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Original Article

Evaluation of ventricular muscle function of patients with coronary heart disease via dual-energy CT combined with resting myocardial transmural perfusion ratio

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Abstract: Objective: Dual-energy CT combined with resting myocardial transmural perfusion ratio has been used as a one-stop and noninvasive imaging examination method for coronary heart disease. To analyze value of dual-energy CT combined with resting myocardial transmural perfusion ratio in coronary heart disease. Methods: A total of 192 patients with coronary heart disease received dual-energy CT coronary angiography and static CT perfusion examination. According to degree of coronary artery stenosis, patients were divided into normal group, mild stenosis (≤50%) group, moderate stenosis (51-75%) group and severe stenosis (≥76%) group. The resting myocardial transmural perfusion ratio was calculated according to gray value of each myocardial tomographic image, and correlation between resting myocardial transmural perfusion ratio and degree of coronary artery stenosis was investigated via Kappa and regression analysis. Results: In terms of stenosis among 576 coronary arterial branches, 145 were normal, 252 had mild stenosis, 112 had moderate stenosis and 67 had severe stenosis. Results of Kappa and regression analysis showed that there is good consistency between the resting myocardial transmural perfusion ratio and degree of coronary artery stenosis. Conclusions: The resting myocardial transmural perfusion ratio of patients with coronary heart disease is negatively correlated with degree of coronary artery stenosis. Dual-energy CT combined with resting myocardial transmural perfusion ratio can improve evaluating ventricular muscle function.

Keywords: Dual-energy CT, resting myocardial transmural perfusion ratio, coronary heart disease, ventricular muscle function

Introduction

In recent years, prevalence rate of cardiovascular risk factors and incidence of coronary heart disease have been increased year by year, and the mortality of urban population in China due to coronary heart disease was about 100.86/100,000 in 2013 [1]. However, a considerable number of patients with coronary heart disease receive inadequate or excessive treatment, which is closely related to the inaccurate evaluation of ventricular muscle function [2]. Currently, coronary angiography is still one main method of reflecting degree of coronary artery stenosis intuitively and accurately, and diagnosing coronary heart disease, but it has obvious invasive trauma and high risk and fails to analyze the influence of coronary artery stenosis on myocardial blood perfusion, so it is difficult to generalize coronary angiography to be a routine screening method for ventricular muscle function of patients with coronary heart disease [3]. Coronary angiography shows that coronary artery stenosis rate of patients with suspected coronary heart disease who have no history of coronary heart disease does not exceed 40% [4]. Based on the above views, the development and application of noninvasive imaging examination method before coronary angiography has become a key link in improving the evaluation efficiency of ventricular muscle function of patients with coronary heart disease.

In recent years, dual-energy CT combined with resting myocardial transmural perfusion ratio has been used as a one-stop and noninvasive imaging examination method for coronary heart disease, and it can assess whether coronary artery stenosis exists and evaluate the degree of stenosis accurately. However, since coronary heart disease-induced myocardial ischemia can be caused by coronary spasm and other non-stenosis factors, it is difficult to evaluate the myocardial perfusion in the percutaneous coronary angioplasty or bypass grafting before and after treatment using dual-energy CT coronary angiography alone [5-8]. At present, static CT perfusion examination is widely used to evaluate myocardial perfusion and understand whether there is ischemia in myocardium dominated by stenotic coronary artery [9]. Based on advantages and disadvantages of the above two examination methods, results of both examinations can be used to diagnose stenotic coronary artery that causes abnormal myocardial blood perfusion, and evaluate ventricular muscle function of patients with coronary heart disease relatively accurately. However, there are few related studies, and no unified conclusion has been made yet.

This study aims to analyze the value of combining the above two examination methods in evaluation of ventricular muscle function of patients with coronary heart disease.

Materials and methods

General materials

Clinical data of 192 patients with clinically suspected coronary heart disease treated in Affiliated Hospital of Hebei University of Engineering from January to December 2016 were retrospectively analyzed. There were 132 males and 60 females aged 36-81 years with an average of 58.23±5.64 years, including 124 of hypertension, 104 of diabetes mellitus and 76 of hyperlipemia. This study was approved by the Ethics Committee of Affiliated Hospital of Hebei University of Engineering.

Inclusion criteria: patients with coronary heart disease, varying degrees of chest tightness, shortness of breath and anterior-chest pain, or a history of angina; patients with no allergic history of iodine contrast agent; patients with sinus rhythm or drug-controlled heart rate no more than 65 times/min; patients with no history of asthma, chronic obstructive pulmonary disease and other respiratory diseases, and who could cooperate in breathing; patients with ST-T abnormalities in electrocardiogram (ECG), positive results in treadmill exercise test, and data of CT coronary angiography and static CT perfusion examination within 1 week after admission.

Exclusion criteria: patients and pregnant women with arrhythmia, allergy to iodine contrast agent, renal insufficiency, congestive heart-failure, hypotension, sick sinus syndrome, or intolerance to intravenous injection using the high-pressure injector, CT coronary angiography or static CT perfusion examination.

To better analyze the data, according to coronary 17-segment model, left anterior descending (LAD), left circumflex artery (LCX) and right coronary artery (RCA), were divided patients into 4 subgroups: normal group (0), mild stenosis (≤50%) group, moderate stenosis (51-75%) group and severe stenosis (≥76%) group. The degree of stenosis in at least one of the three lesions (LAD, LCX and RCA) exceeding 50% was used as a positive diagnostic criterion of coronary artery stenosis [10].

Dual-energy CT examination

All patients received dual-energy CT coronary angiography using the retrospective ECG-gated trigger scanning method via SOMATOM Definition Flash (Siemens, Germany). Scanning range: from 1 cm below the tracheal carina to the diaphragmatic surface of the heart. And 80 mL contrast agent (omnipaque) was injected using a high-pressure syringe via the elbow vein at a rate of 5 mL/s, and 50 mL normal saline was injected in the same way. The aortic root was chosen for small dose test to obtain the expected CT value, and automatic scanning was performed after delay for 5 s. Scanning parameters are as follows: tube voltage: 120 kV, tube current: 380-400 mA, collimator width: 0.625×64 mm, viewing angle: 160 mm×160 mm, single-loop rotation time: 350 ms, and coverage area: 4 cm. The image was analyzed after scanning, and original data were sent to Syngo Multi-Modality workstation (Siemens) for processing to observe the heart chamber and myocardium. The contrast between heart chamber and myocardium was increased using Optimum contrast software. The coronary artery was reconstructed using Circulation software, and degree of coronary artery stenosis was measured quantitatively: degree of coronary artery stenosis = (average of normal coronary artery diameters in the proximal and distal stenoses - coronary artery diameter in the severest stenosis)/average of normal coronary artery diameters in the proximal and distal stenoses [10]. In the above analysis process, coronary artery stenosis was assessed by two experienced physicians using the double-blind method.

Static CT perfusion image analysis

A total of 30 mL omnipaque, the contrast agent, was intravenously injected via the cubital vein at a rate of 5 mL/s using a high-pressure syringe, and 30 mL normal saline was also injected in the same way. Static CT perfusion images were analyzed using myocardial perfusion software Cardiac Tc99m. Images were reconstructed via Butterworth filter back projection. Myocardium was divided into outer, middle and inner layers and images of different layers were obtained [9]. Two experienced physicians interpreted the images using double-blind method and determined area of abnormal myocardial blood perfusion. With the maximum counting area of myocardium of left ventricle as the normal reference area, myocardial perfusion was divided into 4 grades according to coronary 16-segment scoring method (excluding the apical segment in the coronary 17-segment model): 0 point (normal perfusion), 1 point (mild decrease), 2 points (moderate decrease) and 3 points (severe decrease). At the same time, Cardiac Tc99m software was used to analyze each myocardial tomographic image obtained above, and the gray values of different tomographic images were calculated, namely the average myocardial density in each layer, thereby calculating the resting myocardial transmural perfusion ratio using the following formula: resting myocardial transmural perfusion ratio = average density of endocardium/average density of epicardium [11, 12].

Data processing

SPSS 18.0 software was used for experimental data processing. Measurement data conforming to the normal distribution and homogeneity of variance were presented as mean ± standard deviation ($\bar{x}$ ± sd). T-test was used for the measurement data conforming to the normal distribution between two groups, and data were presented as t. Analysis of variance was used for the comparison among groups, and data were presented as F. Chi-square test was used for enumeration data, and data were presented as X^2. Rank sum test was used for ranked data. The consistency between resting myocardial transmural perfusion ratio and degree of coronary artery stenosis was studied via Kappa and regression analysis. The test level was 0.05.

Results

Comparisons of clinical data among four groups of patients with different degrees of coronary artery stenosis

All 192 patients with coronary heart disease received dual-energy CT coronary angiography. Results showed that among 576 branches of coronary artery, there were 145 normal branches and 431 stenotic branches, the latter of which included mild stenosis (≤50%) in 252 branches, moderate stenosis (51-75%) in 112 and severe stenosis (≥76%) in 67 (**Table 1** and **Figure 1**). The overall degree of coronary artery stenosis in patients was evaluated with the most stenotic coronary artery branch as a standard. Eighteen cases were normal, 76 had mild stenosis, 57 had moderate stenosis and 41 had severe stenosis (**Table 1**). Although gender, age, diabetes mellitus, hypertension and hyperlipidemia are recognized high-risk factors for coronary heart disease, patients tended to suffer from coronary heart disease in this study, so there were no significant differences in gender, age, hypertension and diabetes mellitus among the four groups of patients (all P>0.05), but significant differences in the prevalence of hyperlipemia (P<0.05), which may be related to the individual difference.

Static CT perfusion examination results

Static CT perfusion examination was performed for myocardia dominated by the above branches of coronary artery, and perfusion was normal in 200 branches, mildly decreased in 102 branches, moderately decreased in 149, and severely decreased in 125 (**Table 2** and **Figure 2**).

Analysis of correlation between resting myocardial transmural perfusion ratio and degree of coronary artery stenosis

The resting myocardial transmural perfusion ratio had significant differences among LAD, LCX and RCA with different degrees of stenosis

Table 1. Comparisons of clinical data among four groups of patients with different degrees of coronary artery stenosis

Clinical data	Normal	Stenotic			X^2/F	P
		Mild (≤50%)	Moderate (51-75%)	Severe (≥76%)		
LAD (branch, %)	25 (13.02)	58 (30.21)	83 (43.23)	26 (13.54)		
LCX (branch, %)	58 (30.21)	87 (45.31)	16 (8.33)	31 (16.15)		
RCA (branch, %)	62 (32.29)	107 (55.73)	13 (6.77)	10 (5.21)		
Total number of branches (branch, %)	145 (25.17)	252 (43.75)	112 (19.44)	67 (11.63)		
Case (n, %)	18 (9.38)	76 (39.58)	57 (29.69)	41 (21.35)		
Male (n, %)	10 (55.56)	49 (64.47)	42 (73.68)	31 (75.61)	3.649	0.302
Age ($\bar{x}$ ± sd)	56.6±6.2	57.1±5.7	58.9±8.5	60.5±9.9	2.175	0.092
Hypertension (n, %)	10 (55.56)	53 (69.74)	39 (68.42)	22 (53.66)	4.030	0.258
Diabetes (n, %)	12 (66.67)	44 (57.89)	33 (57.89)	15 (36.59)	6.982	0.072
Hyperlipidaemia (n, %)	8 (44.44)	20 (26.32)	29 (50.88)	19 (46.34)	9.595	0.022

Note: LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

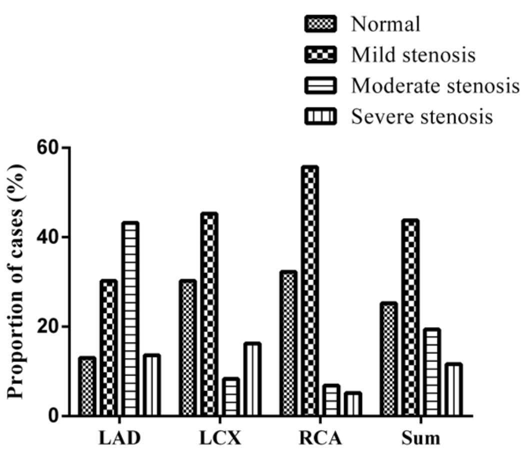

Figure 1. Proportional distribution of different degrees of coronary artery stenosis in four groups. LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

(all P<0.05). See **Table 3**. Kappa consistency and regression analysis were performed for degree of coronary artery stenosis and resting myocardial transmural perfusion ratio, and results showed that resting myocardial transmural perfusion ratio was negatively correlated with corresponding degree of coronary artery stenosis, with Kappa consistency coefficients of 0.675, 0.493 and 0.585, and correlation coefficients of 0.768, 0.549 and 0.730 (all P<0.05), indicating that there is a good correlation between resting myocardial transmural perfusion ratio and degree of coronary artery stenosis. See **Table 4**.

Discussion

Considering that degree of coronary artery stenosis in patients with coronary heart disease has no linear positive correlation with degree of abnormal myocardial perfusion, if single anatomical imaging or functional imaging technique is adopted, coronary artery lesions can be only reflected from one level, such as anatomical lesions or functional lesions, which is difficult to accurately assess ventricular muscle function, resulting in excessive or inadequate treatment [2, 3]. Coronary CT angiography can intuitively display the degree and site of coronary artery disease, and also well display the branch vessels, so it has been recognized as an imaging examination method for coronary disease. However, coronary angiography also has some shortcomings, such as the assessment of calcified plaque and imaging quality. The dual-energy CT is further optimized in the scan rate, imaging quality and radiation dose compared with coronary CT. A major advantage of dual-energy coronary CT scan lies in that it can quantify the percentage of coronary artery calcification in plaques more accurately, get rid of haunting artifact and increase the accuracy of evaluating vascular calcification. Scanning speed, imaging quality and radiation dose of dual-energy CT are further optimized, and dual-energy CT coronary angiography can display coronary artery stenosis and calcification clearly, and its efficiency of evaluating whether there is coronary artery stenosis and stenosis degree is comparable to that of coronary angiography,

Table 2. Static CT perfusion examination results (branch, %)

Coronary artery type	Normal	Abnormal degree of myocardial perfusion		
		Mildly decreased	Moderately decreased	Severely decreased
LAD	40 (20.83)	14 (7.29)	75 (39.06)	63 (32.81)
LCX	76 (39.58)	29 (15.10)	48 (25.00)	39 (20.31)
RCA	84 (43.75)	59 (30.73)	26 (13.54)	23 (11.98)
Total	200 (34.72)	102 (17.71)	149 (25.87)	125 (21.70)

Note: LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

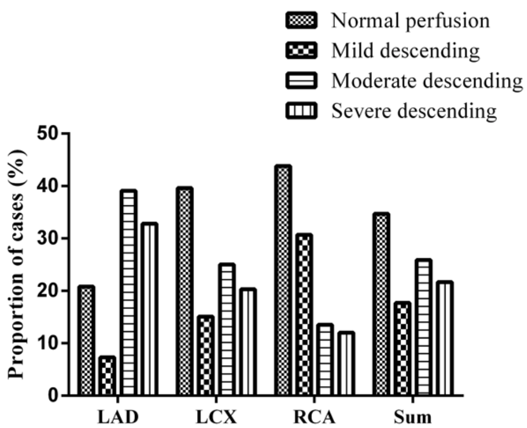

Figure 2. Proportional distribution of different perfusion degrees of coronary artery in four groups. LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

so it is widely recognized in clinic [13]. However, dual-energy CT coronary angiography fails to obtain information about abnormal myocardial perfusion and determine whether there is ischemia in myocardium dominated by stenotic coronary artery branch, and it is difficult to assess myocardial viability [14, 15]. According to the above situations, it is necessary to evaluate cardiac function of patients before and after treatment according to the abnormal myocardial perfusion, thus guiding coronary angiography and interventional therapy. If myocardial perfusion imaging is used additionally, the radiation dose is large [16]. Dual-energy CT can obtain static CT perfusion images via one-time scanning to understand myocardial perfusion [17, 18]. Zhu et al. pointed out in a study on evaluation of myocardial perfusion abnormality via resting myocardial transmural perfusion ratio that incidence of major cardiovascular events in normal myocardial perfusion did not exceed 2%, suggesting that resting myocardial transmural perfusion ratio played an important role in evaluating ventricular muscle function of patients with coronary heart disease [16]. Based on the above view and integrated advantages and disadvantages of CT coronary angiography and static CT perfusion images, the above-mentioned two kinds of examination techniques are combined to complement each other's advantages, to evaluate ventricular muscle function from degree of coronary artery stenosis and abnormal degree of myocardial perfusion. Here, dual-energy CT coronary angiography was used to assess degree of coronary artery stenosis, resting myocardial transmural perfusion ratio was used to evaluate the influence of coronary artery stenosis on myocardial perfusion, and the correlation between resting myocardial transmural perfusion ratio and coronary artery stenosis was analyzed, helping improve efficiency of evaluating ventricular muscle function of patients with coronary heart disease.

This study showed that the resting myocardial transmural perfusion ratio of most patients with suspected coronary heart disease was negatively correlated with the degree of coronary artery stenosis, in other words, the resting myocardial transmural perfusion ratio was decreased with the increased degree of coronary artery stenosis, which is the same as the research viewpoint of most scholars [8, 16]. However, some studies have pointed out that the resting myocardial transmural perfusion ratio of a minority of patients with coronary heart disease is not negatively correlated with the degree of coronary artery stenosis, which may be related to the fact that only three larger branches of coronary artery (LAD, LCX and RCA) were enrolled, because LAD, LCX and RCA had overlapping blood-supply sites [19, 20]. At the same time, it can also explain the low correlation between perfusion ratio and stenosis rate. In addition, there are many branches of LCX and collateral anastomosis between LAD and RCA, so the correlation between LCX perfusion ratio and stenosis rate is the weakest. In this

Table 3. Comparison of resting myocardial transmural perfusion ratio among four groups of patients with different degrees of coronary artery stenosis

Coronary artery type	Normal	Stenotic			F	P
		Mild (≤50%)	Moderate (51-75%)	Severe (≥76%)		
LAD	1.17±0.12	1.16±0.09	1.05±0.10	0.98±0.10	29.760	0.000
LCX	1.16±0.11	1.15±0.08	1.10±0.09	1.08±0.07	6.977	0.000
RCA	1.15±0.13	1.13±0.11	1.09±0.08	1.07±0.11	2.747	0.044

Note: LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

Table 4. Kappa consistency and regression analysis of resting myocardial transmural perfusion ratio with corresponding degree of coronary artery stenosis

Coronary artery type	Kappa	Regression equation
LAD	0.675	Y=0.768 X+0.12
LCX	0.493	Y=0.549 X+0.18
RCA	0.585	Y=0.730 X+0.14

Note: LAD: left anterior descending artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

study, 4 patients with coronary artery stenosis <25% had moderate and severe abnormalities in myocardial perfusion, and range of myocardial defects caused by decreased myocardial perfusion was larger. Such myocardial ischemia occurring under no coronary artery stenosis can be caused by coronary spasm, and it is common in females and patients with diabetes mellitus and coronary heart disease [21, 22]. Besides the case with negative results of dual-energy CT coronary angiography, increased resting myocardial transmural perfusion ratio might also be related to blood glucose, blood pressure, blood lipids and other risk factors [23]. In conclusion, routine evaluation of resting myocardial transmural perfusion ratio can realize early diagnosis of patients with mild stenosis that cannot be found in angiography, so as to intervene early and prevent the occurrence of malignant cardiovascular events, such as myocardial infarction. Therefore, the application of the two methods can adapt to different clinical situations and synergistically improve the level of evaluating ventricular muscle function.

In various noninvasive imaging examination techniques of coronary heart disease, dual-energy CT one-time dynamic continuous perfusion scanning is performed to obtain the CT coronary angiography and static CT perfusion images, to understand degree of coronary artery stenosis and myocardial hemodynamics, which is significant in evaluating ventricular muscle function of patients with coronary heart disease and predicting occurrence of long-term adverse cardiac events [11]. Kong et al. found after a long-term follow-up study for more than 8 years that in the prognostic evaluation and treatment guidance of patients with coronary heart disease through resting myocardial transmural perfusion ratio, the average annual mortality rate of patients with extreme abnormality of myocardial perfusion is higher than that of patients with normal imaging [24]. Otsuka et al. found that in patients with suspected coronary heart disease, the possibility of major serious adverse cardiac events in those with smaller resting myocardial transmural perfusion ratio was higher than that in those with normal ratio [25]. Similarly, Lu et al. found that resting myocardial transmural perfusion ratio can assess the myocardial perfusion abnormality and ventricular muscle function, which is conducive to evaluating the prognosis of patients and predicting serious complications [26].

Coronary heart disease patients with coronary artery stenosis >50% often have multiple vascular lesions, in which case concordance rate of combined methods in evaluating ventricular muscle function is higher [16, 17]. However, degree of coronary artery stenosis in some patients is inconsistent with the abnormal degree of myocardial perfusion [16]. The reason for the above condition was related to the coronary artery stenosis caused by calcified plaque. Current studies argue that stability of coronary calcified plaque is better than that of other types of plaque, because formation of coronary calcified plaque needs a long time, and collateral circulation is formed easily, which is conducive to compensating the coronary calcified plaque-induced decline in myocardial perfusion without affecting ventricular muscle function [27]. There is abnormal myocardial perfusion and smaller resting myocardial transmural perfusion ratio in some patients with degree of coronary artery stenosis of 26-50%, and site of stenotic coronary artery is basically corresponding to that of abnormal myocardial perfusion [28]. It has also been reported that coronary artery stenosis of 50% is considered as critical value for diagnosis of coronary heart disease, while that of less than 50% is defined as the negative perfusion result [29, 30]. However, in this study, there was still myocardial perfusion abnormality in coronary heart disease patients with coronary artery stenosis of less than 50%, and most of them had unstable plaques, leading to abnormal myocardial perfusion and decreased resting myocardial transmural perfusion ratio, and risk of acute coronary events was higher than that of patients with stable plaques. Even if the resting myocardial transmural perfusion ratio isn't reduced, clinical intervention is needed in time due to poor stability of plaque [31]. Through combining the above two examination methods, resting myocardial transmural perfusion ratios of myocardia dominated by LAD, LCX and RCA were all decreased with the increase of stenosis degree, with significant differences in the resting myocardial transmural perfusion ratios of myocardia dominated by LAD, LCX and RCA with different stenosis degrees, suggesting that severe coronary artery stenosis in patients with coronary heart disease had a significant influence on myocardial perfusion, and the resting myocardial transmural perfusion ratio was negatively related to degree of coronary artery stenosis, helping evaluate ventricular muscle function. However, small sample size might lead to slight fluctuations in relevant coefficients, follow-up survey results were lacked, and correlation between degree of coronary artery stenosis evaluated via dual-energy CT coronary angiography and the resting myocardial transmural perfusion ratio failed to be analyzed. Therefore, it is necessary to increase sample size, conduct prospective comparative study with nuclide or magnetic resonance imaging myocardial perfusion and improve research program.

In conclusion, the resting myocardial transmural perfusion ratio of patients with coronary heart disease is negatively correlated with the degree of coronary artery stenosis. Dual-energy CT combined with resting myocardial transmural perfusion ratio could synergistically improve level of evaluating ventricular muscle function. At the same time, CT coronary angiography was integrated with static CT perfusion image, thus improving the accuracy of research.

Disclosure of conflict of interest

None.

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