Original Article

Diagnostic Myocardial Perfusion Imaging to Detect the Anatomical Location of Coronary Artery Disease Compared With Invasive Coronary Angiography

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ABSTRACT

Background: Although invasive coronary angiography (CAG) is the gold standard for the diagnosis of coronary artery disease (CAD), myocardial perfusion imaging (MPI) is also used in suspected cases. In this study, we sought to determine the diagnostic value of MPI in the anatomical localization of CAD.

Methods: In a retrospective study, all patients with an intermediate to high probability of CAD who had positive single-photon emission computed tomography MPI and subsequently underwent CAG between January 2016 and January 2017 were evaluated.

Results: A total of 210 patients at a mean age of 60.2±10.6 years underwent MPI and CAG. Abnormal anterior segments in MPI had a positive predictive value (PPV) of 68.1% to detect a diseased left anterior descending artery (LAD), and the negative predictive value (NPV) of similar segments for a concomitant LAD and right coronary artery (RCA) involvement was the highest (90.4%). Abnormal inferior segments in MPI had PPVs of 65.1% and 47% for the LAD and the RCA, respectively. The NPV was 81.8% for a concomitant LAD and RCA involvement and it was greater than either of each alone. Among the patients with abnormal posterior segments, the RCA and the left circumflex artery (LCX) had a PPV of 66.7%, which was greater than that of a concomitant RCA and LCX involvement. The NPV for either RAC or LCX alone or both arteries together was similar.

Conclusions: MPI provides a relatively good diagnostic accuracy to detect abnormal segments matched to the involved coronary arteries in CAG. However, diagnostic accuracy was more pronounced in matching single-vessel CAD compared with double-vessel CAD. (Iranian Heart Journal 2019; 20(2): 62-68)

KEYWORDS: Coronary artery disease, Myocardial perfusion imaging, Coronary angiography

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therosclerosis is a multifactorial disease attributed to some conventional risk factors. 1-3 and it leads to development of coronary artery disease (CAD). The exact prevalence of CAD as manifestation of atherosclerosis is unknown, particularly in an asymptomatic population.⁴ With the implementation of noninvasive imaging modalities such as echocardiography, computed tomography coronary angiography, myocardial perfusion imaging (MPI), positron emission tomography, and cardiovascular magnetic resonance imaging, there have been higher numbers of CAD cases among patients with suspected ischemic heart diseases.

Although invasive coronary angiography (CAG) is the gold standard for the diagnosis of CAD, the application of imaging modalities in patients with suspected acute coronary syndrome (ACS) with an inconclusive electrocardiogram and cardiac biomarkers is recommended by the guidelines.^{6,7} Of those imaging modalities, MPI is a widely-used and cost-effective tool which is of great diagnostic value for the evaluation of patients with known or suspected CAD,8 or even for the left ventricular function. Despite its good diagnostic accuracy in different studies, 10 the sensitivity and specificity of MPI can be varied, which may be attributable to the study population. In the present study, we sought to evaluate the diagnostic value of MPI in the localization of CAD among patients with suspected CAD who had positive MPI findings and subsequently underwent invasive CAG.

METHODS

Study Protocol

In a retrospective study, all patients who had an intermediate to high probability for CAD underwent single-photon emission computed tomography (SPECT) MPI and subsequently underwent CAG between January 2016 and January 2017 were evaluated. The inclusion criteria included patients older than 18 years old with stable angina and positive MPI for the diagnosis of CAD who subsequently underwent

invasive CAG. Patients with a prior myocardial infarction, a recent or recurrent ACS, valvular heart diseases, and heart failure were excluded from the study. Our local ethics committee at Iran University of Medical Sciences approved the study protocol.

Diagnostic Modalities

In all the patients, nuclear scaning was performed using the rest-stress protocol SPECT MPI (with technetium-99m sestamibi) along with the symptom-limited exercise test or the pharmacological stress test. Data were obtained using a Philips Forte SPECT camera (Philips Healthcare, the Netherlands), followed by making reconstructions presenting in a polar map format based on segmental territories.

All patients with a positive MPI underwent invasive CAG to identify the probable lesions in the coronary arteries. All CAG procedures were undertaken based on the Judgkin technique and were analyzed without knowledge of MPI results. A significant CAD was defined as at least 1 coronary artery with >50% stenosis. For each artery, the most severe stenosis was identified.

Anatomical Territories

The result of SPECT MPI was categorized into 3 segments as follows:

- 1) anterior and anteroseptal
- 2) inferior
- 3) posterior

And the result of invasive CAG was matched for each of the mentioned segments as follows:

- 1) left anterior descending artery (LAD), right coronary artery (RCA), alone and both together
- 2) LAD, RCA, alone and both together
- 3) RCA, left circumflex artery (LCX), alone and both together

Statistical Analysis

All the data were presented as mean \pm SD or numbers (percentages). The diagnostic performance of MPI was also compared with that of CAG so as to identify patients with significant CAD in defined anatomical territories and its relevant coronary artery

branch. All the analyses were performed using the SPSS statistical software for Windows, version 18.0 (Chicago, IL, SPSS Inc). Two-sided *P* values were calculated.

RESULTS

A total of 210 patients with abnormal MPI who subsequently underwent CAG were analyzed. The patients' mean age was 60.2±10.6 years, and 124 patients (59%) were male. Other medical histories are summarized in Table 1. Fifty-four (25.7%)patients had normal coronary arteries without significant involvement of the arteries. The number of patients with triple-vessel, double-vessel, and single-vessel CAD was 54 (25.7%), 50 (23.8%), and 46 (21.9%), respectively. The LAD was involved the most (64.3%). The concomitant involvement of the LAD and the RCA was more frequent than other doublevessel CADs. The significant involvement of the left main CAD was detected in 6 (2.9%) patients.

The patients with the involvement of the anterior and anteroseptal walls of the heart in MPI had a positive predictive value (PPV) of 68.1% to detect a diseased LAD. The PPV of the RCA or a concomitant LAD and RCA involvement was less than that of the LAD alone. In addition, the negative predictive value (NPV) of MPI with involved anterior and anteroseptal segments was the highest (90.4%) in the patients with a concomitant significant LAD and RCA involvement (Table 2). The patients with abnormal inferior segments in MPI had PPVs of 65.1% and 47% for diseased

LAD and RCA in CAG, respectively. However, the NPV was 81.8% for a concomitant LAD and RCA involvement, and it was greater than that of the LAD or RCA alone (Table 3). Among the patients with posterior wall abnormalities in MPI, the RCA and the LCX had a similar PPV (66.7%), and it was greater than that of a concomitant RCA and LCX involvement. On the other hand, the NPV for either RAC or LCX alone or both arteries together was similar (Table 3).

Table 1. Patients' characteristics and overall findings in the imaging evaluation

the imaging evaluation	Value				
Total patients	210				
Age (y)	60.2 ± 10.6				
Male gender	124 (59%)				
Hypertension	120 (57.1%)				
Diabetes mellitus	119 (56.7%)				
Dyslipidemia	93 (44.3%)				
Current smoking	65 (31%)				
Familial history of CAD	97 (46.2%)				
Prior myocardial infarction	70 (33.3%)				
Diseased vessel in CAG					
Normal	54 (25.7%)				
1 VD	46 (21.9)				
2 VD	50 (23.8%)				
3 VD	54 (25.7%)				
CAG findings					
LAD	135 (64.3%)				
RCA	93 (44.3%)				
LCX	83 (39.5%)				
LM	8 (3.8%)				
LAD and LCX	21 (10%)				
LAD and RCA	25 (11.9%)				
LCX and RCA	4 (1.9%)				
LM and RCA	6 (2.9%)				
LAD, LCX, and RCA	54 (25.7%)				

Values are presented as mean ± SD or number (%). CAD, Coronary artery disease; CAG, Coronary angiography; VD, Vessel disease; LAD, Left anterior descending artery; RCA, Right coronary artery; LCX, Left circumflex artery; LM, Left main coronary artery

Table 2. Diagnostic performance of MPI to detect coronary arteries perfusing the anterior and anteroseptal walls of the heart

	CAG	MPI for the Anterior and Anteroseptal Walls		Sensitivity	Specificity	PPV	NPV	P value
		Positive	Negative					
LAD	Positive	79	56	58.5%	50.7%	68.1%	59.6%	0.200
	Negative	37	38					
RCA	Positive	63	30	67.7%	54.7%	54.3%	68.1%	0.001
	Negative	53	64					
LAD and RCA	Positive	16	9	64%	45.9%	13.8%	90.4%	0.348
	Negative	100	85					

MPI, Myocardial perfusion imaging; CAG, Coronary angiography; PPV, Positive predictive value; NPV, Negative predictive value; LAD, Left anterior descending artery; RCA, Right coronary artery

Table 3. Diagnostic performance of MPI to detect coronary arteries perfusing the inferior wall of the heart

	CAG	MPI for the Inferior Wall		Sensitivity	Specificity	PPV	NPV	<i>P</i> value
		Positive	Negative					value
LAD	Positive	108	27	80%	22.6%	65.1%	38.6%	0.649
	Negative	58	17					
RCA	Positive	78	15	83.9%	24.8%	47%	65.9%	0.126
	Negative	88	29					
LAD and RCA	Positive	17	8	- 68%	19.4%	10.2%	81.8%	0.148
	Negative	149	36					

MPI, Myocardial perfusion imaging; CAG, Coronary angiography; PPV, Positive predictive value; NPV, Negative predictive value; LAD, Left anterior descending artery; RCA, Right coronary artery

Table 4. Diagnostic performance of MPI to detect coronary arteries perfusing the posterior wall of the heart

	CAG	MPI for the Posterior Wall		Sensitivity	Specificity	PPV	NPV	<i>P</i> value
		Positive	Negative					value
RCA	Positive	2	91	2.1%	56%	66.7%	99.1%	0.432
	Negative	1	116					
LCX	Positive	2	81	2.4%	60.9%	66.7%	99.2%	0.333
	Negative	1	126					
RCA and LCX	Positive	2	2	50%	98.5%	40%	99%	0.643
	Negative	3	203					

MPI, Myocardial perfusion imaging; CAG, Coronary angiography; PPV, Positive predictive value; NPV, Negative predictive value; RCA, Right coronary artery; LCX, Left circumflex artery

DISCUSSION

Although CAG is the gold standard for the evaluation of CAD, noninvasive modalities have been used first for the selection of proper patients who need to undergo such an invasive procedure. The use of MPI has been dramatically increased in European countries. Based on a meta-analysis, MPI has been associated with an average sensitivity of 87% and a specificity of 73% for the detection of CAD diagnosed by angiography; however, there has been a post-test referral bias leading to a decrease in the specificity of MPI. 11 On the other hand, a previous study showed that without post-test referral bias, MPI had less sensitivity and slightly higher specificity. ¹² Due to study designs and population sizes, the amounts of sensitivity and specificity have been varied among studies. The main factors influencing the different diagnostic values include referral bias, the intensity of the the use of anti-anginal test. medications before the test, the absence of clinical information upon interpreting scan, tracer activity below the diaphragm, some technical issues related to MPI, image quantification, and concomitant electrocardiogram-gating. The retrospective nature of our study precluded a distinction between low- and high-risk probabilities of CAD among patients referred for MPI; we, therefore, used only positive MPI reports to detect the anatomical significance of MPI compared with that of invasive CAG.

The diagnosis of CAD by noninvasive imaging such as MPI and stress echocardiography is based on the assessment of myocardial territories perfused by distinct coronary arteries and the physiological significance of CAD, not the anatomical extent of CAD. However, multi-slice computed tomography angiography (CTA) is another noninvasive imaging method which has been used for the evaluation of atherosclerosis and subsequent CAD similar to invasive CAG. Stein et al found a strong NPV for CTA capable of excluding significant CAD and, thus, concluded that CTA findings should

be also strengthened by concomitant use of pretest clinical probability assessments. In a large study comparing CTA and SPECT MPI, with the increasing severity of stenosis detected by CTA, there was an increase in abnormal MPI tests, suggesting that normal coronary arteries on CTA had a high PPV for a normal MPI.¹⁵

Schwartz et al¹⁶ matched anatomically invasive CAG to SPECT MPI in order to evaluate the diagnostic value of SPECT MPI for the detection of CAD in the distribution of firstorder branches. They demonstrated that SPECT MPI had intermediated sensitivity, specificity, and accuracy to detect CAD in the distribution of first-order coronary arteries values=67%). In addition, this sensitivity of MPI was higher in patients without a prior history of coronary artery bypass surgery. In our study, an abnormal MPI at the anterior and anteroseptal territories had a PPV of 68.1% to detect CAD in the LAD and it was higher than that value for the RCA; nonetheless, the RCA had more sensitivity and both LAD and RCA together had the least accuracy. An abnormal MPI in the inferior segment had a PPV of 65.1% to detect a diseased LAD and it was found to have a sensitivity of 83.9% to detect the involved RCA. For the abnormal SPECT MPI at the posterior wall, the RCA and LCX had similar PPVs (66.7%), but it had the highest sensitivity for diseased RCA and LCX together (50%). In summary, all MPI segments as defined in our study had the highest PPV for the detection of single-vessel CAD. In addition, the NPV was highest for double-vessel CAD at each segment for the anterior and inferior segments. However, in the patients with posterior wall abnormalities in MPI, the NPV was similar for single and double-vessel CAD. We think that the latter finding may be explained by very small cases with an abnormal MPI in the posterior wall compared with the other 2 segments. Further large-scale studies are warranted to explore the exact diagnostic accuracy of MPI

Study Limitations

This study has some limitations that need to be taken into account in the interpretation of the results. Firstly, our sample size is relatively small and our test accuracies may not be generalizable to other populations. Secondly, if only patients with abnormal MPS undergo angiography, then the observed sensitivity and specificity will be 100% and 0%, respectively. Accordingly, we have not been able to use the findings of the current study for the overall diagnostic accuracy of MPI compared with invasive CAG, as the old standard method. Thirdly, due to the small sample size and the nature of MPI reports in our department, we categorized our population into the anatomical territories mentioned in the methods. All MPI segments and matched coronary arteries can be presented in another way for more precision; however, this classification was based on our saved MPI reports and cannot be changed in another categorization. Further studies are required to find the precise diagnostic performance of SPECT MPI in the detection of matched anatomical CAD diagnosed invasive CAG.

CONCLUSIONS

MPI **SPECT** provides relatively good diagnostic accuracy to detect abnormal segments matched to the significant involvement of coronary arteries in CAG. The diagnostic values were more pronounced in matching single-vessel CAD compared with double-vessel CAD.

Conflict of Interest: The authors have no conflict of interest.

REFERENCES

1. Dehghani MR, Rezaei Y, Taghipour-Sani L. Superiority of total white blood cell count over other leukocyte differentials for predicting long-term outcomes in patients with non-st elevation

- acute coronary syndrome. Biomarkers. 2014;19:378-384
- 2. Dehghani MR, Rezaei Y, Taghipour-Sani L. White blood cell count to mean platelet volume ratio as a novel non-invasive marker predicting long-term outcomes in patients with non-st elevation acute coronary syndrome. Cardiology journal. 2015;22:437-445
- **3.** Dehghani MR, Taghipour-Sani L, Rezaei Y, Rostami R. Diagnostic importance of admission platelet volume indices in patients with acute chest pain suggesting acute coronary syndrome. Indian heart journal. 2014;66:622-628
- **4.** Enbergs A, Burger R, Reinecke H, Borggrefe M, Breithardt G, Kerber S. Prevalence of coronary artery disease in a general population without suspicion of coronary artery disease: Angiographic analysis of subjects aged 40 to 70 years referred for catheter ablation therapy. European heart journal. 2000;21:45-52
- **5.** Garg P, Underwood SR, Senior R, Greenwood JP, Plein S. Noninvasive cardiac imaging in suspected acute coronary syndrome. Nature reviews. Cardiology. 2016;13:266-275
- 6. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, Douglas PS, Foody JM, Gerber TC, Hinderliter AL, King SB, 3rd, Kligfield PD, Krumholz HM, Kwong RY, Lim MJ, Linderbaum JA, Mack MJ, Munger MA, Prager RL, Sabik JF, Shaw LJ, Sikkema JD, Smith CR, Jr., Smith SC, Jr., Spertus JA, Williams SV. 2012 accf/aha/acp/aats/pcna/scai/sts guideline for the diagnosis and management of patients with stable ischemic heart disease: A report of the american college of cardiology foundation/american heart association task force on practice guidelines, and the american college of physicians, american association for thoracic surgery, preventive cardiovascular nurses association, society for cardiovascular angiography and interventions, and society of thoracic surgeons. Journal of the American College of Cardiology. 2012;60:e44-e164
- 7. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, Wijns W, Zahger D. Esc guidelines for the management of acute

- coronary syndromes in patients presenting without persistent st-segment elevation: The task force for the management of acute coronary syndromes (acs) in patients presenting without persistent st-segment elevation of the european society of cardiology (esc). European heart journal. 2011;32:2999-3054
- **8.** Malek H, Yaghoobi N, Hedayati R. Artifacts in quantitative analysis of myocardial perfusion spect, using cedars-sinai qps software. Journal of nuclear cardiology: official publication of the American Society of Nuclear Cardiology. 2017;24:534-542
- 9. Shojaeifard M, Ghaedian T, Yaghoobi N, Malek H, Firoozabadi H, Bitarafan-Rajabi A, Haghjoo M, Amin A, Azizian N, Rastgou F. Comparison of gated spect myocardial perfusion imaging with echocardiography for the measurement of left ventricular volumes and ejection fraction in patients with severe heart failure. Research in cardiovascular medicine. 2016;5:e29005
- 10. Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise spect imaging? A meta-analysis of diagnostic test performance. Jama. 1998;280:913-920
- 11. Underwood SR, Anagnostopoulos C, Cerqueira M, Ell PJ, Flint EJ, Harbinson M, Kelion AD, Al-Mohammad A, Prvulovich EM, Shaw LJ, Tweddel AC. Myocardial perfusion scintigraphy: The evidence. European journal of nuclear medicine and molecular imaging. 2004;31:261-291
- 12. Johansen A, Hoilund-Carlsen PF, Christensen HW, Vach W, Jorgensen HB, Veje A, Haghfelt T. Diagnostic accuracy of myocardial perfusion imaging in a study population without post-test referral bias. Journal of nuclear cardiology: official publication of the American Society of Nuclear Cardiology. 2005;12:530-537
- 13. Sajjadieh A, Hekmatnia A, Keivani M, Asoodeh A, Pourmoghaddas M, Sanei H. Diagnostic performance of 64-row coronary ct angiography in detecting significant stenosis as compared with conventional invasive coronary angiography. ARYA atherosclerosis. 2013;9:157-163

- **14.** Stein PD, Yaekoub AY, Matta F, Sostman HD. 64-slice ct for diagnosis of coronary artery disease: A systematic review. The American journal of medicine. 2008;121:715-725
- **15.** Han PP, Fang W, Tian YQ, Gao Y, Yang MF, Zhang XL, Shen R, Sun XX, Qiao SB, Lv B, Yang YJ, He ZX. Comparison of coronary ct angiography and stress/rest myocardial perfusion spect imaging in a chinese population. Clinical nuclear medicine. 2013;38:798-804
- 16. Schwartz JG, Johnson RB, Aepfelbacher FC, Parker JA, Chen L, Azar RR, Parker RA, Danias PG. Sensitivity, specificity and accuracy of stress spect myocardial perfusion imaging for detection of coronary artery disease in the distribution of first-order branch vessels, using an anatomical matching of angiographic and perfusion data. Nuclear medicine communications. 2003;24:543-549