

Clinical Study

Comparative Analysis between SPECT Myocardial Perfusion Imaging and CT Coronary Angiography for Diagnosis of Coronary Artery Disease

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The study aims to discuss the relationship and difference between myocardial perfusion imaging (MPI) using SPECT and CT coronary angiography (CTCA) for diagnosis of coronary artery disease (CAD). Five hundred and four cases undergoing MPI and CTCA were comparatively analyzed, including fifty six patients undergoing invasive coronary angiography in the same period. Among patients with negative MPI results, negative or positive CTCA occupied 84.7% or 15.3%, respectively. Among patients with positive MPI, positive or negative CTCA occupied 67.2% or 32.8%, respectively. Among patients with negative CTCA, negative or positive MPI occupied 94.4% or 5.6%, respectively. Among patients with positive CTCA, positive or negative MPI occupied 40.2% or 59.8%, respectively. Negative predictive value was relatively higher than the positive predictive value for positive CTCA eliminating or predicting abnormal haemodynamics. And there was no significant difference for sensitivity, specificity, and accuracy of MPI or CTCA in diagnosing CAD. Both MPI and CTCA have good diagnostic performance for CAD. They provide different and complementary information for diagnosis and evaluation of CAD, namely, detection of ischemia versus detection of atherosclerosis, which are quite different but have a definite internal link for each other.

1. Introduction

Myocardial perfusion imaging (MPI) with single-photon emission computer tomography (SPECT) is the most commonly used and well-documented noninvasive method for diagnosis and risk stratification of coronary artery disease (CAD) [1]. The location and extent of ischemia can be reliably and semiquantitatively obtained using MPI, which plays an important role for patient management. The latest advancements for computed tomography (CT), such as faster gantry, multidetector array, and even dual-source detectors, make it possible to noninvasively and intuitively obtain anatomic morphology of coronary arteries, especially contributing to identifying the magnitude, distribution, and composition of coronary atherosclerosis. It has been documented that CT coronary angiography (CTCA) has

high accuracy in detection of obstructive CAD comparing with invasive coronary angiography (ICA) [2]. As non-invasive diagnostic methods of CAD for both MPI and CTCA, how to correctly recognize the respective role and relationship between them in diagnosing and evaluating CAD is a very important question concerned by clinicians. This study aims to discuss and evaluate the relationship and difference between SPECT MPI and CTCA through comparative analysis.

2. Materials and Methods

2.1. Study Population. Five hundred and four consecutive patients with suspected or known CAD were enrolled in this study. All cases underwent CTCA and MPI within 30 days. The mean age of the study population was 56.7 ± 8.7 y,

with 326 patients being male (64.7%). Fifty six patients (man 56 women 18) among all cases also underwent ICA within 30 days, and the mean age for the group was 57.5 ± 9.2 y. ICA was finally performed after CTCA and MPI, with the sequence of CTCA and MPI depending on the individual clinical situation. The exclusion criteria were as follows: acute coronary syndrome (ACS), known old myocardial infarction (OMI), frequent premature beat, atrial fibrillation, contraindications for iodinated contrast agent, serious coronary calcification and motion artifacts affecting measures of stenoses, and patient with revascularization (including percutaneous coronary intervention or bypass graft). All patients gave formal written consent approved by our Institution Ethics Committee.

2.2. MPI

2.2.1. Imaging Acquisition. All patients underwent a 2-day stress/rest electrocardiography-gated MPI protocol. Exercise stress/rest gated MPIs were performed on a SPECT scanner (GE Millennium VG5 SPECT) before or after CTCA. Beta-blockers, calcium channel blockers, and nitrates were discontinued at least 24 h before MPI. The exercise stress tests were performed according to a modified Bruce's protocol on a bicycle ergometer with a 12-lead ECG, and blood pressure measurements were taken at the baseline and every 2 min during the whole procedure. The endpoints for the stress tests included any one of the following indexes: reaching target heartbeat ($(220 - \text{age in years}) \times 85\%$), ischemic ST-segment horizontal or downslope depression of ≥ 2 mm, emergence of typical angina, severe cardiac arrhythmia, hypertension ($\geq 240/120$ mmHg), and a fall of systolic pressure ≥ 40 mmHg. At the peak of exercise, a 925-MBq dose of ^{99m}Tc -MIBI was injected into the bloodstream through the vein, and the patient continued to pedal for an additional 1 min. The ECG and blood pressure were monitored before and throughout the test and again after the injection. The acquisition for stress gated-SPECT study was performed about 1 h after injection. Rest studies started acquisition about 1.5 h after injection by using the same amount of doses. The acquisition parameters were listed as follows: a low-energy, high-resolution collimator; a 20% symmetric window at 140 keV; a 64×64 matrix; an elliptic orbit with step-and-shoot acquisition at 6° intervals over 180° from the right anterior oblique 45° to left posterior oblique 45° ; 25 s dwell time per stop. Acquisitions were gated at 8 frames per R-R cycle with a 50% window of accepted heart rate.

2.2.2. Image Reconstruction and Interpretation. All data were transferred to an eNTEGRA workstation and reconstructed using an iterative reconstruction algorithm (2 iterations and 10 subsets, Butterworth prefiltering function, a gradient order of 5.0, and a frequent cutoff of 0.25) without X-ray attenuation correction. Images were reconstructed into short axial, horizontal axial, and vertical long axial sections. At the same time, polar maps, wall motion, and wall thickening were obtained using a special software package (ECT toolbox and Multidim).

Semiquantitative visual judgment was made by consensus of two experienced observers aware of the size, weight, and gender of the patients but not the results of their CTCA or ICA assessments. The left ventricular myocardium was divided into 17 segments according to the American Heart Association [3]. Each segment was scored automatically by use of ECToolbox software based on a 5-point scoring system (0, normal uptake; 1, mild decreased uptake; 2, moderate decreased uptake; 3, severely decreased uptake; 4, absence of uptake). The sum of the stress scores of all segments (SSS) and the sum of the rest scores of all segments (SRS) were determined from these values. A summed difference score (SDS) was calculated as the difference between SSS and SRS. $\text{SDS} > 1$ was defined as reversible perfusion defect indicating ischemia. The results of MPIs were divided into two categories: negative MPI, defined as having homogenous radioactive distributions in myocardium and no defective segments noticed for both stress and rest scans; positive MPI, including reversible and fixed perfusion defects. Reversible pattern of localized segments of decreased perfusion at stress were no longer seen or demonstrated partial improvement at rest. Fixed pattern showed that localized segments of decreased perfusion were unchanged between the stress and rest images. Reversible perfusion defects were considered to represent myocardial ischemia. Fixed perfusion defects with concurrent regional wall motion abnormalities were considered to be myocardial scar.

2.3. CTCA

2.3.1. Image Acquisition. All scans were performed on a 64-slice CT scanner (GE Light Speed VCT). Patients were required to fast 4 h before CT imaging. Patients with pre-scan heart rates above 65 b.p.m. needed to take a beta-blocker (Betaloc tablets, 25–100 mg). Before starting scans, patients were required to take 0.5 mg nitroglycerin sublingually. The acquisition parameters included 350 ms rotation time, 120 KV tube voltage, 650–800 mA tube current, and 0.6 mm collimation. Scan scope range was between the carina of the trachea and 2 cm below the diaphragm. The total scan time was about 12 s. In brief, a bolus of 20 mL contrast agent iohexol (350 mg/mL) was delivered intravenously through an antecubital vein at a flow rate of 4 mL/s using high-pressure injector for prescan. Bolus tracking technique was performed with a region of interest placed in the ascending aorta to record the peak time of enhancement and confirm the delay time of starting acquisition. A bolus of 70–80 mL of iohexol was then intravenously injected into the bloodstream at a speed of 4–5 mL/s through an antecubital vein. At the same time, the patients were required to hold their breath throughout the scanning procedure.

2.3.2. Image Reconstruction and Interpretation. The acquired data were transferred to a GE Advanced Workstation, and a late diastole phase (75% R-R time) was automatically reconstructed. If the qualities of reconstructed images were not satisfactory, the images of 45%–85% R-R time were reconstructed and reviewed to select the best reconstructed

TABLE 1: Characteristics of the population for positive and negative groups of MPI and CTCA.

Parameters	Positive MPI (<i>n</i> = 67)	Negative MPI (<i>n</i> = 437)	<i>P</i> value	Positive CTCA (<i>n</i> = 112)	Negative CTCA (<i>n</i> = 392)	<i>P</i> value
Age	54.0 ± 10.8	51.8 ± 11.8	<i>P</i> > 0.05	49.8 ± 11.8	50.6 ± 11.9	<i>P</i> < 0.05
Prior myocardial infarction	None	None	—	None	None	—
Prior coronary revascularization	None	None	—	None	None	—
Risk factors for CAD						
Diabetes mellitus	19	10	<i>P</i> < 0.05	18	11	<i>P</i> < 0.05
Hypertension	55	32	<i>P</i> < 0.05	60	27	<i>P</i> < 0.05
Hypercholesterolemia	34	213	<i>P</i> > 0.05	89	158	<i>P</i> < 0.05
Family history of CAD	42	56	<i>P</i> < 0.05	51	47	<i>P</i> < 0.05
Smoking history	23	88	<i>P</i> < 0.05	35	76	<i>P</i> < 0.05

images which clearly depicted coronary arteries. Finally, the images were displayed on screen in the form of multiple planar reformations (MPRs), virtual rendering volume (VR), and maximal intensity projection (MIP). The images were visually and independently evaluated by two experienced readers (with more than three years of experience in cardiovascular imaging) who were both blinded to the MPI findings. Upon reaching a consensus, the two readers agreed on the final diagnosis. Coronary arteries were subdivided according to a 15-segment model proposed by the American Heart Association [4]. Each segment was visually assessed and reported as $\geq 50\%$ or $< 50\%$ and allocated to the left main (LM), left anterior descending (LAD), left circumflex (LCX), and right coronary arteries (RCAs). The narrowest lesion was regarded as a final diagnosis for diffuse or multiple stenoses in a single vessel. Visual assessment of vessel narrowing of 50% or greater for at least one main vessel was defined as significant stenosis (positive CTCA), otherwise negative CTCA.

2.4. ICA. Conventional ICA was according to the standard Judkins catheter technique. Multiple views for each coronary artery were obtained digitally and stored in a designated workstation after intracoronary application of iodinated contrast agent. The angiograms were observed and evaluated by two experienced interventional cardiologists who were blinded to the CTCA and MPI findings. The readers agreed on the final diagnosis upon reaching a consensus. Visual assessment of vessel narrowing of 50% or greater for at least one main vessel was defined as significant stenosis (positive ICA), otherwise negative ICA.

3. Data Analysis and Statistics

The percentages of positive or negative CTCA among patients with positive or negative MPI results were calculated, and the percentages of positive or negative MPI among patients with positive or negative CTCA results were also calculated.

Abnormal perfusion area (defect) was allocated to coronary artery territories according to the reference as described previously [5]. Defects in the anterior wall and septal wall

TABLE 2: The relations between MPI and CTCA results.

CTCA	MPI		Total
	Positive	Negative	
Positive	45	67	112
Negative	22	370	392
Total	67	437	504

were allocated to the left anterior descending coronary artery (LAD); defects in the lateral wall, to the right coronary artery (RCA). Defects affecting both LAD region and LCX region were considered as left main artery (LM) lesion. In the watershed regions, allocation was determined according to the main extension of the defect onto the lateral, anterior, or inferior wall. The number of cases with vessel narrowing of $\geq 50\%$ on CTCA with corresponding perfusion defect on MPI was calculated for positive predictive value of CTCA, and the number of cases with vessel narrowing of $< 50\%$ without corresponding perfusion defect was also calculated for negative predictive value of CTCA.

Using ICA as referenced standard, diagnostic sensitivity, specificity, and accuracy of MPI or CTCA for CAD were calculated and statistically compared, respectively. Mean values were compared using the double-tailed *t*-test, and comparison of statistical differences between enumeration data was performed using Chi-square test. A *P* value of < 0.05 was considered significant. Data were analyzed using STATA software version 13.0.

4. Results

The clinical characteristics of patients for different groups are shown in Table 1.

4.1. Relation between MPI and CTCA. The results for CTCA with corresponding MPI were showed in Table 2. Using MPI results as referred criteria, the positive predictive value for positive CTCA predicting abnormal haemodynamics is low (40.2%), but its negative predictive value for eliminating perfusion abnormalities is relatively high (94.4%), and the

TABLE 3: The diagnostic indexes of MPI and CTCA and comparison between them in 56 patients.

Indexes	MPI	CTCA	<i>P</i> values
True positive	24	27	
True negative	20	22	
False positive	5	3	
False negative	7	4	
Sensitivity	82.8%	90.0%	0.67* (0.19)
Specificity	74.1%	84.6%	0.34* (0.90)
Accuracy	78.6%	87.5%	0.21* (1.59)

* Chi-square test, value of χ^2 in brackets.

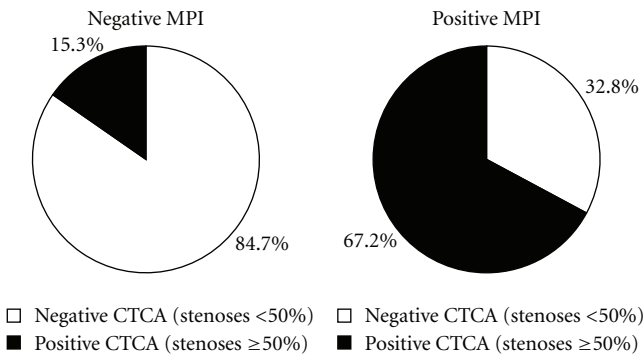


FIGURE 1: The percentages of negative or positive CTCA among patients with negative or positive MPI results.

difference between them has statistic significance ($\chi^2 = 90.3$, $P < 0.01$).

Among patients with negative MPI results, negative or positive CTCA occupied 84.7% or 15.3%, respectively. Among patients with positive MPI results, positive or negative CTCA occupied 67.2% or 32.8%, respectively. Among patients with negative CTCA results, negative or positive MPI occupied 94.4% or 5.6%, respectively; among patients with positive CTCA results, positive or negative MPI occupied 40.2% or 59.8%, respectively. The above results were represented on Figures 1 and 2 in the form of pie charts.

4.2. Comparison of MPI and CTCA to Conventional ICA in 56 Patients. With ICA results regarded as reference, the performance indexes of MPI and CTCA detecting CAD were listed in Table 3. The data showed that both MPI and CTCA had good sensitivity, specificity, and accuracy for the detection of obstructive CAD compared with ICA ($P > 0.05$).

It was important to note that one patient with balanced three-vessel stenoses (narrowing of 80% for LAD, LCX, and RCA) was missed by MPI among seven negative patients who underwent SPECT compared with ICA. Figure 3 presents a typical case of a 55-year-old man with intermittent angina pectoris for half a year. Anatomic and physiologic information provided by CTCA and MPI showed that interventional therapy should be directed to the lesion in the proximal segment of LAD. The patient finally received stent

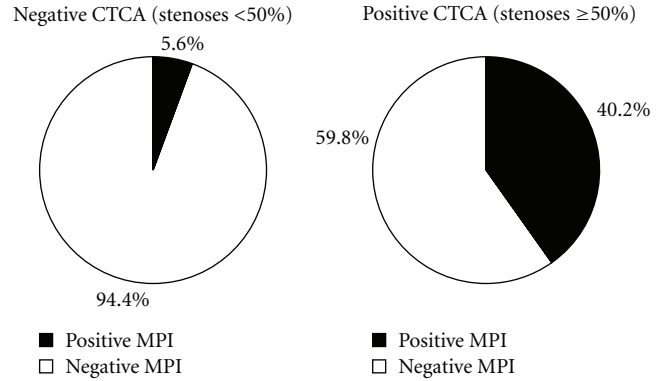


FIGURE 2: The percentages of negative or positive MPI among patients with negative or positive CTCA results.

implantation for the lesion located in the LAD with success. A typical case is shown in Figure 3.

5. Discussion

The diagnostic principle of CAD is very different for MPI and CTCA, and MPI has abilities to show the extent and severity of ischemia by visual or semiquantitative method, but it cannot show the morphology and plaques of coronary arteries. CTCA can directly depict the site and severity of coronary lesions. In addition, the length of stenosis, distribution, magnitude, and even composition of plaque can be precisely revealed and classified (calcified versus noncalcified) [6, 7]. But CTCA does not directly provide the hemodynamic significance related to the abnormalities of coronary arteries, which is very important in developing the therapeutic strategies for CAD. The coronal stenoses found on CTCA do not always lead to decreased perfusion to the myocardium. Previous study [8] showed that the severity of coronary stenosis was only a moderate surrogate among factors affecting myocardial blood perfusion, not sole decisive factor. Other factors affecting myocardial perfusion include length and shape of narrowing, eccentricity of plaque, and serial stenosis. Salm et al. [9] reported that MPI was normal in 50% of angiographically significant lesions. Particularly, lesions with an intermediate stenosis severity may have a great variability in hemodynamic significance [10].

In this study, negative MPI occupying 59.8% among patients with positive CTCA indicated that more than 50% ratio among patients with obvious stenoses ($\geq 50\%$) on CTCA did not have hemodynamic significance of myocardial perfusion. Our results are consistent with the finding reported by Schuijff et al. [11], and it showed that only 45% of patients with an abnormal MSCT had abnormal MPI, even in patients with obstructive CAD on MSCT, 50% still had a normal MPI. Just as what is mentioned in Schuijff's study, myocardial perfusion imaging and MSCT provide different and complementary information on CAD, namely, detection of atherosclerosis versus detection of ischemia. Coronary

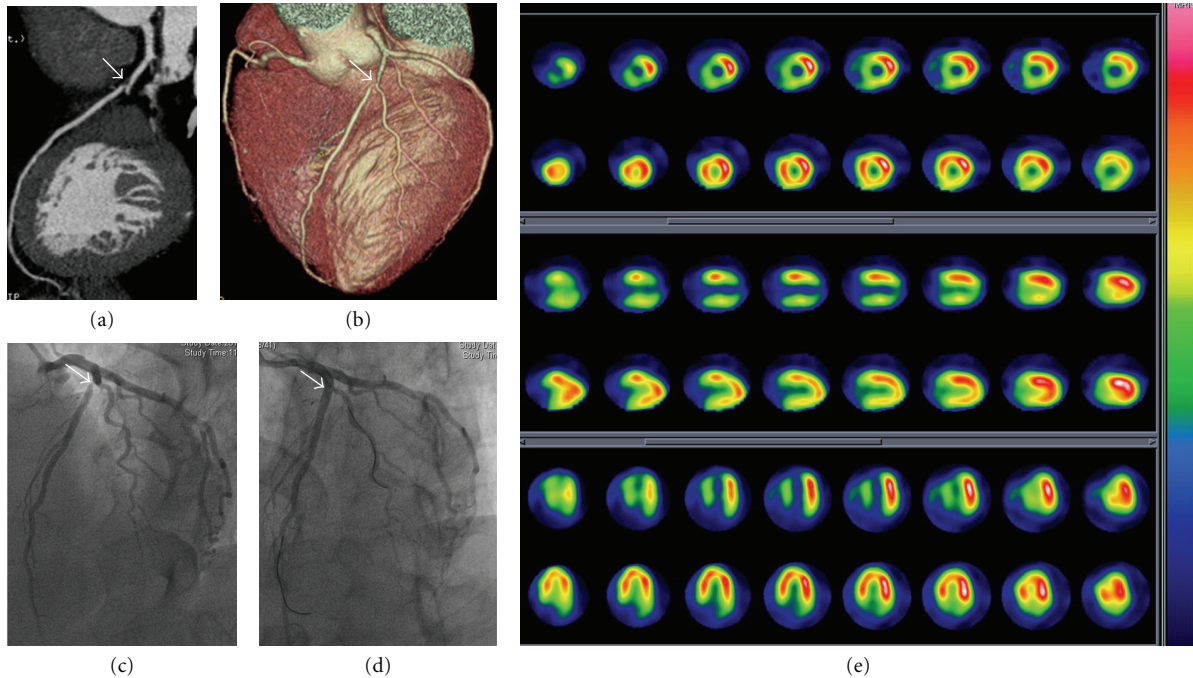


FIGURE 3: Patient with stenosis in the proximal segment of LAD classified as $\geq 50\%$ on CTCA related with large and reversible perfusion defects (ischemia) in apex, anterior, and septal wall on MPI. (a) and (b) Multiple reformation (MPR) and maximal intensity projection (MIP) on CTCA showed noncalcification plaque in the proximal segment of LAD adjacent to the ostia of diagonal branch causing a significant stenosis (arrows), and no positive results on other main arteries were found. (c) ICA of left coronary arteries showed severe stenosis (arrow) in the same segment of LAD compared with CTCA. (d) ICA of left coronary arteries showed successful stenting (arrow) for the lesion in the proximal segment of LAD. (e) SPECT MPI study at stress (odd row) and rest (even row) showed large and reversible perfusion defects in the area of apex, anterior and septal wall corresponding to the territory of LAD, indicating large and severe myocardial ischemia.

stenosis itself usually does not sufficiently predict corresponding hemodynamic abnormality. Whether coronary stenosis causes corresponding abnormal hemodynamics or not possesses considerable variations, especially for moderate stenoses (narrowing between 40% and 70%).

As the results found in this study, it clearly shows that CTCA has higher negative predictive value for eliminating perfusion defects. Hausleiter et al. [12] had proposed that coronary multislice CT could be a suitable means for the management of patients with an intermediate pretest likelihood of significant CAD. Invasive angiography would not be necessary if coronary MSCT angiography demonstrates normal coronary arteries. But the positive predictive value for CTCA reflecting haemodynamics was revealed to be relative low from this study. Therefore, functional imaging still needs to be done to reveal pathophysiologic changes related to coronary lesions. With coronary stenosis worsening, the severity of stenosis could be one of the most critical factors affecting corresponding myocardial perfusion [9, 13].

It should be kept in mind that negative MPI does not exclude coronary atherosclerosis and/or coronal stenoses, even existence of obvious stenoses, but patients with negative MPI results are usually thought to have a low risk of hard cardiac events. Patients with angiographically confirmed CAD, but negative MPI results have been shown to have similar low event rates [14, 15]. CTCA provides with very different information on CAD compared with MPI, which has abilities

to detect plaque burden of coronary atherosclerosis and severity of stenoses at early stage. With plaque burden and stenosis worsen, the prevalence of corresponding abnormal hemodynamics is increasing, but coronal plaque burden and stenosis are not synonyms for myocardial ischemia.

CTCA not only has the abilities to diagnose stenoses of coronary artery, but also shows the prognostic value for CAD. The study from van Werkhoven et al. [16] indicated that MSCT is an independent predictor of events and provides incremental prognostic value to MPI, combined anatomical and functional assessment may allow improved risk stratification. In addition, early identification of CAD with CTCA may also be useful for risk stratification. Non-invasive anatomic assessment of plaque burden, location, composition, and remodeling using CTCA may provide prognostically relevant information. This information has been shown to be incremental to the Framingham risk score, coronary artery calcium scoring, and myocardial perfusion imaging [17].

Therefore, MPI and CTCA play a complementary rather than excluding role in diagnosing and evaluating CAD. According to guidelines of American cardiac intervention therapy and radionuclide imaging, noninvasive morphological and functional method should be used before performing revascularization on patients with chronic stable angina, and coronary stenosis with corresponding ischemia is one of the major indications for performing revascularization,

while conservative therapy should be adopted when there are no significant stenoses or corresponding ischemia [18–20]. So the incremental values for guiding therapeutic strategies using combined CTCA and MPI for the detection of CAD are summarized as follows: first, a patient with neither significant coronary stenoses nor perfusion defects should undergo primary prevention and control of risk factors; second, a patient with significant coronary stenoses and no corresponding perfusion defects should undergo aggressive medical therapy and control of risk factors; third, a patient with significant coronary stenoses and corresponding perfusion defects should undergo active revascularization to obtain better prognosis rather than conservative therapy [21, 22]. CTCA and MPI are helpful in making the correct decision to insure patients benefit from treatments when noninvasively obtaining functional and anatomic information on coronary lesions.

It should be aware of the diagnostic principle of MPI being normal or abnormal depending on the relative distribution of radiopharmaceuticals in myocardium, so MPI possibly just detects abnormal territories corresponding to one or two relatively severe stenoses of coronary arteries for patients with three-vessel disease, and MPI even is negative for balanced reduction of perfusion to the myocardium for patients with balanced three-vessel stenoses [23, 24]. Therefore, MPI may miss some patients with balanced three-vessel disease, whereas CTCA is unlikely to miss severe or extensive coronary atherosclerosis [25]. For coronal microvascular disease causing ischemia, such as X syndrome, no matter CTCA or ICA cannot make a direct diagnosis because of limitation of spatial resolution, while MPI can make a diagnosis of myocardial ischemia for X syndrome by detecting ischemia [26, 27].

Although the rate of positive MPI was less than 50% among patients with significant stenoses on CTCA in this study, there was no statistically difference for the indexes of diagnosing CAD between MPI and CTCA in fifty six patients who underwent ICA in the same period. The reason may be related to the different morbidity of CAD between total patients and the patients who underwent ICA. The morbidity and stenotic severity in patients who underwent ICA were probably increased compared with total patients in this study for the reason of primarily being screened by clinicians. As has been stated, stenoses maybe one of main factors affecting corresponding hemodynamics with the severity of coronal stenoses worsen. So the diagnostic performances between MPI and CTCA tend to reach an agreement for patients with higher morbidity and severity of CAD.

In conclusion, both MPI and CTCA have good diagnostic performance for CAD, and they provide different and complementary information for diagnosis and evaluation of CAD, namely, detection of ischemia versus detection of atherosclerosis, which are quite different but have a definite internal link for each other.

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References

- [1] S. R. Underwood, C. Anagnostopoulos, M. Cerqueira et al., "Myocardial perfusion scintigraphy: the evidence—a consensus conference organised by the British Cardiac Society, the British Nuclear Cardiology Society and the British Nuclear Medicine Society, endorsed by the Royal College of Physicians of London and the Royal College of Radiologists," *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 31, no. 2, pp. 261–291, 2004.
- [2] S. Baumüller, S. Leschka, L. Desbiolles et al., "Dual-source versus 64-section CT coronary angiography at lower heart rates: comparison of accuracy and radiation dose," *Radiology*, vol. 253, no. 1, pp. 56–64, 2009.
- [3] M. D. Cerqueira, N. J. Weissman, V. Dilsizian et al., "Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association," *Circulation*, vol. 105, no. 4, pp. 539–542, 2002.
- [4] W. G. Austen, J. E. Edwards, R. L. Frye et al., "A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association," *Circulation*, vol. 51, no. 4, pp. 5–40, 1975.
- [5] O. Gaemperli, T. Schepis, I. Valenta et al., "Functionally relevant coronary artery disease: comparison of 64-section CT angiography with myocardial perfusion SPECT," *Radiology*, vol. 248, no. 2, pp. 414–423, 2008.
- [6] A. Sato, M. Hiroe, M. Tamura et al., "Quantitative measures of coronary stenosis severity by 64-slice CT angiography and relation to physiologic significance of perfusion in nonobese patients: comparison with stress myocardial perfusion imaging," *Journal of Nuclear Medicine*, vol. 49, no. 4, pp. 564–572, 2008.
- [7] T. Cyrus, R. J. Gropler, and P. K. Woodard, "Coronary CT angiography (CCTA) and advances in CT plaque imaging," *Journal of Nuclear Cardiology*, vol. 16, no. 3, pp. 466–473, 2009.
- [8] A. Yerramasu, A. Lahiri, and T. Chua, "Comparative roles of cardiac CT and myocardial perfusion scintigraphy in the evaluation of patients with coronary artery disease: competitive or complementary," *Journal of Nuclear Cardiology*, vol. 17, no. 5, pp. 761–770, 2010.
- [9] L. P. Salm, J. J. Bax, J. W. Jukema et al., "Hemodynamic evaluation of saphenous vein coronary artery bypass grafts: relative merits of Doppler flow velocity and SPECT perfusion imaging," *Journal of Nuclear Cardiology*, vol. 12, no. 5, pp. 545–552, 2005.
- [10] A. Berger, K. J. Botman, P. A. MacCarthy et al., "Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary intervention in patients with multivessel disease," *Journal of the American College of Cardiology*, vol. 46, no. 3, pp. 438–442, 2005.
- [11] J. D. Schuijf, W. Wijns, J. W. Jukema et al., "Relationship between noninvasive coronary angiography with multi-slice computed tomography and myocardial perfusion imaging," *Journal of the American College of Cardiology*, vol. 48, no. 12, pp. 2508–2514, 2006.
- [12] J. Hausleiter, T. Meyer, M. Hadamitzky et al., "Non-invasive coronary computed tomographic angiography for patients

- with suspected coronary artery disease: the Coronary Angiography by Computed Tomography with the Use of a Submillimeter resolution (CACTUS) trial,” *European Heart Journal*, vol. 28, no. 24, pp. 3034–3041, 2007.
- [13] M. L. E. Vicario, L. Cirillo, G. Storto et al., “Influence of risk factors on coronary flow reserve in patients with 1-vessel coronary artery disease,” *Journal of Nuclear Medicine*, vol. 46, no. 9, pp. 1438–1443, 2005.
- [14] P. Soman, A. Parsons, N. Lahiri, and A. Lahiri, “The prognostic value of a normal Tc-99m sestamibi SPECT study in suspected coronary artery disease,” *Journal of Nuclear Cardiology*, vol. 6, no. 3, pp. 252–256, 1999.
- [15] A. Elhendy, A. Schinkel, J. J. Bax, R. T. van Domburg, and D. Poldermans, “Long-term prognosis after a normal exercise stress Tc-99m sestamibi SPECT study,” *Journal of Nuclear Cardiology*, vol. 10, no. 3, pp. 261–266, 2003.
- [16] J. M. van Werkhoven, J. D. Schuijf, O. Gaemperli et al., “Prognostic value of multislice computed tomography and gated single-photon emission computed tomography in patients with suspected coronary artery disease,” *Journal of the American College of Cardiology*, vol. 53, no. 7, pp. 623–632, 2009.
- [17] J. M. van Werkhoven, J. J. Bax, G. Nucifora et al., “The value of multi-slice-computed tomography coronary angiography for risk stratification,” *Journal of Nuclear Cardiology*, vol. 16, no. 6, pp. 970–980, 2009.
- [18] F. J. Klocke, M. G. Baird, B. H. Lorell et al., “ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary—a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging),” *Circulation*, vol. 108, no. 11, pp. 1404–1418, 2003.
- [19] R. C. Hendel, M. R. Patel, C. M. Kramer et al., “ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriate-ness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology,” *Journal of the American College of Cardiology*, vol. 48, no. 7, pp. 1475–1497, 2006.
- [20] S. C. Smith Jr., J. T. Dove, A. K. Jacobs et al., “ACC/AHA guideline of percutaneous coronary interventions (revision of the 1993 PTCA guidelines): executive summary—a report of the American College of Cardiology/American Heart Association task force on practice guidelines(committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty),” *Journal of the American College of Cardiology*, vol. 37, pp. 2215–2239, 2001.
- [21] R. Hachamovitch, S. W. Hayes, J. D. Friedman, I. Cohen, and D. S. Berman, “Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography,” *Circulation*, vol. 107, no. 23, pp. 2900–2906, 2003.
- [22] D. S. Berman, R. Hachamovitch, L. J. Shaw et al., “Roles of nuclear cardiology, cardiac computed tomography, and cardiac magnetic resonance: noninvasive risk stratification and a conceptual framework for the selection of noninvasive imaging tests in patients with known or suspected coronary artery disease,” *Journal of Nuclear Medicine*, vol. 47, no. 7, pp. 1107–1118, 2006.
- [23] W. H. Aarnoudse, K. J. B. M. Botman, and N. H. J. Pijls, “False-negative myocardial scintigraphy in balanced three-vessel disease, revealed by coronary pressure measurement,” *International Journal of Cardiovascular Interventions*, vol. 5, no. 2, pp. 67–71, 2003.
- [24] J. R. Ghadri, A. P. Pazhenkottil, R. N. Nkoulou et al., “Very high coronary calcium score unmasks obstructive coronary artery disease in patients with normal SPECT MPI,” *Heart*, vol. 97, no. 12, pp. 998–1003, 2011.
- [25] G. Choudhary, V. Shin, S. Punjani, N. Ritter, S. C. Sharma, and W. C. Wu, “The role of calcium score and CT angiography in the medical management of patients with normal myocardial perfusion imaging,” *Journal of Nuclear Cardiology*, vol. 17, no. 1, pp. 45–51, 2010.
- [26] M. Saghari, M. Assadi, M. Eftekhari et al., “Frequency and severity of myocardial perfusion abnormalities using Tc-99m MIBI SPECT in cardiac syndrome X,” *BMC Nuclear Medicine*, vol. 6, article 1, 2006.
- [27] J. C. Kaski, G. Aldama, and J. Cosin-Sales, “Cardiac syndrome X: diagnosis, pathogenesis and management,” *American Journal of Cardiovascular Drugs*, vol. 4, no. 3, pp. 179–194, 2004.