Int J Clin Exp Med 2018;11(5):4794-4800
www.ijcem.com /ISSN:1940-5901/IJCEM0075155

Original Article

Single photon emission computed tomography myocardial perfusion imaging for early detection and location of stable angina pectoris

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Received February 28, 2018; Accepted April 4, 2018; Epub May 15, 2018; Published May 30, 2018

Abstract: Objective: To examine the application of single photon emission computed tomography (SPECT) myocardial perfusion imaging in the early detection and location of stable angina pectoris (SAP). Methods: Between January 2014 and May 2017, 150 with initially-diagnosed SAP admitted to our hospital were included in this study as participants. The participants were randomly assigned to receive either SPECT myocardial perfusion imaging or coronary angiography (CA). The findings of SPECT myocardial perfusion imaging and CA were compared. Analyses were made on the practical implications of SPECT myocardial perfusion imaging in the detection of SAP, and the detection and agreement rates of SPECT for severity of coronary stenosis. Results: For 150 patients with SAP, SPECT myocardial perfusion imaging and coronary angiography varied insignificantly in the detection of positive results of SAP and identification of the severity of coronary stenosis ($P > 0.05$). The sensitivity of SPECT nuclide myocardial perfusion imaging in the detection of SAP was 87.7% (93 of 106), the specificity was 84.1% (37 of 44), the rate of positive prediction was 93% (93 of 100), and the rate of negative prediction was 74% (37 of 50). Compared with CA, the total agreement rate of SPECT myocardial imaging in the detection and location of coronary artery lesions in patients with SAP was 81.8%. Conclusion: SPECT myocardial perfusion imaging is of significance in the early detection of SAP, and it can accurately locate the sites of the stenotic lesions. Hence it is worthy of extensively clinical application.

Keywords: Stable angina pectoris, single photon emission computed tomography, myocardial perfusion imaging, diagnosis, location

Introduction

Stable angina pectoris (SAP) is a common cardiovascular disease. It is a syndrome of acute and transient myocardial oxygen imbalance as a result of severe coronary stenosis and increased myocardial load based on stable coronary atherosclerotic plaques [1-3]. The diagnosis of SAP is primarily based on the patient's complaints of the history because the patient has missed the timing of SAP-onset, and ECG is difficult to capture objective information. Coronary angiography (CA) can intuitively and accurately reflect the severity of coronary stenosis, but it is difficult to estimate the trend of disease development and predict adverse events according to the presence of plaques. Even worse, invasion of CA results in significant traumas and high risks. Thus, it is impossible for CA to be used as a routine screening test [4, 5]. As a substantive branch of nuclear medicine, single photon emission computed tomography (SPECT) myocardial perfusion imaging is more applicable than invasive CA to early identification of SAP severity and location of lesions [6, 7]. Currently, SPECT myocardial perfusion imaging plays a dominant role in early detection of SAP, assessment of myocardial perfusion, confirming whether the myocardium dominated by coronary stenosis is ischemic as well as the location of the "criminal" coronary artery branch. Nevertheless, studies regarding SPECT myocardial perfusion imaging are rare and the results derived are still under debate. Therefore,

the current study aimed to examine the practical implication of SPECT myocardial perfusion imaging in the early detection and location of SAP.

Materials and methods

Patients

This study was approved by the Hospital Ethics Committee and all the patients provided written informed consent. The patients admitted to our hospital and preliminarily diagnosed with SAP were recruited into this study from January 2014 to May 2017. Patients were eligible if they had suspected SAP, typical symptoms, and signs of SAP, cardiac function of classes I to III, no history of acute myocardial infarction, and met the criteria for SPECT myocardial perfusion imaging and CA. Furthermore, they had to voluntarily comply with the study. Patients were excluded if they had suspected unstable angina pectoris, a history of acute myocardial infarction associated with concomitant major organ dysfunction syndrome involving the liver and the kidney or malignancy, had cardia function of class IV, arrhythmia, or congestive heart failure, associated with concomitant severe hypotension or sick sinus syndrome. Of 150 included patients, 89 were males and 61 were females, with a mean age of (59.7±6.5) years. Smoking was reported in 86 patients (57.3%), diabetes mellitus in 63 patients (42%), hypertension in 75 patients (50%), and hyperlipemia in 39 (26%). The enrolled patients had symptoms and signs consistent with those of SAP described in the guidelines for the diagnosis of stable angina pectoris released by the European Society of Cardiology [8]. The patients firstly underwent SPECT myocardial perfusion imaging, and then CA for examining the severity of coronary stenosis.

Detection methods

All the patients underwent SPECT myocardial perfusion imaging, namely, adenosine-stress-$^{99}Tc^{m}$-MIBI myocardial tomography. The details are shown as follows: The instruments included a GE Hawkeye SPECT scanner and a matched low-energy general purpose collimator; the reagents comprised adenosine triphosphate disodium injection (Liaoning Keji Pharmaceutical, China; specification: 10 mg/mL), and $^{99}Tc^{m}$-methoxy isobutyl isonitrile ($^{99}Tc^{m}$-MIBI; Shanghai GMS, China) used as tracers. The agents including theophylline and dipyridamole that might influence adenosine-stress myocardial perfusion imaging were discontinued within 48 h before imaging. The patients were not allowed to drink alkali beverage containing theophylline ingredients. Two venous pathways were constructed. Adenosine triphosphate disodium injection was infused evenly into one pathway using a syringe pump for 5 min at 0.15 mg/kg/min. Over the infusion period, the patient's vital signs and symptoms were monitored closely. If severe angina, significant ST-T segment abnormities, systolic blood pressure > 200 mmHg, atrioventricular block of II or above, or other intolerant symptoms were present in the patient, adenosine disodium triphosphate injection was discontinued immediately. Bolus injection of $^{99}Tc^{m}$-MIBI (740MBg) into the other venous pathway began 3 min after discontinuation of adenosine disodium triphosphate injection. After 0.5-h tracer injection, the patient was instructed to eat a high fat meal. One hour later, myocardial perfusion imaging was performed. Data acquisition was conducted at a rate of one frame every 6 degrees on a 64*64 matrix. One frame time was 30 s. Twenty-four hours later, $^{99}Tc^{m}$-MIBI was injected for stress myocardial perfusion imaging in the submaximal treadmill exercise test. During the stress myocardial perfusion imaging, the heart rates of the patients were controlled and rest SPECT images were acquired. The images were reconstructed by the filtered back projection method and the images were acquired from multiple layers.

Image analysis

SPECT images were read by two experienced physicians in a double-blind manner. The aberrant myocardial perfusion regions were identified with the left ventricular region with maximum count as a normalized reference. Imaging of each segment of the left ventricle, and the blood supply regions in the left anterior descending (LAD), left circumflex (LCX), and right coronary artery (RCA) were observed on the basis of the 17-segment model recommended by the American Heart Association. The presence of more than 3 consecutive layers of rarefaction or defects in over two layer images toward different directions in the same segment of the myocardium and the rarefaction or defects accounting for over 15% of the area of

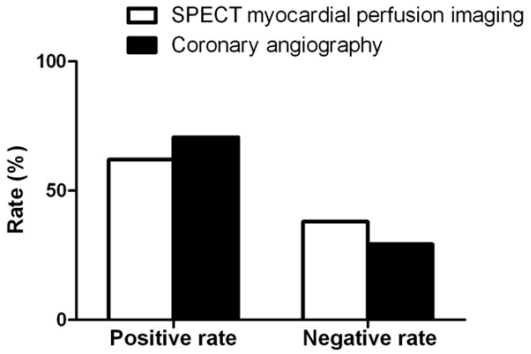

Figure 1. Comparison of the positive and negative rates of 150 patients with initially-diagnosed SAP on SPECT myocardial perfusion imaging and CA.

Table 1. Findings of SPECT myocardial perfusion imaging and CA for suspected SAP

Coronary angiography	SPECT myocardial perfusion imaging		Total
	Negative	Positive	
Negative	37	7	44
Positive	13	93	106
Total	50	100	150

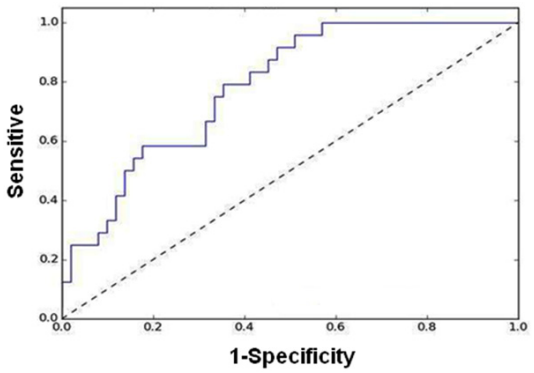

Figure 2. ROC curves for SPECT myocardial perfusion imaging in the detection of SAP.

the left ventricle cavity were considered as positive result of SAP by SPECT [3]. The coronary artery lesions and involved scope were localized according to the coronary artery blood supply regions.

Outcome measures

All the patients underwent CA 14 d after SPECT myocardial perfusion imaging. The findings were judged by two experienced physicians unaware of the general data of the participants in the study. Visually contrasted with the surrounding normal blood vessels, stenosis (≥50%) of any coronary artery was specified as positive finding [4]. The findings of SPECT myocardial perfusion imaging and CA were compared, and an analysis was performed to clarify the validity of SPECT myocardial perfusion imaging in the detection of SAP and accuracy of detecting coronary stenosis with different severity and localizing coronary artery stenosis.

Statistical analysis

The experimental data were processed with the application of the SPSS software, version 18.0. Count data were compared with the Chi-square tests. With the CA findings as reference, the receiver operating characteristics (ROC) curves were employed to evaluate the significance of SPECT myocardial perfusion imaging in detection of SAP. $P<0.05$ was set as significantly different.

Results

Detection of SAP on SPECT myocardial perfusion imaging

CA detected 106 of the 150 patients with suspected SAP, with a positive rate of 70.7% (106 of 150), and 44 without SAP, with a negative rate of 29.3% (44 of 150). Among the patients who were identified by SPECT myocardial perfusion imaging and later reviewed by CA, 62% (93 of 150) patients were positive for SAP and 38% (57 of 150) were negative for SAP, and the results were insignificant from the proportions of the patients detected by CA alone ($\chi^2=2.523$, $P=0.112$; **Figure 1**).

Among 150 patients with suspected SAP, the findings of CA were considered as the gold standard. The sensitivity of SPECT myocardial perfusion imaging in the detection of SAP was 87.7% (93 of 106), whereas the specificity was 84.1% (37 of 44). The positive prediction rate was 93% (93 of 100) and the negative prediction rate was 74% (37 of 50), as shown in **Table 1**. The ROC curve analysis revealed that the value for the area under the curve (AUC) was 0.812, and the difference was statistically significant ($P<0.001$), indicating that SPECT myocardial perfusion imaging is of value in detecting SAP (**Figure 2**).

Table 2. Coronary stenosis of patients with SAP on the two screening tools

Screening testing	Coronary stenosis (n, %)	
	<70%	> 70%
Coronary angiography	32 (34.4)	61 (65.6)
SPECT myocardial perfusion imaging	28 (30.1)	65 (69.9)
χ^2	0.394	
P	0.530	

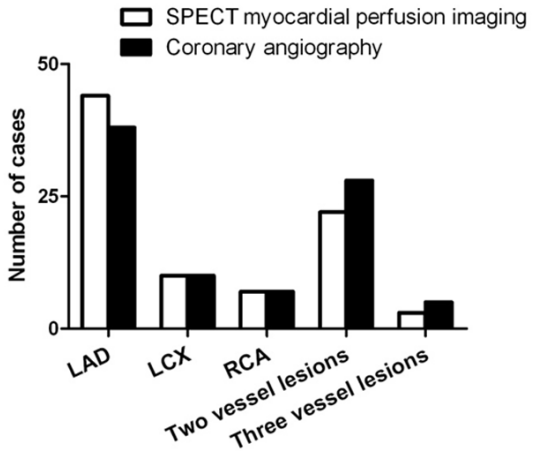

Figure 3. Detection of coronary stenosis by SPECT myocardial perfusion imaging.

Coronary stenosis profile in patients with SAP by SPECT myocardial perfusion imaging

With the findings of CA as the gold standard, 93 cases of positive results were detected by SPECT myocardial perfusion imaging, including 28 cases of coronary stenosis (<70%) and 65 cases of coronary stenosis (> 70%). The results differed insignificantly from those of coronary stenosis detected by CA (P=0.530, **Table 2**).

Detection of coronary stenosis by SPECT myocardial perfusion imaging

Figure 3 shows on CA, 38 of the 93 patients with SAP had the lesions localized in LAD, 10 in LCX, and 7 in RCA; 28 patients had 2-vessel lesions, and 5 had 3-vessel lesions. On SPECT myocardial perfusion imaging, 44 patients had the lesions localized in LAD, 10 in LCX and 7 in RCA; 22 patients had 2-vessel lesions, and 3 had 3-vessel lesions.

Similar results of disease diagnosis and detection by SPECT myocardial perfusion imaging and CA demonstrated that the agreement rates were 89.5% (34 of 38) for lesions in LAD, 70% (7 of 10) for lesions in LCX, and 100% (7 of 7) for lesions in RCA. The agreement rates were 75% (21 of 28) for 2-vessel lesions, and 60% (3 of 5) for 3-vessel lesions. The total agreement rate of SPECT myocardial imaging was 81.8%.

Safety analysis

During SPECT myocardial perfusion imaging, no major cardiovascular events occurred in all the patients. They showed stable vital signs. Mild dizziness, chest tightness and nausea were present in some patients, but the symptoms were tolerable and lasted for a short duration. They were significantly improved after symptomatic treatment or after the completion of examination. Additionally, no other adverse events were present at 24-h follow-up.

Discussion

The prognosis of SAP is affected by severity of coronary stenosis, the myocardial ischemia-involved range and the cardiac functions. In early diagnosis, more attention should be attached to the primary evaluation and detection of the lesions, and guiding the treatment of the criminal coronary arteries. CA is considered one of the most accurate tools for detection of SAP, but it is difficult to exactly locate the microvascular lesions. With the surrounding normal vessels as reference, there are defects in determining the severity of coronary stenosis by the visual contrast method. Additionally, CA is invasive and at high risk, so it is difficult to extensively use. Studies have demonstrated that less than 40% of SAP patients who had no history of coronary artery disease were positive for SAP on CA [9]. This indicates that before detection of SAP by CA, it is necessary to have a preliminary evaluation by non-invasive cardiac testing. The result of another study substantiates that CA is less likely to detect coronary stenosis in patients with normal findings on SPECT myocardial perfusion imaging [10]. Kowalczyk et al. held that SPECT myocardial perfusion imaging is of great significance in evaluating the prognosis of patients with stable coronary heart disease [11]. In the current study, among the 150 patients with suspected SAP, 106 had positive results on CA, with a positive rate of 70.7%, while 62.0% (93

of 150) were identified by SPECT. Although SPECT myocardial perfusion imaging detected fewer patients with SAP than CA, the difference was not statistically significant. Moreover, the result of ROC curves indicated that the AUC value was 0.812, suggesting that SPECT myocardial perfusion imaging is of great value in detecting SAP. All this implies that the noninvasive cardiac testing by SPECT myocardial perfusion imaging can be utilized for preliminary screening of patients with suspected SAP. If the images were normal on SPECT myocardial perfusion imaging, then it was unnecessary to take further CA. In this manner, invasive injury induced by coronary angiography can be reduced significantly.

The pathological characteristics of SAP are that SAP occurs with cardiac overload and relieves at rest. During SPECT myocardial perfusion imaging, myocardial ischemia can be triggered by injection of adenosine agents, and then the SAP patients can receive reasonable and quick screening [12, 13]. SPECT myocardial perfusion imaging fully reflects the myocardial perfusion level and myocardial viability. The severity of coronary stenosis is determined according to the extent of myocardial defects [14-16]. In the previous literature, SPECT myocardial perfusion imaging has proven to accurately predict the sites, range, and severity of myocardial ischemia. The stenotic coronary arteries are localized by the 17-segment method specified by the American Heart Association [17]. The literature regarding the validity of SPECT myocardial perfusion imaging in the detection of SAP reveals that the research on the sensitivity, specificity, and positive prediction has not yet reached a unified conclusion [18, 19]. In the current study, 87.7% (93 of 106) of SAP patients were detected by SPECT myocardial perfusion imaging, with a specificity of 84.1% (37 of 44), a positive prediction rate of 93% (93 of 100) and a negative prediction rate of 74% (37 of 50), suggesting that SPECT myocardial perfusion imaging has high sensitivity and specificity in detecting SAP. All this indicates that SPECT myocardial perfusion imaging can be employed as one of the important tools for screening and early detection of SAP.

As far as coronary stenosis assessment is concerned, the result of this study showed SPECT myocardial perfusion imaging identified 30.1% of cases of coronary stenosis (<70%) and 69.9% of cases of coronary stenosis (> 70%). However, the difference was not statistically significant when compared with CA. SPECT myocardial perfusion imaging detected fewer cases of coronary stenosis (<70%) than CA. This might be due to the unclear hemodynamic impairment in SAP patients with milder coronary stenosis on SPECT myocardial perfusion imaging. Additionally, overall, PECT myocardial perfusion imaging detected 81.8% of coronary artery lesions which had been detected by CA, suggesting that SPECT myocardial perfusion imaging can accurately localize the stenotic lesions of patients, avoiding unnecessary CA and optimizing the medical resources.

In the process of SPECT myocardial perfusion imaging, the safety of adenosine triphosphate disodium injection and $^{99}Tc^{m}$-MIBI use have been generally recognized in clinical research worldwide. It is characterized by less toxic effect, faster metabolism, but no accumulative effects [20]. In the present study, PECT myocardial perfusion imaging contributed to few adverse events and the patients recovered well after symptomatic treatment, implying that SPECT myocardial perfusion imaging is safe in the detection of SAP.

In summary, SPECT myocardial perfusion imaging is of practical implication in the early diagnosis of SAP. It can accurately position the sites of stenotic lesions, and is safe, easy to operate, and minimally invasive, so it is worthy of extensive use. However, this study had a small sample size and lacked follow-up results. It did not evaluate the role of SPECT myocardial perfusion imaging in detection of SAP from the perspective of prognosis and in combination with other screening tests. Multi-center studies with larger sample sizes will be needed for further validation.

Disclosure of conflict of interest

None.

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