

Influence of cardiac stress protocol on myocardial perfusion imaging accuracy: The role of exercise level on the evaluation of ischemic burden

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Background. Some specifics of cardiac stress protocols, i.e., stressor used or exercise level achieved, may impact myocardial perfusion imaging (MPI) accuracy.

Methods. Four-hundred and seventy-five patients were submitted to MPI and coronary angiography. MPI was performed after exercise (303 patients) or dipyridamole stress (172 patients). A coronary stenosis $\geq 70\%$ was considered significant. In case of exercise test, a peak heart rate (HR) $< 85\%$ of the maximal age predicted was considered submaximal and categorized as follows: $> 75\%$ and $< 85\%$ (“Group 1”); $< 75\%$ (“Group 2”).

Results. At coronary angiography, 312/475 (66%) patients showed significant stenosis. In the overall population, MPI showed a high accuracy in unmasking significant coronary stenosis, independently of the stress protocol adopted (AUC .76 for exercise vs .78 for vasodilator; $P = \text{NS}$). However, in case of an exercise stress test, a significant interaction between peak %HR and MPI diagnostic power was evident. While an elevated accuracy was still maintained in “Group 1” patients (AUC .79; P vs maximal exercise = NS), a significant drop was demonstrated in “Group 2” patients (AUC .66; P vs maximal exercise = .012, and P vs “Group 1” = .042).

Conclusions. The accuracy of MPI is not influenced by the stress protocol adopted. Exercise MPI maintains an elevated accuracy as long as the %HR remains $> 75\%$. (J Nucl Cardiol 2016;23:1114–22.)

Key Words: Myocardial perfusion imaging • ischemic heart disease • exercise stress test • pharmacological stress test • CZT

See related editorial, pp. 1123–1127

INTRODUCTION

Myocardial perfusion imaging (MPI) on single-photon emission computed tomography (SPECT) is considered as a reference method for the evaluation of patients with suspected or known coronary artery disease (CAD),¹ offering the opportunity to combine a semi-quantitative assessment of regional myocardial perfusion and to derive measures of the hemodynamic relevance of a coronary stenosis.² When performed in association with an exercise stress test, SPECT-MPI allows integrating left ventricular (LV) perfusion and functional information with the assessment of relevant measures of patients

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global cardio-respiratory fitness and effort tolerance, which in turn may predict adverse outcome.^{3,4}

Nevertheless, despite the theoretical superiority of an exercise stress test, a relevant proportion of MPI evaluations is performed under a pharmacological stressor, i.e., a vasodilator, that gives the chance to perform a standardized stress protocol also in patients with contraindication to exercise testing, i.e., non-interpretable ECG, or unable to exercise sufficiently.⁵

To this respect, it is classically believed that in the case of a submaximal exercise protocol, i.e., with <85% of the predicted maximal heart rate (HR), the accuracy of SPECT-MPI would fall significantly, due to a higher incidence of false-negative results.^{6,7} Specifically, in these cases, a pharmacological stressor is generally considered as a more reliable test for the evaluation of ischemic susceptibility.^{5,8}

However, although a similar accuracy in unmasking the presence of relevant CAD has been reported, the two stress test modalities are characterized by a significantly different prognostic impact, since an exercise SPECT appears to better predict patients' long-term outcome.⁹

Moreover, some studies have also suggested how SPECT-MPI may still hold an acceptable diagnostic accuracy also when performed after a submaximal exercise stress test.^{10–12}

To this respect, despite some previous evidences,^{11,12} a consistent evaluation of the effects of cardiac stress protocol parameters, i.e., exercise tolerance, on MPI diagnostic accuracy in a large population of patients with suspected ischemic heart disease (IHD) is still warranted.

We sought to assess the relationships between cardiac stress protocols and MPI diagnostic accuracy in patients with suspected or known CAD and to determine the interaction among exercise tolerance and MPI-related diagnostic power.

MATERIALS AND METHODS

Patient Population

Among the patients referred to our institution between 2011 and 2014 for myocardial scintigraphy on a cadmium-zinc-telluride (CZT) camera followed by coronary angiography, we retrospectively selected all the subjects (475 patients) with anginal chest pain and known (160 patients, 34%) or suspected CAD (315 patients, 66%). Specifically, 85 patients (all with normal ejection fraction (EF) and a summed stress score <5) were submitted to computed tomography (CT) coronary angiography, while the remaining 390 underwent invasive coronary angiography, according to our routine clinical protocol and/or as indicated by the referring physicians. A coronary stenosis $\geq 70\%$ was considered significant. The time interval between coronary angiography and CZT study was ≤ 3 months. Exclusion criteria were hemodynamic instability, severely

symptomatic heart failure, myocardial inflammatory disease, and more than moderate valvular disease. The study was approved by the Local Ethical Committee and conformed to the Declaration of Helsinki on human research. Written informed consent was obtained from every patient after explanation of the protocol, its aims, and potential risks.

Stress Protocols

Patients discontinued beta-blockers, calcium-antagonists, and nitrates from 24 to 48 hour before testing. Three-hundred and three patients (64%) underwent symptom-limited bicycle exercise test (stepwise increments of 25 W every 2 minute) while 172 patients (36%) dipyridamole stress testing (.56 mg/kg IV over 4 minute). Of the patients undergoing exercise stress test, 95 reached >85% of the age-predicted maximum HR, while 208 did not. Among those, in 129 (62%) patients, exercise test was ended because of stress-induced severe chest pain and/or significant ST segment depression. The stress protocol was completed in each patient without adverse events. In each patient, the rate pressure product at peak stress (HR \times systolic blood pressure) was computed and considered maximal if $\geq 30,000$.¹³

Acquisition Protocol

Patients underwent stress/rest CZT (Discovery NM 530c; GE Healthcare, Haifa, Israel) imaging according to a single-days protocol with the administration of 185–222 MBq of ^{99m}Tc-tetrofosmin during stress and 370–444 MBq at rest. Patients with known prior myocardial infarction were injected at rest after sublingual administration of nitrates.^{14,15}

Stress-CZT imaging was performed 10–15 minute after injection of the radiopharmaceutical with an acquisition time of 7 minute. Patients were injected at rest 30 minute after the end of the first acquisition and then after an interval of 30–45 minute, a second acquisition was carried out for 6 minute. Image acquisition times were calculated in order to obtain a number of counts generally acquired by the same CZT camera after a standard tracer injection.¹⁴ Patients were imaged in the supine position with arms placed over their head without any detector or collimator motion. All images were acquired with a 32 \times 32 matrix and a 20% energy window centered at the 140 keV photopeak of ^{99m}Tc (pixels width 4 mm).

List mode files were acquired, and images were reconstructed on a standard workstation (Xeleris II; GE Healthcare, Haifa, Israel) using a dedicated iterative algorithm with 50 iterations.¹⁵ A Butterworth post-processing filter (frequency .37, order 7) was applied to the reconstructed slices. The tomographic studies were also re-projected into 60 planar projections to emulate a standard SPECT layout. Images were reconstructed without scatter or attenuation correction.

Analysis of Perfusion Images

Perfusion images were semi-quantitatively scored according to the 17-segment LV model and a five-point scale (0-normal, 1-equivocal, 2-moderate, 3-severe reduction in radioisotope uptake, and 4 absence of detectable tracer uptake)

and the summed stress score and summed rest score were calculated. Accordingly, the summed difference score (SDS), a measure of stress-induced reversible myocardial ischemia, was computed in every patient and considered pathological if >3 .¹⁶ The same analysis was performed on a per-vessel basis and the difference score of each coronary territory calculated. Two experienced nuclear cardiologists performed the semi-quantitative analysis independently, and consensus was reached on all analyses.

Analysis of Gated Images

LV functional analysis was performed on 16-frame reformatted images using commercially available software (Corridor4DM, Invia, Ann Arbor, MI). End-diastolic volume (EDV), end-systolic volume, EF, and peak filling rate (PFR, EDV second⁻¹) were calculated in every patient^{15,17,18} both at rest and during stress. In order to quantitate the magnitude of stress-induced LV functional impairment, the “% Stress-to-Rest” ratios of EF and PFR were calculated.

Invasive and CT Coronary Angiography

Invasive coronary angiography was performed using standard techniques and multiple projections. Coronary angiograms were quantified with a dedicated computer software (Advanced Vessel Analysis, Innova 3DXR for Advanced Workstations; GE Healthcare) using an automatic edge-contour detection algorithm to compute stenosis severity. CT coronary angiography was performed on a 64-slice scanner (GE Discovery VCT; GE Healthcare) or on a 320-slice scanner (Aquilion one, Toshiba). The data were then transferred to dedicated workstations for post-processing. Stenosis severity was measured on Multiplanar Reformatting Images using an automatic interactive program to quantify coronary luminal narrowing and expressed with intervals of 5%.¹⁹ In vessels showing multiple stenosis in series, only the most severe was considered.

Statistical Analysis

Continuous variables were expressed as mean \pm SD and categorical variables as percentages. Groups were compared for categorical data using Fisher’s exact test and for continuous variables using analysis of variance followed by Fisher’s protected least significant difference for multiple comparisons. All tests were 2-sided; a $P < .05$ was considered significant. The accuracy of CZT-derived SDS in unmasking the presence of significant coronary stenosis was assessed at receiving operating characteristic (ROC) analysis and the area under the curve (AUC) and the relative 95% CI were determined. Specifically, the interaction between specific stress protocols, exercise vs vasodilator test, and CZT accuracy was determined. Moreover, in patients submitted to an exercise stress test, the impact of exercise level and diagnostic accuracy was determined. Therefore, patients with a submaximal exercise ($<85\%$ of predicted maximal HR) were divided according to the median value of %HR distribution and categorized as

follows: “Group 1” ($<85\%$ and $>75\%$ of predicted %HR), and “Group 2” ($<75\%$ of predicted %HR).

Statistical analyses were performed using JMP (SAS Institute Inc, version 4.0.0) and Stata (version 13, StataCorp, College Station, TX).

RESULTS

Characterization of the Population

The characteristics of the overall study population are reported in Table 1. As expected, patients who underwent a vasodilator stress test were significantly older ($P < .001$) and relatively more obese ($P = .003$) than those submitted to an exercise test. At coronary angiography, 312/475 (66%) patients presented a significant coronary stenosis in one (129, 41%), two (106, 34%), or three (77, 25%) vessels with no significant difference between the two patients categories. Specifically, coronary findings at CT and invasive angiography, as considered separately, are reported in Table 2.

Association Between Stress Protocol and MPI Accuracy: Exercise Vs Vasodilator

In the overall population, a significant association between increasing CAD extent and more impaired measures of myocardial perfusion and function was evident (Table 3). Accordingly, the interaction among the different MPI stress protocols and patients clinical and functional variables was further investigated. There was not any significant difference regarding resting LV functional parameters between patients who underwent an exercise or a vasodilator stress test (Table 4). However, patients submitted to an exercise test more frequently showed signs of myocardial ischemia on stress ECG ($P = .008$) as well as significantly higher values of SDS and stress-induced LV functional impairment (Table 4). Interestingly, the difference in terms of ischemic burden on MPI between exercise and vasodilator stress was limited to patients with multi-vessel disease (SDS: 7 ± 4 in vasodilator vs 8 ± 4 in exercise stress, $P = .05$) while disappeared in those with single-vessel CAD.

Nevertheless, at ROC analysis (Figure 1), the two stress modalities showed a similar accuracy in unmasking the presence of significant coronary stenosis.

Interaction Among Exercise Level and MPI Accuracy

Of the 208 patients who performed a submaximal exercise level, 103 attained a %HR $>75\%$ (“Group 1”), while 105 were injected despite a %HR $<75\%$ (“Group 2”).

Table 1. Characteristics of the study population

Parameter	Overall (475 patients)	Exercise stress test (303 patients)	Vasodilator stress test (172 patients)	<i>P</i> value
Demographics and CV risk factors				
Age (years)	69 ± 10	67 ± 10	72 ± 9	<.001
Male gender, <i>n</i> (%)	367 (77)	239 (79)	128 (74)	.305
Pre-test probability of CAD, %	65 ± 17	67 ± 13	63 ± 20	.492
Family history of CAD, <i>n</i> (%)	153 (32)	95 (31)	58 (34)	.610
Diabetes, <i>n</i> (%)	189 (40)	128 (42)	61 (35)	.172
Hypercholesterolemia, <i>n</i> (%)	244 (51)	160 (52)	84 (49)	.445
Hypertension, <i>n</i> (%)	336 (71)	207 (63)	129 (73)	.142
Smoking, <i>n</i> (%)	64 (13)	42 (14)	22 (13)	.781
Body mass index	29 ± 5	29 ± 5	30 ± 6	.003
Coronary anatomy				
Normal coronary arteries, <i>n</i> (%)	163 (34)	94 (31)	69 (40)	.100
Single-vessel disease, <i>n</i> (%)	129 (27)	83 (27)	46 (27)	
Multi-vessel disease, <i>n</i> (%)	183 (39)	126 (42)	57 (33)	

P values < .05 should be reported in bold

Table 2. Coronary anatomy on invasive and CT angiography

Parameter	Invasive angiography (390 patients)	CT angiography (85 patients)	<i>P</i> value
Coronary anatomy			.004
Normal coronary arteries, <i>n</i> (%)	120 (31)	43 (51)	
One-vessel disease, <i>n</i> (%)	108 (28)	21 (25)	
Two-vessel disease, <i>n</i> (%)	95 (24)	11 (13)	
Three-vessel disease, <i>n</i> (%)	67 (17)	10 (11)	

The latter patients were significantly older (69 ± 9 years and 66 ± 9 years for “Group 2” and “Group 1,” respectively) and more frequently obese (31% and 35%, for “Group 1” and “Group 2,” respectively) than subjects that performed a maximal exercise (66 ± 10 years and 20% obese; *P* < .05 for both). No significant difference in the incidence of stress-induced clinical or ECG-graphical signs of ischemia was evident between the groups. Similarly, no significant difference in the extent of significant CAD was evident between “Group 2” patients and those who performed a maximal exercise. As expected patients, individual RPP at peak stress was strictly related to the attained exercise level (25,777 ± 4405 bpm-mmHg in patients with a maximal exercise, 21,178 ± 4849 bpm-mmHg

in “Group 1”, and 117,543 ± 4388 bpm-mmHg in “Group 2”; *P* < .001), with only 2/103 (2%) and 0/105 (0%) patients reaching a RPP ≥ 30,000 in “Group 1” and “Group 2,” respectively.

The interaction among exercise level and CZT accuracy in unmasking significant CAD was assessed (Figure 2). While “Group 1” patients showed a similar diagnostic accuracy as those with a maximal exercise, in patients with significantly impaired HR response (“Group 2”), MPI diagnostic power was considerably diminished because of a significantly lower sensitivity (71% in “Group 2” vs 85% in “Group 1” and 84% in “maximal exercise”; *P* = .023 vs “Group 1” and *P* = .044 vs “maximal exercise”). To this respect, in

Table 3. Relationship between MPI data and coronary anatomy

Parameter	Normal coronary arteries (163 patients)	Single-vessel disease (129 patients)	Multi-vessel disease (183 patients)	P value
Myocardial perfusion				
Summed rest score, <i>n</i>	1 ± 3	4 ± 5 ^{**} , ^{††}	6 ± 7 ^{**} , ^{††}	<.001
Summed stress score, <i>n</i>	4 ± 4	9 ± 5 ^{**} , ^{††}	14 ± 7 ^{**} , ^{††}	<.001
Summed difference score, <i>n</i>	3 ± 2	5 ± 3 ^{**} , ^{††}	7 ± 4 ^{**} , ^{††}	<.001
Left ventricular systolic function				
Ejection fraction at rest, %	56 ± 13	53 ± 14	52 ± 15 ^{**}	.017
Ejection fraction after stress, %	57 ± 12	53 ± 14	50 ± 15 ^{**} , [†]	<.001
“Stress/rest” ejection fraction, %	99 ± 8	99 ± 11	95 ± 10 ^{**} , ^{††}	<.001
Left ventricular diastolic function after stress				
Peak filling rate at rest, mL	2.7 ± .7	2.5 ± .7 ^{**}	2.3 ± .7 ^{**}	<.001
Peak filling rate after stress, mL	2.8 ± .8	2.4 ± .7 ^{**}	2.3 ± .7 ^{**} , [†]	<.001
“Stress/rest” peak filling rate, %	106 ± 25	100 ± 21 [*]	96 ± 19 ^{**}	<.001

* *P* < .05 and ** *P* < .01 vs “normal coronary arteries”

† *P* < .05 and †† *P* < .01 vs “single-vessel disease”

“Group 2” patients, the underestimation of the ischemic burden was particularly evident in the presence of multi-vessel CAD (Figure 3).

Interestingly, as the analysis was limited to the patients with submaximal exercise but clinical evidence of stress-induced myocardial ischemia (angina and/or ST segment depression), CZT-MPI presented a similar accuracy in unmasking significant CAD in both “Group 1” (AUC .84, 95% CI .73-.92) and “Group 2” (AUC .76, 95% CI .63-.85; *P* = NS) subjects. On the other hand, in patients in whom exercise was ended because of fatigue the accuracy of CZT-MPI was significantly higher in “Group 1” (AUC .74, 95% CI .62-.83) than in “Group 2” (AUC .54, 95% CI .41-.67, *P* = .04) patients.

DISCUSSION

Our study shows that MPI performed on a dedicated CZT camera has an elevated accuracy in unmasking the presence of significant CAD, independently from the stress protocol employed. Specifically, the present results suggest that an excellent diagnostic power is maintained also in the case of a moderately submaximal exercise stress test, as long as the 75% of the maximal predicted HR is reached.

MPI and CAD: The Value of the Stress Test Protocol

MPI on SPECT has become a reference for the non-invasive estimation of the presence of significant CAD,⁵

allowing an accurate evaluation of regional myocardial blood flow regulation together with quantitative measures of LV function.^{1,15,17} To this respect, when combined with an exercise stress test, MPI offers the chance to acquire information on both individual ischemic threshold and on key parameters of patients’ effort tolerance, allowing deriving prognostically relevant measures of patients’ cardio-respiratory fitness.^{3,4}

Nevertheless, in a relevant proportion of patients (as high as 26%), an exercise stress test is not clinically feasible⁹; in this case, a pharmacological stress test, generally through a coronary vasodilator, may offer a similar accuracy in unmasking significant CAD.⁵

Our study sought to compare the relative accuracy of the two main MPI stress test protocols in the detection of significant CAD with the use of a novel dedicated camera equipped with stationary CZT detectors. As a matter of fact, those cameras are characterized by a significantly higher photon sensitivity and spatial resolution than standard SPECT devices, theoretically offering a more accurate evaluation of regional myocardial perfusion, despite a rapid acquisition time and a significantly reduced radiation burden.^{14,20}

The present results confirmed the elevated accuracy of MPI in unmasking significant CAD, independently from the stress protocol used. Interestingly, the accuracy of CZT-MPI was maintained also in patients with a moderately reduced exercise tolerance (75% < %HR < 85%) even in the absence of clinical evidences of myocardial ischemia, suggesting its possible clinical role also in patients with a submaximal exercise stress test.

Table 4. Relationship between stress protocol and MPI-related parameters

Parameter	Overall (475 patients)	Exercise stress test (303 patients)	Vasodilator stress test (172 patients)	P value
Symptoms and ECG changes				
Stress-induced typical angina, n (%)	174 (37)	112 (37)	62 (36)	.921
Positive ECG during stress, n (%)	134 (28)	98 (32)	36 (20)	.008
Myocardial perfusion				
Summed rest score	4 ± 6	4 ± 5	4 ± 6	.523
Summed stress score	9 ± 7	10 ± 7	9 ± 7	.331
Summed difference score	5 ± 4	6 ± 4	5 ± 4	.006
Left-ventricular Systolic function				
Ejection fraction at rest, %	54 ± 14	54 ± 14	52 ± 14	.088
Ejection fraction after stress, %	53 ± 14	53 ± 14	53 ± 14	.578
“Stress/rest” ejection fraction, %	98 ± 10	97 ± 10	99 ± 9	.017
Left-ventricular diastolic function after stress				
Peak filling rate at rest, mL	2.5 ± .7	2.5 ± .7	2.4 ± .7	.153
Peak filling rate after stress, mL	2.5 ± .8	2.5 ± .8	2.5 ± .8	.877
“Stress/rest” peak filling rate, %	101 ± 22	98 ± 15	106 ± 31	<.001

P values < .05 should be reported in bold

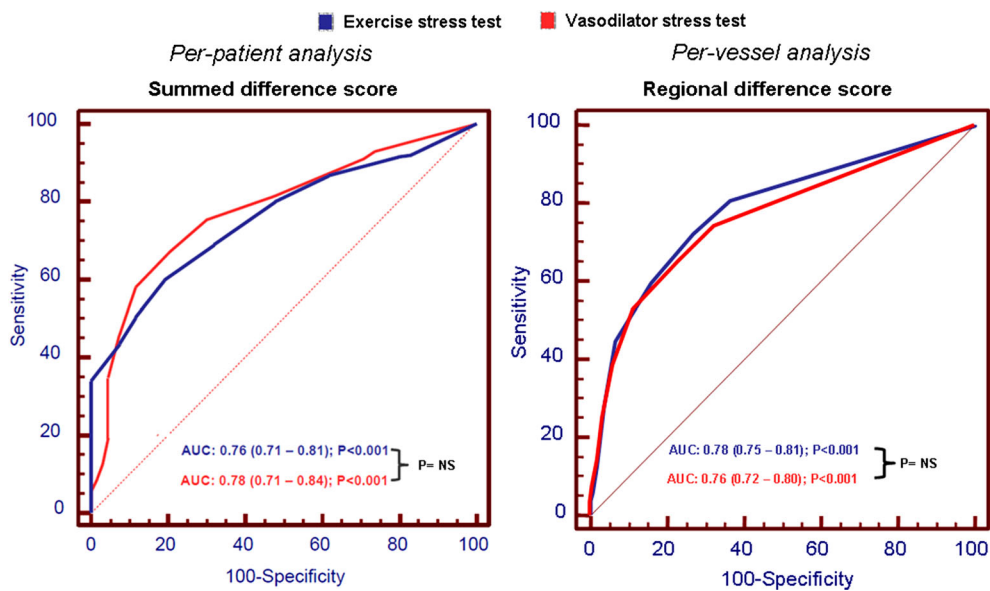


Figure 1. Accuracy of CZT-MPI in unmasking the presence of significant coronary stenosis according to the adopted stress protocol at “per-patient” (left) and “per-vessel” (right) analyses.

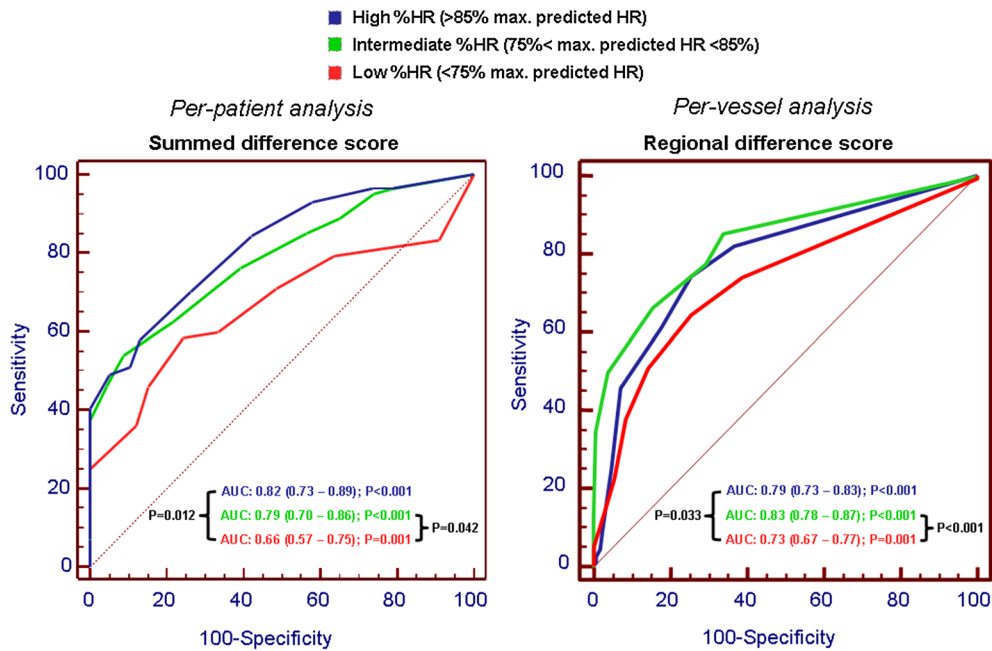


Figure 2. Accuracy of CZT-MPI detecting significant coronary stenosis according to patients exercise tolerance at ‘per-patient’ (left) and ‘per-vessel’ (right) analyses.

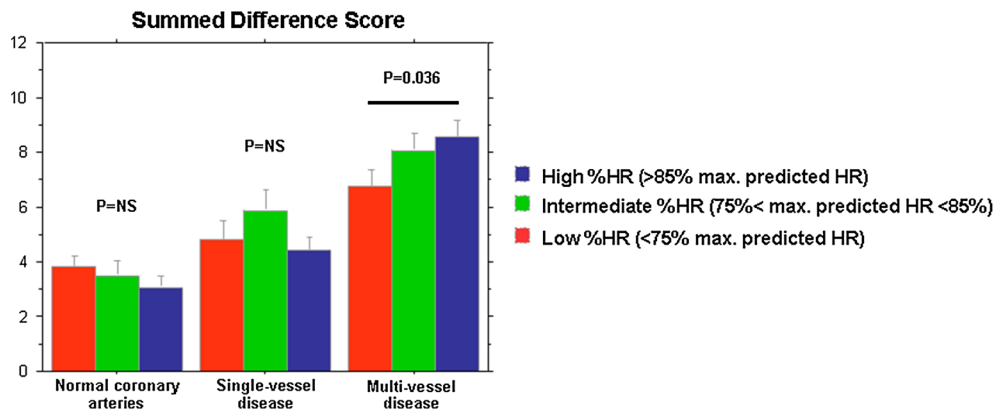


Figure 3. Relationships between the extent of coronary artery disease and summed difference score according to the patients individual exercise tolerance.

Cardiac Workload and MPI Accuracy

It is generally believed that a submaximal exercise stress MPI has a limited accuracy in detecting significant CAD,^{6,7} although this concept has been questioned by some.¹¹ Accordingly, in these patients, a pharmacological stress test is generally warranted, either alone or in conjunction with low-level exercise.^{7,21} On the other hand, the significant inferiority of vasodilator MPI with respect to exercise stress SPECT in terms of patients’ risk stratification has been repeatedly highlighted, and the clinical value of different accessorial information that an exercise stress test allows to obtain demonstrated.^{3,4,12,22}

As previously reported, despite the theoretical diagnostic limitations of a submaximal exercise stress test, in a relevant proportion of patients (as high as 1 every 4), the widely accepted boundary of the 85% of the predicted maximal HR is not reached due to symptoms or physical exhaustion,⁸⁻¹⁰ making the trade-off between reduced diagnostic power and enhanced patients risk stratification, a clinically relevant question. Interestingly, it could be possible that the relatively superior accuracy and photon sensitivity of the recently introduced CZT-dedicated cardiac cameras^{14,18} could help to partially overcome these limitations, allowing a ‘diagnostic’ MPI also in case of a relatively submaximal exercise level.

As a matter of fact, our data indicate that in a relevant proportion of patients with a nominally submaximal exercise level, the diagnostic accuracy of a state-of-the-art MPI with a novel CZT camera is maintained. On the other hand, in case of a significantly reduced cardiac workload, such as when <75% of the maximal HR is reached, a significant drop in accuracy is demonstrated because of a significantly lower diagnostic sensitivity. Specifically, our results indicate that, in the presence of clinical evidences of myocardial ischemia, the accuracy of exercise MPI remains elevated independently from the attained exercise level. On the other hand, in patients in whom exercise is terminated because of fatigue an acceptable accuracy is maintained as soon as the 75% of the predicted maximal HR is reached.

These results suggest that the conversion to a pharmacological stress test might be omitted in the case of a moderately submaximal exercise tolerance, allowing obtaining this exercise-related accessorial information on cardio-respiratory fitness also in patients usually submitted to a pharmacological stress test. This consideration might hold particularly true when a dedicated cardiac CZT camera is used for MPI since its increased sensitivity might allow a better assessment of myocardial ischemic burden also in patients with relatively submaximal exercise stress test. On the other hand, in patients who reach less than the 75% of the target HR without clinical signs of ischemia, the administration of low doses of atropine might increase MPI accuracy⁷ even though the predicted maximal HR is not reached, allowing to improve the diagnostic power in detecting CAD.

Interestingly, in the present study, CZT-MPI showed a relatively lower accuracy than previously reported.¹⁴ This result may be related to the fact that in our study, MPI was considered positive only in the presence of reversible myocardial ischemia. In fact, while the inclusion of myocardial scar as a diagnostic criterion would have increased the diagnostic power of MPI, ischemia represents by far a more clinically indicated measure of abnormal myocardial perfusion.

LIMITATIONS

The retrospective nature of the study may introduce the problem of a possible selection bias of the patients. However, as all the consecutive anginal patients submitted to CZT-MPI and coronary angiography were selected, the impact of this limitation should be considered low. Moreover, due to the consistent number of patients studied, the present data represent a close picture of the actual population of subjects submitted to MPI. The evaluation of post-stress measures of LV systolic and diastolic function is performed 10-15 minute after stress completion, probably underestimating the

real magnitude of stress-induced LV functional impairment. However, considering the intrinsic timing of the present imaging protocol, a more precocious assessment of LV function seems unrealistic.

Moreover, in patients with preserved LV systolic function and limited myocardial ischemia (18% of the population), coronary anatomy was evaluated only at CT coronary angiography and some coronary stenoses could have been overlooked. Since this study was performed on a dedicated cardiac camera equipped with a relatively new technology of stationary CZT detectors, the present results might not be directly transferred to tradition SPECT devices. For instance, the specifics of the acquisition protocol employed and the radionuclide doses injected in the present study have been already validated in CZT cameras^{14,15,17,18} but cannot be adopted when traditional SPECT devices are adoperated.⁵ Finally, in the present study, the gold-standard used for the assessment of MPI accuracy was entirely anatomical. To this respect, we recognize that the use of a functional reference standard, such as invasive fractional flow reserve, would have better depicted the hemodynamic severity of a given coronary lesion. Accordingly, a relatively conservative positivity criterion for coronary angiography ($\geq 70\%$ stenosis) was selected in order to better identify only the clinically relevant coronary lesions.²³

CONCLUSIONS

In patients with suspected IHD, MPI offers an elevated accuracy in unmasking the presence of significant CAD independently of the stress test protocol employed, i.e., exercise or vasodilator. A significant diagnostic power is maintained also in the case of a mildly submaximal exercise stress test as soon as a >75% of the predicted maximal HR is reached. These results might lead to a better protocol selection in patients submitted to MPI, expanding the indications of exercise test.

NEW KNOWLEDGE GAINED

In patients with suspected or known coronary artery disease, myocardial perfusion imaging showed an elevated accuracy in unmasking the presence of significant coronary stenosis, independently of the stress protocol employed, i.e., exercise vs pharmacological, and also in the case of a moderately submaximal exercise test.

Disclosure

Alessia Gimelli, Riccardo Liga, Emilio Maria Pasanisi, Mirta Casagrande, Michele Coceani, and Paolo Marzullo declare no relationships with industry or conflicts of interest.

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