the endpoint consisting in coronary stenosis >50% rather than obstructive stenosis >70%. We chose this low cut-off of coronary stenosis because , in the emergency setting and in daily clinical care, physicians need to separate high-risk from very low-risk patients. Thus, the role of nuclear scan strategy could be extended from the simple ruling out of acute myocardial ischemia to the wider detection of coronary artery disease. Eventually, the scan strategy could be considered cost-effective in patients at risk of short-term coronary events when early discharge is the main priority.

Of note, the major reasons for subjecting patients to pharmacological nuclear scan rather than exercise-ECG usually include the presence of baseline ECG alterations like as bundle-branch block and pacing. Additional general reason to choose a nuclear scan evaluation is the need to quantify the ischemic area. However, our data demonstrated that, patients presenting basal nonischemic echocardiography alterations when compared with patients without, could benefit of scan strategy because they showed eight-fold risk of adverse events. Finally, also hypertensive patients with eventually structural heart disease could benefit of scan strategy because of high sensitivity and NPV in this subset of patients with 5-fold risk of adverse events. Other studies indicate the potential cost-effectiveness of MPI related to a decrease in the number of patients requiring admission and by a more appropriate selection of diagnostic procedures; the rate of coronary angiography in low-risk patients can also be reduced.

In view of the relatively limited availability of nuclear imaging and economic issues, selection of patients who could effectively benefit from a nuclear scan strategy represents an attractive option, especially in the emergency department of a crowded public health care delivery setting. Thus, the results of this study update the diagnostic implementation of costly nuclear scan strategy with stress adenosine-SPECT over dipyridamole-SPECT in patients unable to exercise and presenting a poor acoustic window, eventually with hypertension or nondiagnostic echocardiography alterations.

### Limitations of the study

The presence of both perfusion defects and abnormal wall motion analysis to consider as positive an otherwise equivocal nuclear scan, which was aimed to reduce false positives, could result in overestimating mild ischemia images. Thus, the relatively low PPV of pharmacological-SPECT in our series could be due to an overestimation of perfusion defects as nontransmural myocardial perfusion defects (minimal perfusion abnormalities of suspected diaphragmatic or breast attenuation artifacts or equivocal attenuation). Sometimes, the resolution of the technique cannot distinguish subendocardial from a full-thickness defect. In addition, The outcome evaluation based on dichotomy (normal/abnormal tests) and the need of subjecting patients to coronary angiography may be a limitation of any screening workup. However, in emergency setting and in CP patients, physicians need to consider to incorporate nuclear scan technology into daily clinical care, which aims to admit or discharge the patient.

The results of this cohort of patients are not extensible to a symptomatic general population, because of the exclusion of patients with a prior diagnosis of coronary artery disease, resting echocardiographic moderate-to-severe left ventricular dysfunction, or regional moderate-to-severe wall motion abnormalities. In addition, small areas of ischemic myocardium (3-5% of the left ventricle) may not be detected by MPI. The results of this study were obtained from single center patients and need validation in other centers. Thus, the optimal use of pharmacological stress SPECT in patients with CP and nondiagnostic ECG needs to be confirmed in a properly designed study beyond the preliminary results of this analysis.

## Conclusion

Nuclear scan strategy with adenosine-SPECT adds incremental prognostic value over dipyridamole-SPECT in CP patients with serial normal ECG and normal troponin who are unable to perform physical stress. Costly scan strategy is more appropriate in special populations including patients with hypertension and

with nonischemic echocardiography alterations. In these patients, stress-MPI is effective in separating high-risk patients who need admission from very low-risk patients who may be discharged, eventually saving time and avoiding unnecessary angiograms or hospitalizations.

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**How to cite this article:** Conti A, Mariannini Y, Canuti E, Petrova T, Innocenti F, Zanobetti M, *et al*. Nuclear Scan Strategy and Outcomes in Chest Pain Patients Value of Stress Testing with Dipyridamole or Adenosine. World J Nucl Med 2014;13:94-101.

**Source of Support:** Nil, **Conflict of Interest:** None declared.