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ORIGINAL RESEARCH

A Clinical Tool to Identify Candidates for Stress-First Myocardial Perfusion Imaging

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ABSTRACT

OBJECTIVES This study sought to develop a clinical model that identifies a lower-risk population for coronary artery disease that could benefit from stress-first myocardial perfusion imaging (MPI) protocols and that can be used at point of care to risk stratify patients.

BACKGROUND There is an increasing interest in stress-first and stress-only imaging to reduce patient radiation exposure and improve patient workflow and experience.

METHODS A secondary analysis was conducted on a single-center cohort of patients undergoing single-photon emission computed tomography (SPECT) and positron emission tomography (PET) studies. Normal MPI was defined by the absence of perfusion abnormalities and other ischemic markers and the presence of normal left ventricular wall motion and left ventricular ejection fraction. A model was derived using a cohort of 18,389 consecutive patients who underwent SPECT and was validated in a separate cohort of patients who underwent SPECT (n = 5,819), 1 internal cohort of patients who underwent PET (n=4,631), and 1 external PET cohort (n = 7,028).

RESULTS Final models were made for men and women and consisted of 9 variables including age, smoking, hypertension, diabetes, dyslipidemia, typical angina, prior percutaneous coronary intervention, prior coronary artery bypass graft, and prior myocardial infarction. Patients with a score ≤1 were stratified as low risk. The model was robust with areas under the curve of 0.684 (95% confidence interval [CI]: 0.674 to 0.694) and 0.681 (95% CI: 0.666 to 0.696) in the derivation cohort, 0.745 (95% CI: 0.728 to 0.762) and 0.701 (95% CI: 0.673 to 0.728) in the SPECT validation cohort, 0.672 (95% CI: 0.649 to 0.696) and 0.686 (95% CI: 0.663 to 0.710) in the internal PET validation cohort, and 0.756 (95% CI: 0.740 to 0.772) and 0.737 (95% CI: 0.716 to 0.757) in the external PET validation cohort in men and women, respectively. Men and women who scored ≤1 had negative likelihood ratios of 0.48 and 0.52, respectively.

CONCLUSIONS A novel model, based on easily obtained clinical variables, is proposed to identify patients with low probability of having abnormal MPI results. This point-of-care tool may be used to identify a population that might qualify for stress-first MPI protocols. (J Am Coll Cardiol Img 2020;13:2193–202) © 2020 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

3D = 3-dimensional

ASNC = American Society of Nuclear Cardiology

AUC = area under the curve

BMI = body mass index

CAD = coronary artery disease

CI = confidence interval

CZT = cadmium-zinc-telluride

MPI = myocardial perfusion imaging

OSEM = ordered-subset expectation maximization

PET = positron emission tomography

SPECT = single-photon emission computed tomography

Myocardial perfusion imaging (MPI) is commonly used for the diagnosis and risk stratification of patients with suspected coronary artery disease (CAD). Traditional single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are commonly performed at rest and with stress. However, there is an increasing interest in stress-first and stress-only imaging to reduce patient radiation exposure and improve patient workflow and experience.

Methods for identifying patients who are most likely to undergo successful stress-first imaging are required. Such methods should include the identification of patients who are most likely to have a normal stress MPI study and forgo rest imaging. The objective of this study was to derive and validate a model that could be easily applied at the "point of referral," which would identify a population more likely to have "normal" MPI and would potentially be candidates for stress-first protocols.

METHODS

Consecutive patients between December 1, 2010 and June 30, 2017 referred to SPECT and PET at the University of Ottawa Heart Institute were prospectively included in the MPI clinical databases. Patients with a history of cardiac transplant or congenital heart disease were excluded from the analysis. After exclusion criteria, 18,389 consecutive patients who underwent SPECT (2009 to 2015) were used as the derivation cohort and 5,819 consecutive patients who underwent SPECT (2015 to 2017) were used for validation. Additionally, 4,631 consecutive patients who underwent PET were used as a secondary validation cohort. Ethics approval was obtained from the Ottawa Health Science Network Research Ethics Board. Furthermore, 7,028 patients were enrolled between 2000 and 2009 and included in a multicenter PET registry (1-6) that was used as an external validation cohort. Ethics approval was obtained for each center, and all centers similarly collected standardized demographic data, medical history, and PET results.

As per clinical routine, patient demographic data, medical history, and cardiac risk factors were recorded for all patients at the time of MPI. Chest pain symptoms were recorded, and typical angina was defined as a composite of substernal location, exertional or emotional stress, and relieved by rest or with administration of nitroglycerin (7). Hypertension was defined as a systolic blood pressure >140 mm Hg or current treatment with antihypertensive medications. Diabetes was defined as a previous clinical diagnosis or current treatment with hypoglycemic medications. Hyperlipidemia was defined as known personal history of hyperlipidemia or current treatment with lipid-lowering agents.

STRESS PROTOCOL. Patients referred to SPECT MPI underwent either exercise (treadmill stress, Bruce protocol) or pharmacological stress, adhering to the American Society of Nuclear Cardiology (ASNC) guidelines and local dipyridamole administration practice (8,9). Pharmacological stress was performed using dipyridamole, and dobutamine stress was used in those with contraindications to vasodilator stress. Dipyridamole was infused at a rate of 0.14 mg/kg/min over 5 min in all cohorts as per local practice, as previously described (10,11). Patients who did not achieve target heart rate with exercise stress were subsequently converted to pharmacological stress. In occasions where pharmacological stress was

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contraindicated (e.g., allergy to dipyridamole), these patients would have been excluded.

SPECT IMAGE ACQUISITION PROTOCOL. SPECT MPI images were acquired in adherence to the ASNC guidelines. Technetium-99m tetrofosmin radiotracer was used with standard rest-stress SPECT protocols as per ASNC guidelines (9). Images were acquired using either dual-headed Na-I gamma cameras (Infinia with Hawkeye [GE Healthcare, Waukesha, Wisconsin] and e-CAM [Siemens Medical Systems, Siemens Healthineers AG, Erlangen, Germany]), or cadmium-zinc-telluride (CZT) cameras (Discovery NM, 530c, GE Healthcare) (Supplemental Table 1). The derivation cohort consisted of a mixture of full-dose studies until February 2012 and primarily half-dose studies after that date. For full-dose studies, the injected radiotracer activity was 300 MBq (8.1 mCi) at rest and 1,000 MBq (27 mCi) at stress for body mass index (BMI) <30 (male patients) or <25 (female patients) and increased to 350 MBq (9.5 mCi) at rest and 1,100 MBq (29.7 mCi) at stress for larger BMI patients. For BMI >30 (female patients) or >35 (male patients), a 2-day protocol was used with 1,100 MBq (29.7 mCi) injected at both rest and stress. The half-dose protocol used exactly one-half of the full-dose activity amounts.

Dual-headed gamma cameras used parallel-hole low-energy high-resolution collimators and acquired images at 25 s per projection for 60 (Infinia) or 64 (e-CAM) projections over 180° for both rest and stress images (full-dose protocol). For the half-dose protocol, acquisition times were changed to 30 s per projection (rest) and 20 s per projection (stress). Studies performed at full-dose tracer with the Infinia camera were reconstructed using an ordered-subset expectation maximization (OSEM) algorithm (2 iterations and 10 subsets for stress, 3 iterations and 4 subsets for rest), whereas half-dose Infinia images were reconstructed with a maximum a posteriori OSEM algorithm performed with Evolution for Cardiac software (GE Healthcare) using 8 iterations and 15 subsets (rest and stress). Post-reconstruction filtering was achieved with 3-dimensional (3D) Butterworth filtering (order 10, 0.3 cycles/cm cutoff) for both half-dose and full-dose Infinia studies. The e-CAM images were reconstructed using an OSEM algorithm (6 iterations, 16 subsets, Butterworth 3D filter with order 5, 0.43 cycles/cm) with Hermes software (Hermes Medical Solutions, Stockholm, Sweden) until July 2015 after which OSEM with resolution recovery (HRecon; Hermes Medical Solutions) was used with 5 iterations and 16 subsets and 3D Butterworth filtering (order 5, 0.32 cycles/cm cutoff).

TABLE 1 Baseline Characteristics of the Derivation Cohort

	All Comers (N = 18,389)	Normal SPECT (n = 11,712)	Abnormal SPECT (n = 6,677)	p Value
Age, yrs	63.9 ± 11.8	63.1 ± 11.7	65.21 ± 11.8	<0.001
BMI, kg/m^2	28.4 ± 5.7	28.3 ± 5.6	28.6 ± 5.7	0.001
Male	10,641 (57.8)	5,684 (48.4)	4,981 (74.4)	<0.001
Hypertension	11,586 (62.9)	6,768 (57.6)	4,824 (72.1)	<0.001
Diabetes	3,842 (20.9)	2,086 (17.8)	1,758 (26.3)	<0.001
Hyperlipidemia	10,507 (57.1)	5,956 (50.7)	4,572 (68.3)	<0.001
Current smoking	3,093 (16.8)	1,829 (15.6)	1,273 (19.0)	<0.001
Past smoking	6,512 (35.4)	3,900 (33.2)	2,624 (39.2)	<0.001
Family history	7,008 (38.1)	4,465 (38.0)	2,555 (38.2)	0.887
History of PCI	3,063 (16.6)	1,177 (10.0)	1,885 (28.2)	<0.001
History of CABG	1,396 (7.6)	404 (3.4)	993 (14.8)	<0.001
History of MI	3,355 (18.2)	1,091 (9.3)	2,264 (33.8)	<0.001
Typical angina	3,184 (17.3)	1,972 (16.8)	1,221 (18.2)	0.014
Pre-test probability	31.8 ± 31.3	30.3 ± 30.4	34.3 ± 32.6	<0.001
Dyspnea	9,548 (51.9)	6,012 (51.3)	3,531 (52.9)	0.044

Values are mean ± SD or n (%). The p values correspond to the comparison of normal vs. abnormal myocardial perfusion imaging subgroups.

BMI = body mass index; CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention; SPECT = single-photon emission computed tomography.

The CZT camera used 19 pinhole collimators and acquired stress and rest images for 3 and 5 min, respectively, for full-dose studies, or 6 and 10 min, respectively, when half-dose protocols were employed. Maximum a posteriori EM software (40 iterations for rest or 50 iterations for stress) and 3D Butterworth filtering (order 7, 0.37 cycles/cm) were used for image reconstruction.

PET IMAGE ACQUISITION PROTOCOL. PET MPI images were acquired using a Discovery 690 or 600 PET-CT scanner (GE Healthcare) with low-dose CT attenuation correction scans acquired at rest. Weight-based dosing of 8 to 10 MBq/kg rubidium-82 was used at rest and stress per ASNC guidelines. Dynamic PET imaging was started with the initial arrival of activity in the scanner field of view. Static (ungated) images were reconstructed from 2 to 8 min using the vendor iterative program (VuePoint HD) with 12-mm 3D Hann post-filter. Electrocardiogram-gated images (8 bins) were reconstructed from 1.5 to 8 min with 16-mm 3D Hann post-filter. External cohort PET image acquisition has been previously described (6).

MPI INTERPRETATION. Visual analysis of SPECT and PET images was performed using Corridor-4DM version 2012 (INVIA Medical Imaging Solutions, Ann Arbor, Michigan). Expert observers reviewed MPI studies and perfusion defects were graded using a 5-point scoring system (0 = normal, 1 = mild, 2 = moderate, 3 = severe, 4 = absent tracer uptake) on a standard 17-segment left ventricular model (7,12).

TABLE 2 Baseline Characteristics of the SPECT, UOHI PET, and External PET Validation Cohorts

	All Comers	Normal	Abnormal	p Value
		SPECT Validation Cohort		
	(n = 5,819)	**(n = 4,025)**	**(n = 1,794)**	
Age, yrs	64.8 ± 11.4	64.0 ± 11.3	66.8 ± 11.5	<0.001
Male	3,445 (59.2)	2,099 (52.1)	1,346 (75.0)	<0.001
BMI, kg/m^2	28.5 ± 6.3	28.5 ± 6.6	28.4 ± 5.4	0.620
Hypertension	3,620 (62.2)	2,244 (55.8)	1,376 (76.7)	<0.001
Diabetes	1,323 (22.7)	805 (20.0)	518 (28.9)	<0.001
Hyperlipidemia	3,452 (59.3)	2,118 (52.6)	1,334 (74.4)	<0.001
Current smoking	856 (14.7)	548 (13.6)	308 (17.2)	0.001
Past smoking	2,102 (36.1)	1,387 (34.5)	715 (39.9)	<0.001
Family history of coronary artery disease	2,348 (40.4)	1,607 (39.9)	741 (41.3)	0.296
History of PCI	1,106 (19.0)	466 (11.6)	640 (35.7)	<0.001
History of CABG	462 (7.9)	134 (3.3)	328 (18.3)	<0.001
History of MI	1,044 (17.9)	371 (9.2)	673 (37.5)	<0.001
Typical angina	1,114 (19.1)	693 (17.2)	421 (23.5)	<0.001
Pre-test probability	35.4 ± 31.9	33.4 ± 30.8	39.7 ± 34.0	<0.001
Dyspnea	3,205 (55.1)	2,210 (54.9)	995 (55.5)	0.819
		UOHI PET Validation Cohort		
	(n = 4,631)	**(n = 1,766)**	**(n = 2,865)**	
Age, yrs	63.9 ± 11.2	60.4 ± 11.1	66.1 ± 10.7	<0.001
Male	2,586 (55.8)	726 (41.1)	1,860 (64.9)	<0.001
BMI, kg/m^2	31.1 ± 7.5	31.9 ± 8.0	30.6 ± 7.1	<0.001
Hypertension	3,357 (72.5)	1,136 (64.4)	2,221 (77.5)	<0.001
Diabetes	1,405 (30.3)	427 (24.2)	978 (34.1)	<0.001
Hyperlipidemia	3,344 (72.2)	1,117 (63.3)	2,227 (77.7)	<0.001
Current smoking	701 (15.1)	240 (13.6)	461 (16.1)	0.023
Past smoking	2,208 (47.7)	770 (43.6)	1,438 (50.2)	<0.001
Family history of coronary artery disease	2,519 (54.4)	973 (55.1)	1,546 (54.0)	0.510
History of PCI	1,298 (28.0)	350 (19.9)	948 (33.2)	<0.001
History of CABG	534 (11.5)	87 (4.9)	447 (15.6)	<0.001
History of MI	1,337 (29.6)	275 (16.0)	1,062 (37.9)	<0.001
Typical angina	872 (18.8)	302 (17.1)	570 (19.9)	0.018
		External PET Validation Cohort		
	(n = 7,028)	**(n = 4,766)**	**(n = 2,262)**	
Age, yrs	63.3 ± 13.1	61.8 ± 13.1	66.5 ± 12.3	<0.001
Male	3,698 (52.6)	2,207 (46.3)	1,491 (65.9)	<0.001
BMI, kg/m^2	30.2 ± 7.3	30.2 ± 7.4	30.0 ± 7.1	0.174
Hypertension	4,764 (67.8)	3,077 (64.6)	1,687 (74.6)	<0.001
Diabetes	1,911 (27.2)	1,086 (22.8)	825 (36.5)	<0.001
Hyperlipidemia	4,485 (63.8)	2,876 (60.3)	1,609 (71.1)	<0.001
Smoking history	1,523 (21.7)	963 (20.2)	560 (24.8)	<0.001
History of PCI	1,220 (17.4)	563 (11.8)	657 (29.0)	<0.001
History of CABG	945 (13.4)	339 (7.1)	606 (26.8)	<0.001
History of MI	1,476 (21.0)	532 (11.2)	944 (41.7)	<0.001
Angina or dyspnea	4,523 (64.4)	3,131 (65.7)	1,392 (61.5)	0.001

Values are mean ± SD or n (%). The p values correspond to the comparison of normal vs. abnormal myocardial perfusion imaging subgroups.
PET = positron emission tomography; UOHI = University of Ottawa Heart Institute; other abbreviations as in Table 1.

A normal study was defined as the absence of perfusion abnormalities or other potential ischemic markers (transient ischemic dilatation, right ventricular uptake, etc.), and the presence of normal left ventricular wall motion and left ventricular ejection fraction. Patients with normal myocardial perfusion but failure to achieve their target heart rate with exercise stress were categorized as equivocal.

STATISTICAL ANALYSIS. Statistical analysis was performed using IBM SPSS software version 24 (IBM Corp., Armonk, New York). Using an outcome of "abnormal" SPECT study interpretation, univariate analysis was performed on demographic and clinical variables collected for all patients at time of testing (13). Using a cutoff of $p > 0.20$, the variables of age, BMI, sex, typical angina, current smoking, previous smoking, hypertension, diabetes, hyperlipidemia, family history of CAD, previous myocardial infarction, previous percutaneous coronary intervention, and previous coronary artery bypass graft were selected for multivariate analysis. In the multivariable logistic regression analysis, statistical significance was defined as $p < 0.05$, and variables within this limit were included in the final model. As per the Framingham Risk Score (14) and the method described by Le Gal et al. (15) for dichotomous variables, a scoring system was developed by assigning weighted points for each variable, and a total score was calculated for each patient. A receiver-operating characteristic curve was generated, and area under the curve (AUC) was calculated with 95% confidence interval (CI) to evaluate discrimination ability of the model against other established models.

RESULTS

A total of 18,389 consecutive rest-stress SPECT MPIs were used as the derivation cohort with a total of 63.7% interpreted as "normal." The mean age of this cohort was 63.9 years of age with a mean BMI of 28.4 and a male proportion of 57.8% (**Table 1**). The results were then validated in a separate cohort of 5,819 consecutive patients who underwent SPECT with similar demographic characteristics, as well as a second validation cohort of 4,631 consecutive patients who underwent PET, and then external validation was performed with a multicenter cohort of 7,028 patients who underwent PET (**Table 2**).

Based on the multivariable analysis (**Table 3**), age, sex, typical angina, smoking, hypertension, diabetes, hyperlipidemia, prior coronary artery bypass graft, prior percutaneous coronary intervention, and prior myocardial infarction were included in the final predictive model (**Table 4**) and points were assigned based on regression coefficients. Multivariate analysis for each sex as a subgroup produced 2 very similar scoring models, with the only difference being the inclusion of typical angina in men only (1 point) and dyslipidemia in women only (1 point), as well as an additional age category in men (55 to 69 years of age). The predictive probability of an abnormal MPI was calculated for each score along with respective positive and negative likelihood ratios (Supplemental Table 2).

The AUC of the receiver-operating characteristic of the derived model was 0.684 (95% CI: 0.674 to 0.694) and 0.681 (95% CI: 0.666 to 0.696) for men and

TABLE 3 Multivariate Analysis Predicting Non-Normal SPECT in Men and Women

	Beta Coefficient	SE	OR	Lower CI	Upper CI	p Value
Men						
Age, yrs						
<55	0					<0.001
55–69	0.117	0.054	1.124	1.012	1.249	0.029
70–84	0.286	0.061	1.331	1.181	1.501	<0.001
>85	0.463	0.130	1.589	1.232	2.048	<0.001
Current smoker	0.272	0.054	1.312	1.180	1.459	<0.001
Hypertension	0.163	0.046	1.177	1.074	1.289	<0.001
Diabetes	0.119	0.050	1.126	1.020	1.243	0.018
Previous infarct	1.081	0.060	2.947	2.619	3.316	<0.001
Previous PCI	0.459	0.059	1.582	1.409	1.776	<0.001
Previous CABG	0.867	0.075	2.379	2.054	2.756	<0.001
Typical angina	0.111	0.056	1.118	1.002	1.247	0.046
Constant	−0.905	0.051	0.405			<0.001
Women						
Age, yrs						
<70	0	0				<0.001
70–84	0.292	0.063	1.339	1.182	1.516	<0.001
>85	0.568	0.131	1.765	1.366	2.280	<0.001
Current smoker	0.237	0.081	1.267	1.082	1.484	0.003
Hypertension	0.319	0.069	1.376	1.202	1.576	<0.001
Diabetes	0.392	0.073	1.480	1.284	1.706	<0.001
Previous infarct	0.935	0.092	2.547	2.126	3.052	<0.001
Previous PCI	0.407	0.101	1.502	1.233	1.830	<0.001
Previous CABG	1.173	0.141	3.232	2.452	4.261	<0.001
Hyperlipidemia	0.181	0.067	1.198	1.051	1.365	0.007
Constant	−2.055	0.060	0.128			<0.001

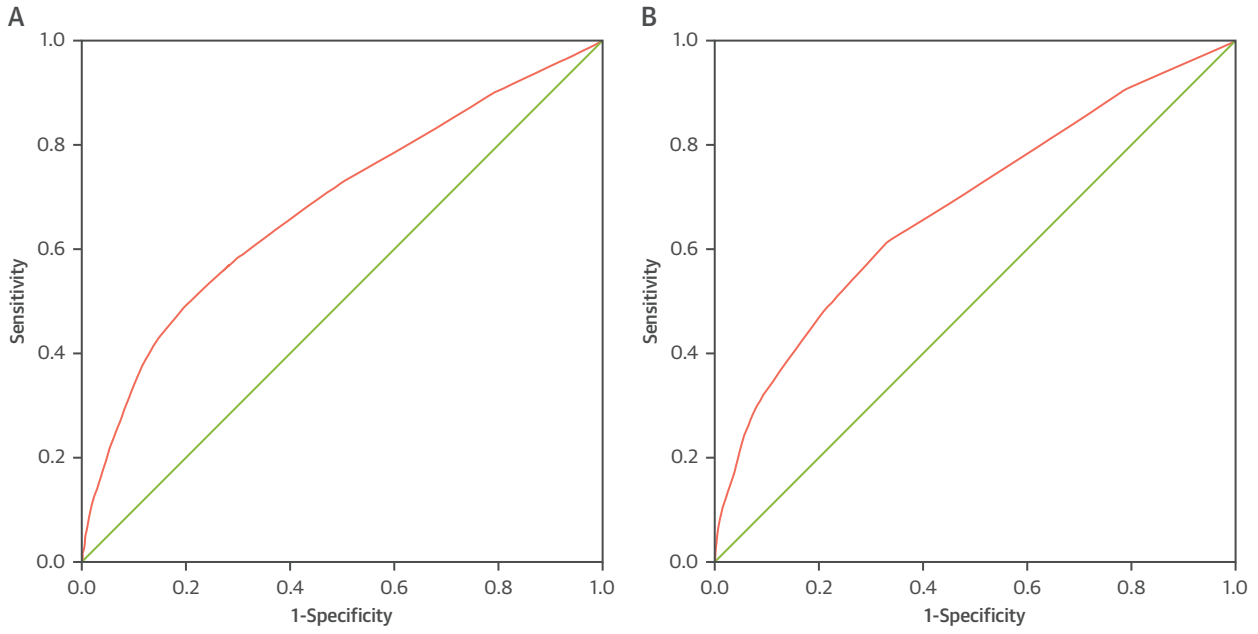
CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

TABLE 4 Clinical Score Model

	Men	Women
Age, yrs		
<55	0	0
55–69	1	0
70–84	3	1
≥85	4	2
Typical angina	1	0
Hyperlipidemia	0	1
Current smoking	2	1
Hypertension	2	2
Diabetes	1	2
History of MI	10	5
History of PCI	4	2
History of CABG	8	6

0 to 1 = low risk for a non-normal myocardial perfusion imaging.
Abbreviations as in Table 1.

FIGURE 1 ROC Curves for Predicting Abnormal SPECT Studies



Receiver-operating characteristic (ROC) curves for the clinical score for prediction of abnormal single-photon emission computed tomography (SPECT) studies in male **(A)** and female **(B)** patients. Area under curve for male patients is 0.684 **(A)** and for female patients is 0.681 **(B)**.

women, respectively (Figure 1). When applied to the SPECT validation cohort, the model yielded an AUC of 0.747 (95% CI: 0.730 to 0.764) and 0.702 (95% CI: 0.675 to 0.730) for men and women, respectively. The PET validation cohort yielded similar results with an AUC of 0.672 (95% CI: 0.649 to 0.696) and 0.686 (95% CI: 0.663 to 0.710) for men and women, respectively. A subanalysis was performed using patients imaged with CZT and NaI cameras separately. The model performed equally well irrespective of camera type. Another subanalysis showed that the model performed equally well in patients with low to intermediate-low pre-test probability of CAD, defined as a pre-test probability of ≤33.3%. This also held true in patients with a pre-test probability of ≤50%.

A score of ≤1 was selected as a threshold based on its sensitivity and specificity of predicting abnormal studies. Based on this threshold, the positive and negative likelihood ratios of having an abnormal SPECT study were 1.15 and 0.48 for men, respectively, and 1.25 and 0.52 for women, respectively. This cutoff identified patients with an abnormal study with a sensitivity of 89.6% in men and 82.2% in women. Conversely, normal studies were identified with a specificity of 70.6% in men and 87.1% in women (Table 5). The predicted and observed probability of having an abnormal SPECT per clinical score is presented in Figure 2.

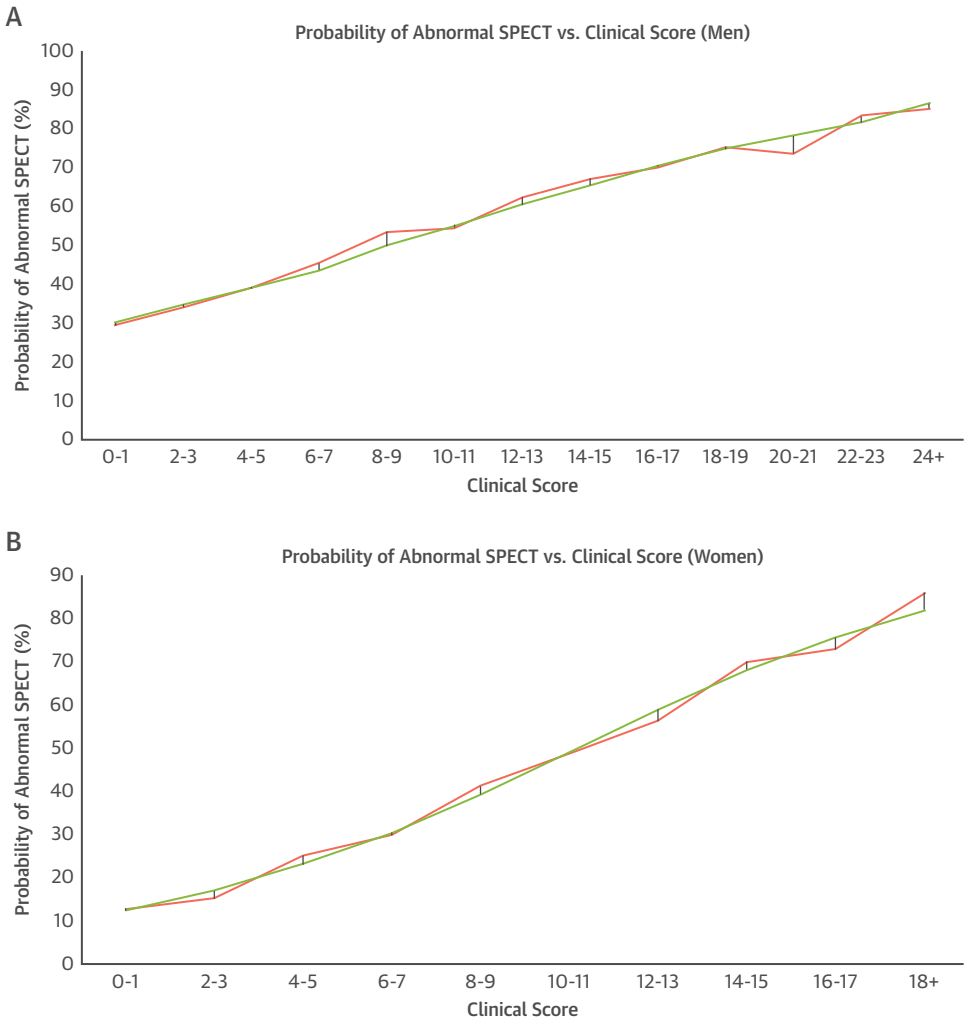
Using this same threshold in the SPECT validation cohort, the positive and negative likelihood ratios and specificity for identifying abnormal SPECT studies were, respectively, 1.20, 0.29, and 84.5% in men, and 1.35, 0.35, and 92.6% in women. In the PET validation cohort, the positive and negative

TABLE 5 Patients With High Likelihood of a Normal MPI Study According to Sex

	Derivation		Validation SPECT		Validation PET	
Model Score (0-1)	Patients	Normal SPECT	Patients	Normal SPECT	Patients	Normal PET
Men	1,763 (16.6)	1,244 (70.6)	542 (15.7)	458 (84.5)	206 (7.9)	112 (54.4)
Women	2,368 (30.5)	2,063 (87.1)	739 (31.1)	684 (92.6)	349 (17.0)	248 (71.6)

Values are n (%).
MPI = myocardial perfusion imaging; other abbreviations as in Table 1.

FIGURE 2 Predicted Versus Observed Probability of Abnormal SPECT Studies



Predicted **(red)** versus observed **(green)** probability of abnormal single-photon emission computed tomography (SPECT) studies in men **(A)** and women **(B)**, respectively. Mean observed versus predicted probability plotted for each score range.

likelihood ratios and specificity were 1.12, 0.33, and 54.4% in men and 1.18, 0.42, and 71.1% in women, respectively. The model performed better in an external cohort of PET patients, with an AUC of 0.752 in men and 0.737 in women.

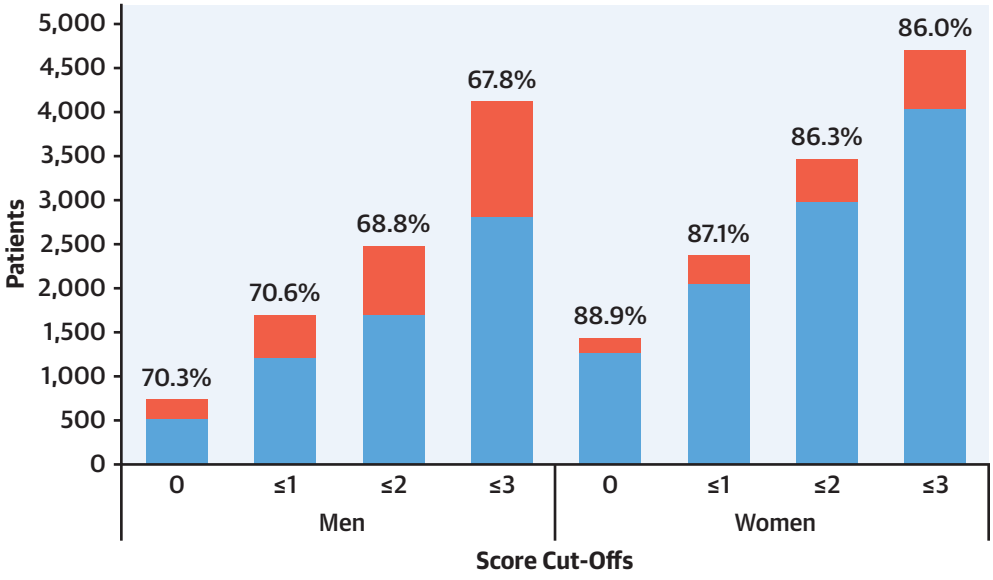
In the derivation cohort, 16.6% of men and 30.5% of women had a score of ≤1. Similarly in the SPECT validation cohort, this score corresponded to 15.7% of men and 31.1% of women (Table 5).

DISCUSSION

In a large cohort of 18,389 patients, we derive and validate a model that may be used to identify a population that is more likely to have a normal MPI study and thus may be considered for a stress-first protocol. This model could be used at the point of care to assist with decision making and image protocoling.

Although a score ≤1 is thought to be strict, this threshold was chosen to minimize abnormal studies. Different institutions may elect to use different thresholds, acknowledging that a higher score threshold would result in decreased sensitivity (Central Illustration, Table 6). The threshold of ≤1 would still be applicable to 16.6% of men and 30.5% of women. Based on the model, men with scores ≤1 are those who are: 1) <70 years of age without cardiac risk

CENTRAL ILLUSTRATION **Model Score and Proportion of Men and Women With Normal and Abnormal SPECT Studies**



Rouhani, S. et al. J Am Coll Cardiol Img. 2020;13(10):2193-202.

Model score and corresponding proportion of men and women with normal **(blue)** and abnormal **(red)** single-photon emission computed tomography (SPECT) studies. Percentage of normal studies indicated for each score.

factors, typical chest pain, or documented CAD or: 2) <55 years of age with either typical angina or diabetes mellitus. Similarly, women with a score ≤1 are those who are: 1) <85 years of age without cardiac risk factors, or; 2) <70 years of age with either dyslipidemia or a smoking history.

Although men and women with scores ≤1 had 70.6% and 87.1% probability of having a normal study, 29.4% of men and 12.9% of women would still require rest imaging. Rest imaging may be required in a greater proportion because our study does not account for all factors that would cause stress-perfusion defects (such as artifact, incomplete attenuation correction, inability to reach peak heart rate).

TABLE 6 Sensitivity and Accuracy of Various Score Thresholds in Men and Women

Score Cutoff	Sensitivity	Proportion of Patients	Patients Requiring Rest Imaging
Men			
≤0	95.6	6.9	29.7
≤1	89.6	16.1	29.4
≤2	84.4	23.3	31.2
≤3	73.2	38.9	32.2
≤4	69.4	43.6	32.7
≤5	58.3	56.9	34.2
Women			
≤0	90.8	18.4	11.1
≤1	82.2	30.5	12.9
≤2	72.3	44.7	13.7
≤3	61.3	60.7	14.0
≤4	48.2	73.0	15.6
≤5	38.2	80.9	16.8

Values are %.

The specificity of the model in SPECT and PET cohorts was different and likely attributable to several factors. First, at our center, there exists a referral and patient selection bias between the 2 modalities (Table 3). Furthermore, the quantification of myocardial blood flow and myocardial flow reserve with PET would potentially affect image interpretation. Also, the higher diagnostic accuracy of PET could have potentially led to more correct diagnoses in similar patients who would have otherwise been falsely categorized (false positive or false negative) with SPECT MPI.

The model was validated against 3 validation cohorts and proved to have similar or superior performance. Differences in its performance characteristics may be due to differences in population and referral bias. However, the results reassure us that the model should perform equally well at other institutions with different populations.

Stress-first protocols have been adopted to improve patient experience, reduce radiation exposure, and optimize resource use. Specifically, stress-first imaging has been shown to reduce radiation exposure to patients by 25% to 80% (16,17), and technologists and nurses by 40% to 50% (18). As the current radiation reduction goal of ASNC is to reduce median doses to <9 mSv (9), and a combination of stress-only imaging with CZT cameras is shown to achieve radiation reduction to 1 mSv (19,20), such protocols will assist in minimizing patient harm and meeting these goals (21). By minimizing the need for rest imaging, this would potentially reduce cost and allow for increased patient throughput as well (16,17).

The indiscriminate use of a stress-first protocol for all-comers may be difficult and may potentially inconvenience patients, and depending on the prevalence of CAD in the population, it could require a significant proportion to return a second day for rest imaging. Therefore, a stress-first protocol would most greatly benefit those who will most likely have a normal MPI. Our model can select patients using easily obtainable clinical information and could be calculated at the time of scheduling or even at the point of care. Another group has examined a model to identify eligible patients for stress-first studies (22). Their study reported a sensitivity and specificity of 57% and 88% in identifying unsuccessful stress-first protocols, with the investigators commenting on its cumbersome nature and demonstrating that it is only marginally more accurate than triaging patients based on CAD status alone (23). Another shortcoming of this prediction score was the assignment of 5 points to male sex, which placed all men in an intermediate risk group. The investigators circumvented this limitation by assigning 4 points to men. Our study separated analyses according to sex, in light of growing awareness on differences in presentation, management, and prognosis between sexes (24). Furthermore, previous studies incorporated variables that may not be immediately available, such as an abnormal electrocardiography and congestive heart failure status, and included 1,996 patients in their derivation cohorts. The model present here was developed to be easily applied at point of care (e.g., by booking staff or implemented into an electronic ordering system) using readily available clinical variables at time of booking and was derived with a very large cohort of 18,389 patients, which is much more robust in terms of sample size. As well, it was validated in 3 large cohorts across both sexes, demonstrating that it is robust across a diverse patient population.

Performing stress-first studies does not detract from the prognostic value of MPI. It has been previously demonstrated that normal stress-first studies carry similar prognostic value in patients with normal stress-rest studies (16,17,25). Selective omission of rest imaging in these patients would be beneficial in reducing image acquisition, processing time, and interpretation time, and it requires lower radiation dosing to the patient.

STUDY LIMITATIONS. This model was derived in a single-center SPECT cohort, and thus the population and prevalence of CAD may differ from the population at other centers. Although this model can be used to predict those more likely to have normal MPI, it does not identify those who may be subject to artifact or incomplete attenuation compensation whereby rest images are still required.

CONCLUSIONS

A novel model, based on easily obtained clinical variables, is proposed to identify patients with low probability of having abnormal MPI results. This point-of-care tool may be used to identify a population that might qualify for stress-first MPI protocols.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: There is an increasing desire to use stress-only or stress-first SPECT MPI where possible. Adoption of these protocols have the advantage of reducing radiation exposure, improving workflow, improving patient experience, and reducing health care costs, without compromising diagnostic accuracy. Identifying patients that would potentially benefit from a stress-first protocol would allow labs to achieve these goals.

TRANSLATIONAL OUTLOOK: This study developed a simple point-of-care method of identifying patients that may benefit from a stress-first study. With the use of electronic medical record information, there may be the future ability to create more accurate models, using other variables available within the electronic medical records, such as electrocardiography, creatinine, biomarkers, antecedent test results, and comorbidities. Integration of such models into an electronic medical record would improve patient selection and patient care.

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KEY WORDS cardiac death, computed tomography, coronary angiography, major adverse cardiac events, myocardial infarction, prognosis

APPENDIX For supplemental tables, please see the online version of this paper.