The use of pre-test and post-test probability values as criteria before selecting patients to undergo coronary angiography in patients who have ischemic findings on myocardial perfusion scintigraphy

Nazlı Pınar Karahan Şen, Recep Bekiş[1], Ali Ceylan[2], Erkan Derebek[1]

Department of Nuclear Medicine, Kırklareli Government Hospital; Kırklareli-*Turkey*
Departments of [1]Nuclear Medicine, [2]Public Health, Faculty of Medicine, Dokuz Eylül University; İzmir-*Turkey*

Abstract

Objective: Myocardial perfusion scintigraphy (MPS) is a diagnostic test which is frequently used in the diagnosis of coronary heart disease (CHD). MPS is generally interpreted as ischemia present or absent; however, it has a power in predicting the disease, similar to other diagnostic tests. In this study, we aimed to assist in directing the high-risk patients to undergo coronary angiography (CA) primarily by evaluating patients without prior CHD history with pre-test and post-test probabilities.

Methods: The study was designed as a retrospective study. Between January 2008 and July 2011, 139 patients with positive MPS results and followed by CA recently (<6 months) were evaluated from patient files. Patients' pre-test probabilities based on the Diamond and Forrester method and the likelihood ratios that were obtained from the literature were used to calculate the patients' post-exercise and post-MPS probabilities. Patients were evaluated in risk groups as low, intermediate, and high, and an ROC curve analysis was performed for the post-MPS probabilities.

Results: Coronary artery stenosis (CAS) was determined in 59 patients (42.4%). A significant difference was determined between the risk groups according to CAS, both for the pre-test and post-test probabilities ($p<0.001$, $p=0.024$). The ROC analysis provided a cut-off value of 80.4% for post-MPS probability in predicting CAS with 67.9% sensitivity and 77.8% specificity.

Conclusion: When the post-MPS probability is ≥80% in patients who have reversible perfusion defects on MPS, we suggest interpreting the MPS as "high probability positive" to improve the selection of true-positive patients to undergo CA, and these patients should be primarily recommended CA. *(Anatol J Cardiol 2016; 16: 512-9)*

Keywords: myocardial perfusion imaging, coronary angiography

Introduction

Coronary heart disease (CHD) is one of the most frequent diseases that can be observed in developed countries. It causes significant morbidity and mortality worldwide. Many diagnostic tests are used in the diagnosis of coronary artery stenosis (CAS), but we also know that some factors such as age, gender, or symptoms have predictive values for detecting the disease (1). Coronary angiography (CA) is still the gold standard method in the diagnosis (2). However, it is an invasive and expensive procedure and carries the risks of mortality even if it is low (3). Therefore, selecting patients who are appropriate for CA has been investigated in several studies (4, 5). Before a diagnostic test, the pre-test probabilities of patients can be estimated. By adding positive or negative likelihood ratios (LRs) and using the Bayes' theorem, we can calculate the post-test probabilities after a test. Thus, the tests are not evaluated alone as positive or negative; they would be evaluated using clinical findings, personal properties, and other test results (6).

Myocardial perfusion scintigraphy (MPS) is frequently used in the diagnosis of CAS. In CAS, cardiac oxygen support decreases, but the need for oxygen increases. This unbalanced metabolism results in ischemia and a reversible perfusion defect seen in stress images (7). Currently, we still interpret MPS as ischemia-positive when a reversible perfusion defect is present. However, it has a power in predicting the disease, similar to other diagnostic tests. In our study, we investigated patients who had positive findings on MPS with their CA results and pre-test probabilities. We calculated the post-test probabilities, thereby evaluating the final probabilities, and investigated what the contribution of this probabilistic approach to the interpretation of the test and what we could do in addition to interpreting MPS as positive or negative.

Address for correspondence: Dr. Nazlı Pınar Karahan Şen, Kırklareli Devlet Hastanesi, Nükler Tıp Bölümü, 39000 Kırklareli-*Türkiye*
Phone: +90 536 514 43 75 Fax: +90 288 214 29 42 E-mail: drpinarkarahan@hotmail.com
Accepted Date: 09.09.2015 **Available Online Date:** 30.11.2015

DOI:10.5152/AnatolJCardiol.2015.6347

Methods

Study design

The study was designed as a retrospective study.

Study population

Patients who had undergone MPS between January 2008 and July 2011 at the Nuclear Medicine Department of Dokuz Eylül University in İzmir were evaluated retrospectively. In total, 139 patients without prior CAS history and a positive result of MPS as ischemia or infarct and who had undergone CA recently (in less than 6 months) after MPS were included in this study. This study was approved by the local Ethical Committee of our University (776-GOA protocol number, 01.11.2012, 2012/35-14 decision number).

Study protocol

All patients underwent a 1-day rest/stress MPS protocol. MPSs were performed on a gated single-photon emission computerized tomography (SPECT) scanner (PHILLIPS dual head gamma camera). Calcium channel blockers and beta-blockers were stopped 48 h before the procedure. Furthermore, nitrate derivative drugs were discontinued 24 h before the procedure, and MPS was performed after a fasting period of at least 6 h. Rest imaging analysis began approximately 1 h after the injection of 8 millicuries Tc-99m MIBI. Three hours after the rest imaging analysis, exercise stress tests were performed on a treadmill according to the MODIFIED BRUCE or BRUCE protocol as a step of MPS. Pharmacological stress test was applied with dobutamine in patients who could not tolerate the exercise test. Twelve-lead electrocardiograms (ECGs) were recorded during the exercise. The endpoints for the stress tests included any one of the following indexes: reaching the target heartbeat [(220 – age in years) × 85%], ischemic ST segment horizontal or downslope depression of ≥3 mm, emergence of angina, severe cardiac arrhythmia, hypertension (≥240/120 mm Hg), and a decrease in systolic pressure of ≥20 mm Hg. At the peak of exercise, a 22 millicuries dose of Tc-99 m MIBI was injected, and the patient continued to exercise for an additional 1 min. The acquisition for the stress imaging study was performed approximately 30 min after the injection. The obtained rest and stress images were processed on the JETSTREAM program and visually assessed on AUTOSPECT and AUTOQUANT 7.0 programs.

Inter-observer variability is known to be good in the interpretation and reporting of MPS (8). The MPS images of 139 patients were visually assessed by six nuclear medicine specialists in our department. The visual assessment criteria for ischemia were hypoperfusional areas in stress images, which were reversible in the rest images. Hypoperfusional areas in both stress and rest images were the criteria for infarcts. Defects, which were interpreted as infarct, were accepted as perfusion defects and a sign of CAS (9, 10). Hypoperfusional areas were also evaluated from the gated images. To exclude breast tissue attenuation, the patients' breasts were fixed to the chest wall by banding during the imaging procedure. In cases where hypoperfusion of the anterior wall was present, both in the stress and rest images, major breast tissue and gated images were considered to exclude breast tissue attenuation from real perfusion defects. In addition, when distinguishing the inferior wall, hypoperfusion from diaphragmatic attenuation was required; static images were obtained in the supine and right lateral decubitus position.

The Diamond and Forrester (DF) method was used to determine pre-test probabilities of all patients (1). This method uses the patient's age (between 30 and 70 years), gender, and chest pain characteristics to estimate the patient's probability of being CAS. Chest pain is classified in three types (typical, atypical, and non-anginal) according to the pain characteristics, namely retrosternal, precipitating with exercise, and relief with rest or nitroglycerin in minutes. This method evaluates female and male patients in four groups according to age (30–39, 40–49, 50–59, and 60–69 years) and four groups according to pain symptoms (typical, atypical, non-anginal, and asymptomatic). The DF method gives a pre-test probability value for the combination of each group. Patients' pre-test probabilities can be obtained using the age, sex, and chest pain data of patients individually. For example, according to the DF method, a 65-year-old female patient with typical angina has 91% pre-test probability of CHD, and a 40-year-old male patient with non-anginal chest pain has 14% pre-test probability of CHD. All patients' pre-test probabilities were obtained individually from the pre-test probability table of the DF method using these parameters (11). One patient, younger than 30 years old, was included in the 30–39 years age group, and 21 patients who were ≥70 years old were included in the 60–69 years age group.

ECGs that were recorded during the exercise stress test were evaluated. Only some of the patients' detailed exercise ECGs were obtainable. In ECG derivations 60–80 milliseconds after the end of the QRS complexes, ≥1 mm horizontal or downsloping ST-segment depressions were investigated. At least 85% of the maximal heart rate for age or below 85% with significant ST segment changes was considered to be adequate; hence, in the patient group, 64 ECGs were included in the study. ST segment depression values of <1 mm were considered as negative, and depressions of ≥1 mm were interpreted as positive. Patients with ≥2 mm ST segment depression were further assessed.

The probabilities after exercise test (post-exercise) of these 64 patients were calculated based on positive and negative LR values that had been reported in the literature. Positive and negative LR values were calculated using the formula written below (12):

Positive LR value=Sensitivity/(1–Specificity)

Negative LR value=(1–Sensitivity/Specificity)

The calculated LR value was 5 for <1 mm ST segment depression, and the negative LR value was 0.555 for <1 mm ST segment depression (13). For a ≥2 mm ST segment depression, the calculated positive LR value was 11.08 (1). For a positive result of MPS, a positive LR value has been stated as 3.56 in the literature (14).

Table 1 demonstrates the reported values obtained from the literature. The LR values used for calculations and the probabilities after exercise were calculated using the formula written below (15, 16):

Pre-test Probability/1–Pre-test Probability=Pre-test Odds

Pre-test Odds×LR=Post-test Odds

Post-test Odds/(Post-test Odds+1)=Post-test probability

If evaluated through an example, the pre-test probability of a 56-year-old female patient with non-anginal chest pain can be calculated before MPS using this formula (Fig. 1). In this example, the adequate exercise test was performed on a treadmill according to the BRUCE protocol before MPS, and in the exercise ECG, a 1 mm ST segment depression was present. This patient's clinical pre-test probability, which was obtained using the DF method, was 8% (11), and the positive LR value for the exercise test from the literature is 5. By inserting these values into this formula, the post-exercise probability value after the exercise test can be calculated as below:

Pre-test Odds=0.08/1–0.08=0.08695652

Post-test Odds=0.08695652×5=0.43478261

Post-test Probability (post-exercise)=0.43478261/(0.43478261+1)=0.30303030=30.30%

The estimated post-exercise values were further used as pre-test probability values before MPS. The diagnostic tests were performed consecutively; therefore, this calculated post-exercise probability is a pre-test probability value that we could use before MPS. The positive LR value of MPS from the literature is 3.56. By putting these values in the formula, the post-MPS probability value of this patient can be calculated as 60.75% as written below:

Table 1. LR values that obtained from the literature (1, 13, 14)

Conditions	LR value	Sensitivity	Specificity
ST <1 mm (negative test)	0.555* (LR-)	50%	90%
1 mm ≤ ST <2 mm	5** (LR+)	50%	90%
ST ≥2 mm	11.08** (LR+)	13.3%	98.8%
MPS (positive test)	3.56** (LR+)	83%	77%

LR - likelihood ratio; MPS - myocardial perfusion scintigraphy; ST - ST segment depression in exercise stress test electrocardiogram; * - Negative LR value=(1–Sensitivity/Specificity); ** - Positive LR value=Sensitivity/(1-Specificity)

Pre-test Odds=0.303/1–0.303=0.43472023

Post-test Odds=0.43472023×3.56=1.54760402

Post-test probability (post-MPS)=1.54760402/(1+1.54760402)=0.60747432=60.75%

Another example of calculating the pre-test probability is a 53-year-old male patient with atypical chest pain (Fig. 2). In this example, the exercise test was performed on a treadmill according to the BRUCE protocol. The exercise test was submaximal with 81% of the maximal heart rate, but a symptom-positive test and a 1 mm ST segment depression were present on the exercise ECG.

The patient's clinical pre-test probability is 59%, which is obtained using the DF method and using the same formula. By inserting the mentioned values into this formula, the post-exercise

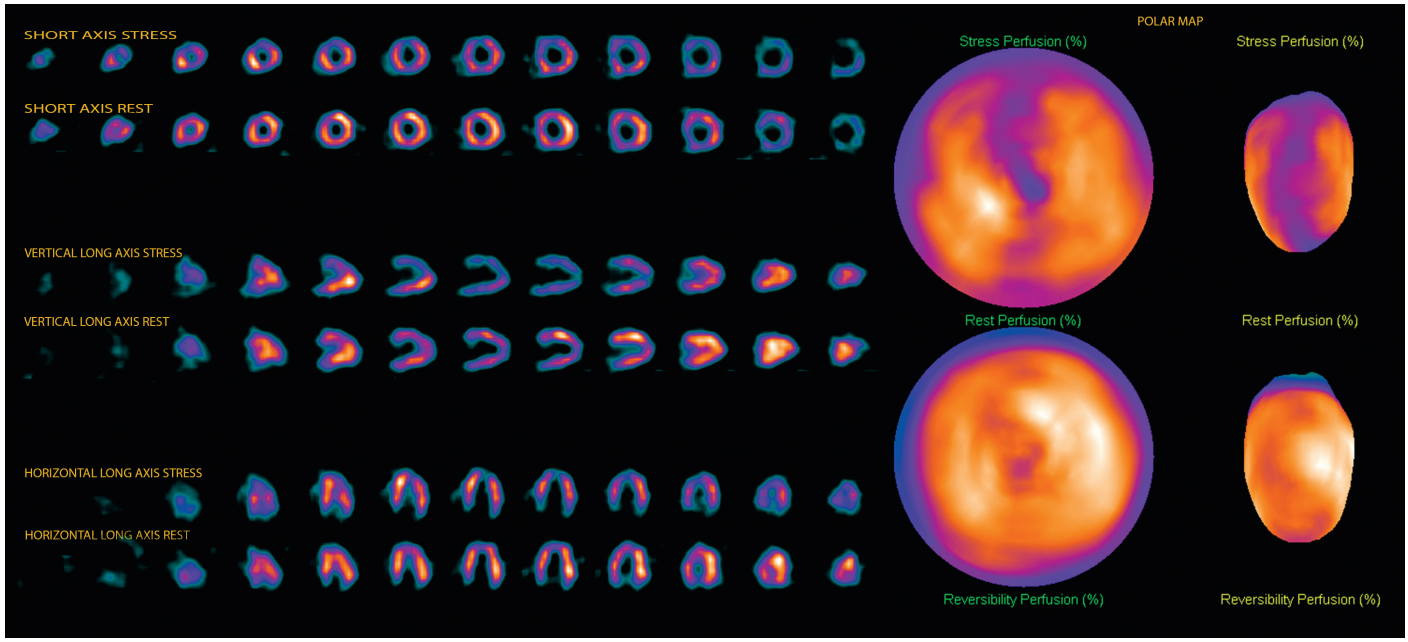

Figure 1. MPS images of a 56-year-old female patient with non-anginal chest pain. Short- axis, horizontal long-axis, vertical long-axis, and polar map images demonstrate hypoperfusion of the anterior wall and a mild hypoperfusion on mid-basal slices of the inferior wall compared with the septal or lateral walls of the left ventricle. The breasts had been fixed to the chest wall both in the rest and stress images to determine breast tissue attenuation. Hypoperfusion was only present in stress images; therefore, this suggested ischemia primarily rather than attenuation. Furthermore, gated images were evaluated, and images were interpreted as anterior wall ischemia and a possible mid-basal inferior wall ischemia. The patient's clinical pre-test probability was determined as 8% and a low risk for pre-test probability. After exercise ECG, the post-exercise probability was calculated to be 30.30%, and the post-test probability was increased to 60.75% after MPS. The patient was classified in the intermediate risk group for post-exercise and post-MPS probability. The patient underwent CA, but the coronary arteries were found to be normal in the CA results

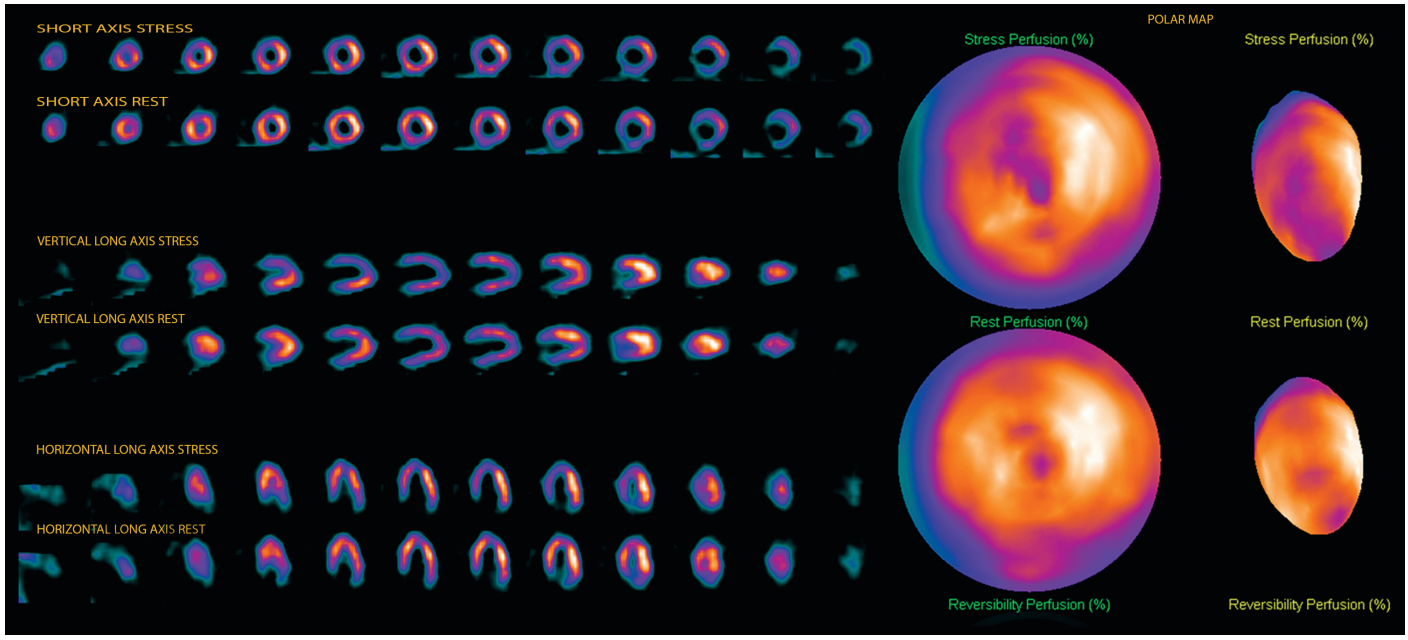

Figure 2. A 53-year-old male patient with atypical chest pain. The patient's clinical pre-test probability was 59%, obtained through the DF method, and the post-exercise probability value was calculated as 87.80%. After the positive result of MPS, the final probability was calculated as 96.24% from the formula. Images demonstrate hypoperfusion of the apex, apical, and mid slices of the anterior and anteroseptal walls on the short-axis, vertical long-axis, horizontal long-axis, and polar map. Hypoperfusional areas were confirmed on gated images. The CA result revealed CAS at the LAD

probability value was calculated as 87.80%. After the positive result of MPS, the final probability was calculated as 96.24% from the formula.

All patients were evaluated using the clinical pre-test and post-test probability values that were calculated after MPS without using the exercise step and only considering the MPS step of the calculation. Sixty-four patients with exercise data were additionally assessed using the exercise data-added probabilities and post-test probability values that had been calculated after only MPS, thereby aiming to evaluate the effect of the exercise data. Furthermore, the patients were classified into three risk groups as low, intermediate, and high (LR, IR, HR) according to the pre-test and post-test probability values (<20%, 20%–80% and ≥80%) (4).

LAD, LCX, and RCA were evaluated separately, and stenosis of a vessel equal or higher than 70% in the CA was accepted as significant CAS according to CA reports. Coronary narrowing below this value or normal coronaries were considered to be negative for CAS.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 15.0 for Windows. The patients' age, gender, type of chest pain, and the risk classes were examined for a significant association between CA results using the chi-square test and the independent samples t-test. A p value of <0.05 was considered significant. The receiver operating characteristics (ROC) curve analysis was used to calculate the threshold of post-MPS probability values for CAS. The presence of significant CAS (≥%70) in CA results was accepted as the gold standard for the ROC analysis. The best cut-off value was obtained from the ROC curve. A perfect test has an area under the curve (AUC) of 1.0, whereas a random chance gives an AUC of 0.5; therefore, an AUC of >0.5 was accepted as worthwhile.

Results

CAD was detected in 59 (42.4%) of 139 patients. The descriptive characteristics of the patients are presented in Table 2. Based on the DF method, when the patients are classified into risk groups, the patient numbers in LR, IR, and HR groups were

Table 2. Descriptive characteristics of patients

	CAS (+)		CAS (-)		*P*
Mean age	60.2±10.5		56.2±11.0		*P*=0.032*
	n	%	n	%	
Gender					
Male	40	67.8%	36	45.0%	*P*=0.008**
Female	19	32.2%	44	55.0%	
Chest pain					
Typical	28	47.5%	14	17.5%	*P*<0.001**
Atypical	16	27.1%	38	47.5%	
Non-anginal	9	15.3%	24	30.0%	
Asymptomatic	6	10.2%	4	5.0%	

CAS - coronary artery stenosis; n - number of patients; % - the percentage of column; * - Independent samples t-test; ** - chi-square test

determined as 38 (27.3%), 68 (48.9%), and 33 (23.7%), respectively. A significant difference was determined between the risk groups according to CAS, both for the pre-test and post-test probabilities. The relation between CAS and risk classes obtained from the pre-test and post-test probabilities in 139 patients and additionally in the exercise group are presented in Tables 3 and 4.

The ROC curve was plotted for 64 patients in the exercise group. Without evaluating the ECGs, according to the post-test probabilities after only MPS, the calculated AUC was 0.656 [95% confidence interval (CI), 0.518–0.793, p=0.34]. If exercise data were added in the same group, the calculated AUC was determined as 0.734 (95% CI, 0.608–0.859, p<0.001) (Fig. 3). The results of the ROC curve analyses demonstrated that exercise-added post-test probabilities were more meaningful. The ROC curve analysis of exercise-added post-test probabilities provided a cut-off value of 80.4% in predicting CAS with 67.9% sensitivity and 77.8% specificity (Table 5).

Discussion

Our study results demonstrate a significant relationship between risk classes and having CAS. The majority of true-positive patients in MPS were detected to be in the HR group (67.9%). Similarly, the ROC curve results also demonstrated that 67.9% of the patients with CAS had a post-test probability of ≥80.4%. These findings suggested calculating the post-test probability in patients who are referred to MPS, and if there is a perfusion defect and the post-test probability is equal or higher than 80%, MPS was reported as "high probability positive." It was found that this method increases the anticipation of the true CAS. Therefore, at the time of interpretation of MPS, the use of probabilities was expected to provide more accurate results.

CAS was determined and required vascular interventions only in one-quarter of patients whom MPS had been interpreted as ischemia, but the post-test probabilities remain under 80%. In addition, 75% of the patients were found to have unnecessarily applied CA. Consequently, in patients with post-test probability <80%, interpretation as "low probability positive" is thought to prevent unnecessary CA. In patients interpreted as "low probability positive" before the decision of CA, smoking, blood lipid levels, hypertension, diabetes, family history, as well as additional risk factors or an additional diagnostic test may be required to be considered.

Table 3. Risk group classification for pre-test and post-MPS probabilities in the groups of 139 patients and CAS ratios

Risk groups	PrP-MPS	CAS		PP-MPS	CAS	
	(n)	n	%	(n)	n	%
LR	38	10	26.3%	8	3	37.5%
IR	68	25	36.8%	60	18	30%
HR	33	24	72.7%	71	38	53.5%
P	*P*<0.001*			*P*=0.024*		

CAS - coronary artery stenosis; HR - high risk; IR - intermediate risk; LR - low risk; n - number of patients; PP – post-test probability; PrP – pre-test probability; * - chi-square test

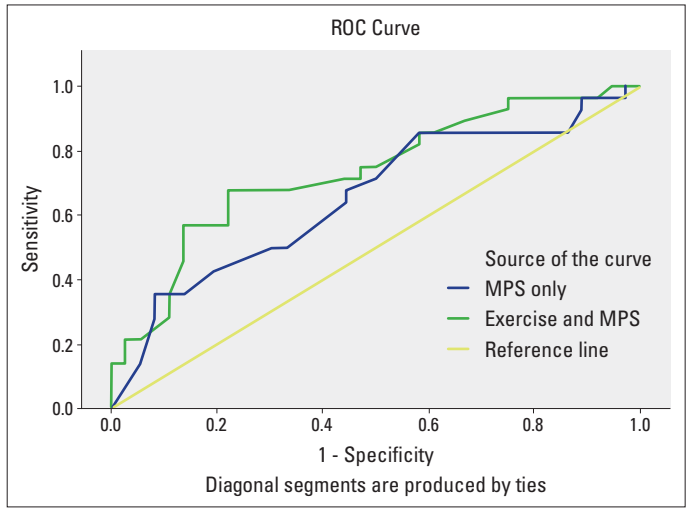

Figure 3. Compartment of the ROC Curve analyses of 64 patients both for the post-test probabilities with and without exercise data

Table 4. Risk group classification for pre-test probabilities, post-exercise, and post-MPS probabilities of 64 patients and CAS ratios in the groups

Risk group	PrP-Exercise	CAS		PP-Exercise	CAS		PP-MPS	CAS	
	(n)	n	%	(n)	n	%	(n)	n	%
LR	20	5	25%	15	3	20%	2	0	0%
IR	31	13	41.9%	30	11	36.7%	34	9	26.5%
HR	13	10	76.9%	19	14	73.7%	28	19	67.9%
P	*P*=0.013*			*P*=0.004*			*P*=0.002*		

CAS - coronary artery stenosis; HR - high risk; IR - intermediate risk; LR - low risk; n - number of patients; PP – post-test probability; PrP – pre-test probability; * - chi-square test

Table 5. ROC Curve analysis of post-test probabilities, MPS with exercise data added (first column), and only MPS without exercise data

Post-MPS	AUC	*P*	Sensitivity	Specificity	Cut-off
PP-MPS (with exercise)	0.734 (0.608–0.859, 95% CI)	*P*<0.001	67.9%	77.8%	80.4%
PP-MPS (only MPS)	0.656 (0.518–0.793, 95% CI)	*P*=0.34	67.9%	55.6%	68.1%

AUC - area under the curve; CI - confidence interval; MPS - myocardial perfusion scintigraphy; P - P value; PP - post-test probability; ROC - receiver operating characteristics

Three basic factors that are used to determine the pre-test probabilities for CAS are age, gender, and type of chest pain. In this study, the mean age of patients with CAS was statistically higher than normal ones, and age was found to be a reliable risk factor in the determination of the disease (p=0.032). Similarly, gender was also found to be a reliable pre-test risk parameter. A significant difference was detected between females and males according to CAS. CAS was detected at significantly higher rates in males (p=0.008). We have known that an increase in age increases the risk of CAS (1). Age >45 years in men and 55 years in women is a strong risk factor for CHD. In terms of gender, a significant difference between females and males for developing CAS is known. In particular, because of the protective effect of estrogen in females, the onset of the disease is seen at later ages than men (17). Typical chest pain is also considered as an important symptom of CAS. Furthermore, typical chest pain has the highest rates of risk, followed by atypical chest pain and non-anginal pain. The absence of pain ensures a lower pre-test risk (1, 18). Consistent with the literature, in our study, CAS was detected at higher rates in patients with typical chest pain than other types of pain or asymptomatic group. According to the pre-test risk values, typical pain was followed by asymptomatic, atypical pain, and non-anginal pain groups. A significant difference was determined between the risk groups according to CAS (p<0.001). In our study, the determination of high rates of CAS in asymptomatic patients was thought to be related with the limited number of patients in this group.

The DF method uses these three main parameters of age, gender, and chest pain characteristics to estimate the patients' probability of having CAS; however, the method does not consider other risk factors such as diabetes mellitus, lipid levels, hypertension, or smoking. In contrast, the Duke clinical scoring method has been improved. This method also takes into consideration the clinical data or the history of prior MI to estimate the pre-test probability (19). However, in the prediction of the disease, the predictive value of other risk factors is known to be less effective than the presence of typical angina (20). A study, which was aimed to develop the method of DF, suggests that particularly the pre-test probability of the DF model unnecessarily estimates high values in women (21). However, currently, the DF method is still frequently used (2, 21). DF is a quick method for the determination of the pre-test risk of CHD, and it is easy to perform and independent from laboratory techniques.

Implementation of diagnostic tests in high or low risk groups is generally not recommended because of the limited contribution to the diagnosis (4). In a study, the pre-test probabilities of patients were determined according to the DF model and then non-invasive cardiac diagnostic tests (stress ECG, MPS, and cardiac cinefluoroscopy) and coronary angiographies were performed. The post-test probabilities were calculated, and the CAS was compared in risk groups comprising the pre-test and post-test probabilities. According to the pre-test probabilities, CAS was determined in 78.9% of the high-risk group and in 9% of the low-risk group patients. The study determined that diagnostic test application in high-risk and low-risk patients with Bayes' theorem could not have made any significant change in the groups. As a result, the implementation of the diagnostic tests would be appropriate in the intermediate risk group. In low-risk patients, diagnostic tests are not recommended to be performed otherwise, and patients with high probabilities are recommended to be guided directly to CAG. Currently, this approach still maintains its validity. Patients primarily recommended for MPS are in the intermediate risk group. In our study, the number of patients with intermediate risk was higher than other risk groups. In another study with 544 patients included with suspected CHD, the prevalence of CAS was determined as 41% in all patients. Patients were classified into risk groups using the DF method, and CAS rates were determined as 27%, 42%, and 70% in DR, IR, and HR groups, respectively (22). In our study, similar rates of CAS were determined in the groups.

It is known that the exercise test has an important role individually among diagnostic tests in the determination of CAS. The diagnostic power of the exercise test and the pre-test probability of CAS have been evaluated in a systematic review. It has been indicated that scoring systems and Bayesian approaches may be helpful in the diagnosis; furthermore, calculating the pre-test probabilities would be helpful in preventing unnecessarily expensive and invasive investigations (23). Physical or pharmacological exercise tests are a routine part of MPS. Considering exercise ECGs before MPS could have an additional effect on post-test probability values in the determination of CAS, as in our study. Therefore, in the evaluation of MPS, exercise data were also considered. According to post-test probability values after MPS, when the exercise data were also evaluated, the CAS rate was determined 0% in the LR group. The findings between the groups were significantly more favorable when the exercise data were considered. Sixty-four patients with exercise data when classified for pre-exercise, post-exercise, and post-MPS probabilities showed significant differences between risk groups according to CAS in gradually increasing levels (p=0.013, p=0.004, and p=0.002, respectively). Furthermore, another supporting finding that demonstrates the value of exercise data in the evaluation of MPS is AUC in ROC. It was found to be more meaningful when the exercise data were added before MPS. In a study, which included 2200 patients without known prior CHD, who were followed after MPS, the probabilities of cardiac events were calculated. The clinical pre-test probability, clinical and post-exercise probability, and the probability after MPS obtained using clinical and post-exercise probabilities were calculated together. The ROC curve was plotted, and the AUC was determined as 0.66, 0.73, and 0.87, respectively, for a cardiac event in the follow-up (24). Compared with our results, the pre-test probability and the post-exercise probability findings were similar, but in this study, the post-MPS AUC was found to be more favorable than our study. A better result after MPS was suggested because only positive MPSs were included in our study. Fur-

thermore, when calculating the pre-test probability values additionally to age, gender, and pain, this study had also considered the blood pressure levels, hyperlipidemia, glucose intolerance, smoking history, and resting ECG. Similarly, when calculating post-test probabilities, the exercise blood pressure, heart rate, and exercise duration were included in the assessment, similar to that in the Duke scoring. Although these data were not used in our study, the obtained diagnostic power of pre- and post-test probabilities were found to be similar to the mentioned study.

As a result, to determine the pre-test probabilities of CAS, it will be appropriate to correctly obtain the patient's age, gender, and pain type data from the history. The patient's probabilities obtained with the addition of exercise data can be used in the interpretation of the test to reduce the rate of false positivity. To facilitate the clinician's perspective, interpreting MPS in patients with post-test probability equal or higher than 80% as "high probability positive" and for patients with post-test probability below 80% reporting as "low probability positive" ensures the review of ischemia on a patient-specific basis and provides more accurate conclusions by evaluating each patient individually rather than interpreting a perfusion defect only.

Study limitations

Failing to reach all patients' exercise data and a limited number of exercise groups are the main limitations of the study. Furthermore, our calculation method is useful only in a selected patient group in whom we can determine the pre-test probability with no prior coronary artery disease history.

Conclusion

Our study highlighted that in patients who have no prior CAS history, the use of our calculating procedure, which considers patient's probabilities obtained with the addition of exercise data, can be used in the interpretation of the test to reduce the rate of false positivity. If the post-test probability is equal or higher than 80% and the patient has a reversible perfusion defect on MPS, images should be reported as "high probability positive," and these patients should be primarily advised for CAG. Otherwise, when the post-test probability is <80%, we suggest reporting "low probability positive" and considering the other risk factors or another diagnostic test before CA. Further prospective studies are needed to confirm our results.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept- N.P.K.S., R.B., E.D.; Design- N.P.K.S., R.B., E.D.; Supervision- N.P.K.S., R.B., E.D.; Data collection &/or processing – N.P.K.S.; Analysis and/or interpretation– N.P.K.S., R.B., E.D., A.C.; Literature search- N.P.K.S., R.B., E.D.; Writing – N.P.K.S., R.B.; Critical review- N.P.K.S., R.B.

References

1. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med 1979; 300: 1350-8. [Crossref]
2. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and the management of patients with stable ischemic heart disease: a report of American College of Cardiology foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society For Cardiovascular Angiography And Interventions, and Society of Thoracic Surgeons. Circulation 2012; 126: e354-471.
3. Noto TJ Jr, Johnson LW, Krone R, Weaver WF, Clark DA, Kramer JR Jr, et al. Cardiac catheterization 1990: a report of the Registry of the Society for Cardiac Angiography and Interventions (SCA&I). Cathet Cardiovasc Diagn 1991; 24: 75-83. [Crossref]
4. Detrano R, Yiannikas J, Salcedo EE, Rincon G, Go RT, Williams G, et al. Bayesian probability analysis: a prospective demonstration of its clinical utility in diagnosing coronary disease. Circulation 1984; 69: 541-7. [Crossref]
5. Melin JA, Wijns W, Vanbutsele RJ, Robert A, De Coster P, Brasseur LA, et al. Alternative diagnostic strategies for coronary artery disease in women: demonstration of the usefulness and efficiency of probability analysis. Circulation 1985; 71: 535-42. [Crossref]
6. Rutherford JD. Cardiology Core Curriculum, A problem-based approach. London: BMJ Books; 2003.
7. Taegtmeyer H. From fetal to fatal metabolic adaptation of the heart to environmental stress. In: Cokkinos DV, Patnos C, Heush G, Taegtmeyer H, editors. Myocardial ischemia from mechanism to therapeutic potential. USA: Springer; 2006. p.11-4. [Crossref]
8. Johansen A, Hoilund-Carlsen PF, Christensen HW, Grupe P, Veje A, Vach W, et al. Observer variability in the evaluation of dual-isotope Tl-201/Tc-99m sestamibi rest/stress myocardial perfusion SPECT in men and women with known or suspected stable angina pectoris. J Nucl Cardiol 2004; 11: 710-8. [Crossref]
9. Strauss HW, Miller DD, Wittry MD, Cerquerica MD, Garcia EV, Iskandrian AS, et al. Procedure guideline for myocardial perfusion imaging 3.3. J Nucl Med Technol 2008; 36: 155-61. [Crossref]
10. Hesse B, Tagil K, Cuoccolo A, Anagnostopoulos C, Bardies M, Bax J, et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. Eur J Nucl Med Mol Imaging 2005; 32: 855-97. [Crossref]
11. Diamond GA, Forrester JS, Hirsch M, Staniloff HM, Vas R, Berman DS, et al. Application of conditional probability analysis to the clinical diagnosis of coronary artery disease. J Clin Invest 1980; 65: 1210-21. [Crossref]
12. Attia J. Moving beyond sensitivity and specificity: using likelihood ratios to help interpret diagnostic tests. Aust Prescr 2003; 26: 111–3.
13. Gibbons RJ, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 2002; 106: 1883-92. [Crossref]
14. de Jong MC, Genders TS, van Geuns RJ, Moelker A, Hunink MG. Diagnostic performance of stress myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis. Eur Radiol 2012; 22: 1881-95. [Crossref]

15. Boo S, Waters CM, Froelicher ES. Coronary heart disease risk estimation in asymptomatic adults. Nurs Res 2012; 61: 66-9. [Crossref]
16. Interpretation of diagnostic data: 5. How to do it with simple maths. Can Med Assoc J 1983; 129: 947-54. [Crossref]
17. Guetta V, Canon RO 3rd. Cardiovascular effects of estrogen and lipid-lowering therapies in postmenopausal women. Circulation 1996; 93: 1928-37. [Crossref]
18. Pryor DB, Harrell FE Jr, Lee KL, Califf RM, Rosati RA. Estimating the likelihood of significant coronary artery disease. Am J Med 1983; 75: 771-80. [Crossref]
19. Pryor DB, Shaw L, McCants CB, Lee KL, Mark DB, Harrell FE Jr, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. Ann Intern Med 1993; 118: 81-90.
20. Chun AA, McGee SR. Bedside diagnosis of coronary artery disease: a systematic review. Am J Med 2004; 117: 334-43. [Crossref]
21. Genders TS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J 2011; 32: 1316-30. [Crossref]
22. Morise AP. Comparison of the Diamond-Forrester method and a new score to estimate the pretest probability of coronary disease before exercise testing. Am Heart J 1999; 138: 740-5. [Crossref]
23. Ashley E, Myers J, Froelicher V. Exercise testing scores as an example of better decisions through science. Med Sci Sports Exerc 2002; 34: 1391-8. [Crossref]
24. Hachamovitch R, Berman DS, Kiat H, Cohen I, Cabico JA, Friedman J, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease, incremental prognostic value and use in risk stratification. Circulation 1996; 93: 905-14. [Crossref]