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Diagnostic value of stress myocardial perfusion imaging in combination with computed tomography angiography for coronary slow flow

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ABSTRACT

Introduction: To date, there are few reports on computed tomography angiography (CTA) in combination with stress myocardial perfusion imaging (SMPI) in the diagnosis of coronary slow flow (CSF).

Methods: A total of 62 patients with suspected CSF who were scheduled to undergo CTA, SMPI and coronary angiography (CAG) from June 2019 to June 2021 were selected. With the results of CAG as the gold standard, the value of CTA plus SMPI in the diagnosis of CSF was analyzed.

Results: Of the 62 patients, 52 (83.87%) were diagnosed with CSF by CAG. The results of the Kappa consistency test showed that SMPI alone, CTA alone and SMPI plus CTA had 0.565, 0.396 and 0.881 consistency, respectively, with CAG in the diagnosis of CSF. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of SMPI plus CTA in the diagnosis of CSF were 98.08% (51/52), 90.00% (9/10), 96.47% (60/62), 98.08% (51/52), and 90.00% (9/10), respectively, all higher than those of SMPI or CTA alone (P<0.05). The areas under the receiver operating characteristic curves of SMPI alone, CTA alone and SMPI plus CTA in the diagnosis of CSF were 0.754, 0.771 and 0.940, respectively.

Conclusion: CTA and SMPI have high diagnostic values for CSF, and the results of their combination have high consistency with those of CAG.

Keywords: angiography, computed tomography, coronary slow flow, imaging, stress myocardial perfusion

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INTRODUCTION

Patients with coronary slow flow (CSF) suffer from typical angina pectoris symptoms, accompanied by continuous progression of the disease. It leads to myocardial ischemia, acute coronary syndrome and even acute myocardial infarction, affecting the prognosis [1, 2]. CSF has been closely related to coronary microvascular disease, inflammatory response and vascular endothelial dysfunction [3, 4]. No specific treatment is available for CSF patients in clinical practice. Therefore, accurate early diagnosis is crucial for CSF patients.

CAG is currently the gold standard for the diagnosis of CSF. Despite high diagnostic accuracy, CAG, as an invasive examination method, cannot be tolerated by some patients, and complications can be easily caused by improper operation or nursing [5, 6]. Therefore, a noninvasive and accurate diagnostic method for CSF is urgently needed now. At present, stress myocardial perfusion imaging (SMPI) has been generally recognized as a reliable noninvasive examination method with high diagnostic value for myocardial ischemia in clinical practice [7]. Moreover, the diagnostic value of SMPI for CSF with high sensitivity has also been verified [8-10]. However, SMPI cannot accurately determine whether the myocardial ischemia symptoms of patients with coronary artery disease are caused by CSF or coronary stenosis, resulting in low diagnostic specificity. Thus, it is necessary to combine SMPI with other diagnostic methods.

Coronary computed tomography angiography (CTA) is a non-invasive volume rendering technology that processes multiple X-ray images by computer, which conducts ECG-gated scanning and image reconstruction following intravenous injection of contrast agent iodine [11]. It is well-documented that CTA has a comparable diagnostic value to CAG for coronary heart disease, and its accuracy in the diagnosis of CSF is also high [12]. Although coronary CTA can clearly display the structural composition of coronary arteries, it cannot determine the status of myocardial blood supply, which reduces

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the diagnostic accuracy for CSF, so the sensitivity of CTA alone remains to be improved [13].

In view of this, the diagnostic value of CTA in combination with SMPI for CSF was analyzed in this study, aiming to provide valuable clinical evidence for future diagnosis.

MATERIALS AND METHODS

General data

This study was approved by the ethics committee of our hospital. A total of 62 patients with suspected CSF who were scheduled to undergo examinations in our hospital from June 2019 to June 2021 were selected. The inclusion criteria were as follows: 1) patients who signed the informed consent form, 2) those with normal immune function and endocrine function, 3) those with normal consciousness and mental state on admission, and good cooperation in the study, 4) those with recurrent chest pain, syncope or palpitations; ECG may show changes such as transient ST segment elevation or even arrhythmia, and 5) those with generally stable vital signs.

The exclusion criteria included: 1) patients complicated with malignant tumors, hematological system disease or immune system disease, 2) those with uncontrollable infectious diseases, 3) those allergic to interventional equipment, anesthetics or contrast media, 4) those with risk of bleeding or coagulation disorders, 5) those with severe liver or kidney dysfunction, 6) those with any coronary artery stenosis of ≥40%, cardiac insufficiency, or cardiac function grade II or above, or 7) those with abnormal baseline ECG.

CTA method

Discovery HD750 system (GE, USA) was used. Before examination, the ventricular rate was controlled at below 70 beats/min. Then 60-80 mL of iopromide injection (100 mL: 62.34 g; Bayer Vital GmbH, Germany) was injected as the contrast medium through the forearm vein at 3 mL/s. Scan was performed from the lower part of tracheal carina to the diaphragmatic surface of heart, with the tube voltage/tube current/tube rotating speed/slice thickness of 120 kVp/150-750 mA/0.35 s/0.625 mm. After scanning, the acquired data were transmitted to the computer workstation for three-dimensional image reconstruction. Then the condition of the coronary artery was carefully observed. Negative results were defined as no obvious plaque and stenosis in left and right coronary arteries and their important branches. Otherwise, CTA positive results were determined.

SMPI method

Single photon emission computed tomography (Beijing GE Hualun Medical Equipment Co., Ltd., China) was used as the imaging instrument, and 99mTc-methoxyisobutyl isonitrile (MIBI) was used as the imaging agent. The patient was instructed to undergo the exercise load test by treadmill exercise as follows. The patient was asked to stand on the treadmill, and the doctor turned on the treadmill after inputting the personal information. First, uniform and level treadmill exercise of grade 1 was performed, and increased by one grade every 3 min.

The load requirements of exercise test were met under the following conditions: 1) The target heart rate reached 85% of the maximum, 2) angina pectoris, severe arrhythmia, dyspnea, shock or heart failure occurred, or 3) ECG showed upsloping ST segment or horizontal ST segment, and they both had downward depression by more than 2 mm, or systolic blood pressure/diastolic blood pressure >220 mmHg/120 mmHg. At this time, the exercise should be stopped, and 740-925 MBq MIBI was intravenously injected, followed by 1-2 min of exercise. One hour after MIBI injection, MPI was performed to acquire the tomographic images, with the matrix/magnification of 128×128/1.23, and 32 frames collected. After background processing by computers, the tomographic images of myocardial vertical and horizontal long-axis and short-axis views were acquired. The normal distribution of 99mTc-MIBI (indicating normal myocardial perfusion at corresponding sites) was regarded as negative result, while the decrease or defect of 99mTc-MIBI distribution in different degrees (indicating decrease or defect of myocardial perfusion at corresponding sites) was considered as positive result.

CAG method

With an appropriate puncture approach (radial artery or femoral artery), CAG was performed using Innova 2000 imaging system (GE, USA) by the Judkins method. The coronary artery blood flow of suspected patients was assessed by the mean TIMI frame count of target vessels, and positive results were defined when the TIMI frame count of no less than one vessel was >27.

Evaluation of outcomes

(1) Diagnostic value of SMPI and CTA: The diagnostic value of SMPI and CTA individually or in combination was analyzed with the CAG results as the gold standard.

(2) Consistency analysis: The consistency of SMPI and CTA individually or in combination in the diagnosis of CSF with CAG was analyzed by the Kappa consistency test.

(3) Diagnostic value: The diagnostic value of SMPI and CTA individually or in combination was analyzed using receiver operating characteristic (ROC) curves.

Statistical analysis

SPSS24.0 software was used for statistical analysis. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and underwent the t-test. The count data were expressed as percentage [n(%)] and underwent the chi-square test. The Kappa consistency test was carried out. Kappa <0.4, 0.4≤ Kappa <0.75 and Kappa ≥0.75 indicated poor, moderate, and better consistency. ROC curves were plotted to detect the diagnostic values of SMPI and CTA individually or in combination for CSF. The areas under the ROC curves (AUCs) of >0.9, 0.7<AUC≤0.9, 0.5<AUC≤0.7, and AUC≤0.5 indicated high, moderate, low, and no diagnostic values. P<0.05 was considered statistically significant.

RESULTS

Baseline clinical data

Among the 62 suspected patients, there were 35 males and 27 females aged 30-75 years, with a mean of (50.10±4.50) years. The body mass index was 22-26 kg/m2, with a mean of (24.50±0.40) kg/m2. The systolic blood pressure on admission ranged from 110 to 145 mmHg, with a mean of (120.20±5.10) mmHg. The diastolic blood pressure on admission was 65-98 mmHg, with a mean of (75.60±3.01) mmHg. Among these patients, 35, 26, and 20 cases were complicated with hypertension, diabetes mellitus, and hyperlipemia, respectively.

CAG results

A total of 52 (83.87%) out of the 62 suspected patients were diagnosed with CSF by CAG.

Results of SMPI and CTA individually or in combination in the diagnosis of CSF

The results of the Kappa consistency test showed that SMPI alone, CTA alone, and SMPI plus CTA had 0.565, 0.396, and 0.881 consistency, respectively, with CAG in the diagnosis of CSF (Table 1-3). Therefore, the combination method had the highest consistency with CAG.

Table 1. Results of SMPI in the diagnosis of CSF

SMPI	CAG		Total	Kappa
	Positive	Negative		
Positive	49	4	53	-
Negative	3	6	9	-
Total	52	10	62	0.565/0.000

CAG: Coronary angiography; CSF: coronary slow flow; SMPI: stress myocardial perfusion imaging.

Table 2. Results of CTA in the diagnosis of CSF

CTA	CAG		Total	Kappa
	Positive	Negative		
Positive	42	3	45	-
Negative	10	7	17	-
Total	52	10	62	0.396/0.001

CAG: Coronary angiography; CSF: coronary slow flow; CTA: computed tomography angiography.

Diagnostic efficiency of SMPI and CTA individually or in combination for CSF

With the results of CAG as the gold standard for the diagnosis of CSF, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of SMPI plus CTA in the diagnosis of CSF were 98.08% (51/52), 90.00% (9/10), 96.47% (60/62), 98.08% (51/52) and 90.00% (9/10), respectively. The values were all higher than those of SMPI or CTA alone (P<0.05) (Table 4).

Diagnostic value of SMPI and CTA individually or in combination for CSF

The AUC values of SMPI alone, CTA alone and SMPI plus CTA in the diagnosis of CSF were 0.754, 0.771 and 0.940, respectively (Table 5 and Figure 1-3). Thus, the combination method had the highest diagnostic value for CSF.

DISCUSSION

SMPI produces myocardial plane and tomographic images by single photon emission computed tomography based on the fact that myocardial cells with normal physiological function can effectively take up radioactive drugs and continuously emit radioactive rays outward [14].

Table 3. Results of CTA+SMPI in the diagnosis of CSF

CTA	CAG		Total	Kappa
	Positive	Negative		
Positive	51	1	52	-
Negative	1	9	10	-
Total	52	10	62	0.881/0.000

CAG: Coronary angiography; CSF: coronary slow flow; CTA: computed tomography angiography; SMPI: stress myocardial perfusion imaging.

Table 4. Diagnostic efficiency of SMPI and CTA individually and in combination for CSF

Method	Sensitivity	Specificity	Accuracy	PPV	NPV
CTA	80.76% (42/52)	70.00% (7/10)	79.03% (49/62)	87.50% (42/48)	50.00% (7/14)
SMPI	94.23% (49/52)	60.00 (6/10)	88.71% (55/62)	92.45% (49/53)	66.67% (6/9)
CTA + SMPI	98.08% (51/52)	90.00% (9/10)	96.47% (60/62)	98.08% (51/52)	90.00% (9/10)
χ2	10.471	2.616	10.152	11.392	11.345
P value	0.005	0.270	0.006	0.022	0.023

CSF: Coronary slow flow; CTA: computed tomography angiography; NPV: negative predictive value; PPV: positive predictive value; SMPI: stress myocardial perfusion imaging.

Table 5. Diagnostic value of SMPI and CTA individually and in combination for CSF

Method	AUC	SE	P value	95% CI
CTA	0.754	0.091	0.012	0.576-0.932
SMPI	0.771	0.098	0.007	0.579-0.963
CTA + SMPI	0.940	0.057	0.000	0.829-0.999

AUC: area under the ROC curve; CI: confidence interval; CTA: computed tomography angiography; SE: standard error; SMPI: stress myocardial perfusion imaging.

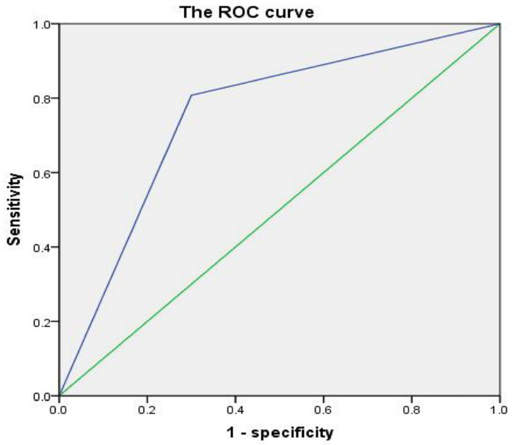

Fig. 1. Receiver operating characteristic (ROC) curve of computed tomography angiography (CTA) for diagnosis of coronary slow flow (CSF).

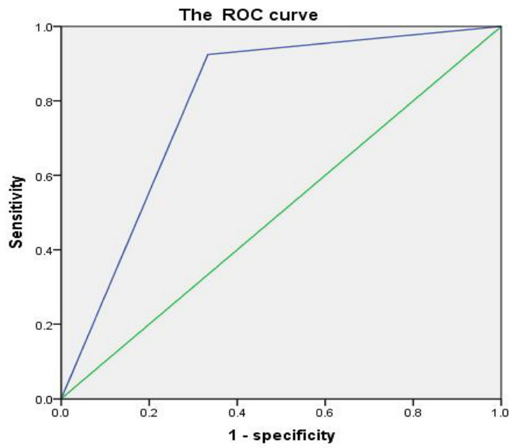

Figure 2. Receiver operating characteristic (ROC) curve of stress myocardial perfusion imaging (SMPI) for diagnosis of coronary slow flow (CSF).

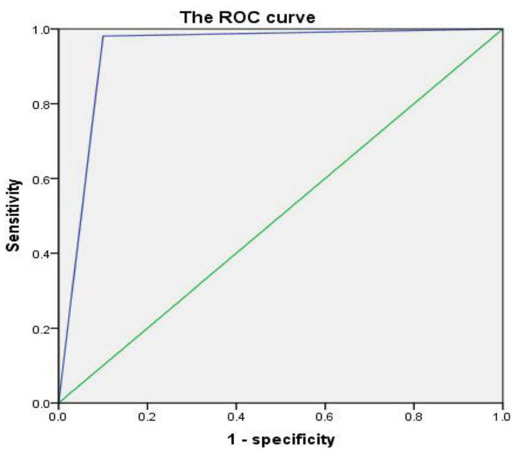

Figure 3. Receiver operating characteristic (ROC) curve of stress myocardial perfusion imaging (SMPI) plus computed tomography angiography (CTA) for diagnosis of coronary slow flow (CSF).

Usually in a resting state, myocardial cells can maintain the myocardial blood supply and oxygen supply even in the case of severe coronary stenosis, in which case it is difficult to detect coronary artery disease or myocardial ischemia [15]. In an exercise state, the myocardial oxygen consumption significantly increases. The normal coronary artery obviously dilates (about 3-5 times as much as usual), while the abnormal coronary artery can only dilate to a limited extent or cannot dilate. At this time, the blood flow in the target coronary artery cannot increase or increases less significantly than the normal coronary artery, resulting in blood redistribution in the myocardium. In other words, the blood in the diseased coronary artery flows to the normal coronary artery, and the distributions of imaging agents in diseased and normal myocardial arteries become significantly different. Therefore, SMPI can be performed to visualize the presence or absence of CSF and its location, extent and degree, which significantly improves the sensitivity and accuracy in CSF diagnosis [16, 17].

CTA can simultaneously display the images of superficial and internal lesion structures, and then produce three-dimensional images by combining post-processing operations such as multiplanar reconstruction, volume reconstruction and curved planar reformation, which helps to effectively determine the opening and course of coronary arteries, the presence or absence of stenosis or occlusion, and whether the intravascular stent is patent. Coronary CTA, which creates three-dimensional images to display the coronary artery structure and function, can achieve high diagnostic accuracy [18]. Compared to traditional CAG, coronary CTA is characterized by noninvasiveness, rapid diagnosis, low cost and simple operation, and thus has been widely applied in the clinical diagnosis of patients with coronary heart disease [19].

In this study, SMPI alone, CTA alone, and SMPI plus CTA had 0.565, 0.487, and 0.881 consistency, respectively, with CAG in the diagnosis of CSF. The diagnostic value (accuracy, sensitivity, specificity, negative and positive predictive values) of SMPI plus CTA for CSF was superior to that of SMPI or CTA alone. Hence, CTA plus SMPI had a higher consistency with CAG and a higher diagnostic value for CSF. Probably, SMPI can show the condition of coronary myocardial ischemia, and then CTA can display the structure and function of coronary arteries, so whether the myocardial ischemia symptoms of coronary artery disease-positive patients are caused by CSF or coronary stenosis indeed occurs can be effectively determined. As a result, the combination greatly augments the diagnostic accuracy and consistency with CAG [20, 21]. Furthermore, the AUC values of SMPI alone, CTA alone and SMPI plus CTA in the diagnosis of CSF were 0.754, 0.771, and 0.940, respectively, which verified the above conclusion. Therefore, SMPI plus CTA has an elevated diagnostic value for patients with suspected CSF.

In conclusion, CTA and SMPI have a high diagnostic value for CSF, and the results of this combination have high consistency with those of CAG. Nevertheless, this study is limited. The sample size is small, without clinical follow-up. Besides, the medication of the patients was not considered. Further studies are ongoing in our group to confirm our conclusion.

ABBREVIATIONS

AUC- area under the ROC curve
CAG- coronary angiography
CSF- coronary slow flow
CTA- coronary computed tomography angiography
ECG- electrocardiogram
MIBI- 99mTc-methoxyisobutyl isonitrile
ROC- receiver operating characteristic
SIMPI- stress myocardial perfusion imaging

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AUTHORS' CONTRIBUTION

XG- study design.
DZ- data analysis.
YZ and JS- data collection
RJ- writing the manuscript.

CONFLICT OF INTEREST

None to declare.

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