Value of One-stop Cardiac Examination with 640-slice Dynamic Volume CT in coronary artery disease

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Aims and objectives

Currently, the indications of traditional multi-slice spiral CT (MSCT) in cardiac examinations mainly include revealing coronary artery stenosis, evaluation of coronary artery atherosclerotic plaque, postoperative evaluation of coronary stenting, evaluation of coronary artery bypass graft, coronary artery anomalies and variations, left ventricular function and other aspects of the cardiac functions. For multidetector CT (MDCT), one of the most important applications is myocardial perfusion. A few studies have demonstrated that under the drug load, dynamic MDCT can be applied to detect myocardial ischemia and myocardial blood perfusion[1]. Due to its unique advantages, when applied in clinical practice, 320-row MDCT can provide the computed tomography angiography (CTA) of the cardiac myocardial perfusion of the entire heart during one cardiac cycle. This is exceptionally helpful for assessing whether certain vascular lesion has an impact on the cardiac function. Many scholars have explored observing two indicators, the physiological cardiac ejection function and the morphology of coronary vessels, in one cardiac examination [2]. Yet there are few reports on one-stop cardiac examination that simultaneously observes the coronal vascular morphology, evaluates the cardiac ejection function and assesses the myocardial function. The goal of the present study was to explore the clinical application value of one-stop cardiac examination in coronary angiography, left ventricular function analysis and analysis of resting-state left ventricular transmural perfusion ratio (TPR).
Methods and materials

1. Participants and inclusion materials

A total of 130 cases of clinically diagnosed or suspected coronary artery disease collected from June 2013 to June 2014 were enrolled in this study, including 63 females and 67 males, with a mean age of $61.4\pm10.4$ years. The inclusion criteria included the following: typical or atypical chest pain, treadmill exercise test or ECG abnormalities, and known coronary heart disease. The exclusion criteria included the following: arrhythmias or rapid heart rates (heart rate > 90 beats/min), severe imaging artifacts that precluded the images being used for diagnosis, severe heart, liver or kidney dysfunction and iodine allergy. This study was approved by the research ethics committee for exemption from written consent, the patients only need sign the consent form for CT angiography examination.

2. Examination methods

2.1 CT examination

(1) Patient preparation: Prior to the examination, the patients were asked about their disease history and their general conditions, and the patients signed the informed consent for CT angiography. The patients were subjected to breathe training to maintain the heart rate below 80 beats/min. For patients with a rapid heart rate, 25-50 mg metoprolol was administered under the supervision of the physician. An 18 G indwelling catheter was placed in the cubital vein, and before the start of the examination, a nitroglycerin tablet was given sublingually.

(2) Scan range: From tracheal bifurcation to the diaphragmatic surface of the heart. Aquilion One 640-slice dynamic volume CT scanner (Toshiba, Japan) was used for coronary volume scanning.

(3) Contrast agent: 50-70 mL iopamidol (370 mg/mL) was used as the contrast agent. The dosage used was adjusted according to the body mass index (BMI) (body weight/height squared, kg/m²) of the patient. The intravenous bolus injection of the 50-70 mL contrast agent was administered into the cubital vein using a two-tube high-pressure injection syringe at a flow rate of 5.0 mL/s. Next, at the same rate a bolus injection of 20-30 mL saline was administered to reduce the contrast agent artifacts in the right ventricle and to save the contrast agent.

(4) Scanning protocol: tube voltage 120-135 kV, tube current 400-450 mA, detector width 16cm (320*0.5 mm), field of view FOV-M, rotational speed 0.35 s/r. Retrospective ECG-gated full cardiac cycle scan was performed, and the parameter was set to conduct continuous scan of 1-2 cardiac cycles (beats). The CT monitoring level was set to the
descending aorta. Automatic trigger of the scan was applied. SureStart contrast agent tracking technology was used. The descending aorta contrast agent threshold was 150 Hounsfield Unit (HU); when this threshold was reached the scan was triggered. The patient held his/her breath for approximately 5 s. During the scanning process, ECG was simultaneously recorded. For each patient, during the CT examination, the scanner automatically generated volume CT dose index (CTDI) and the dose length product (DLP).

(5) Image post-processing: In this study, CFA#Cardiac Functional Analysis#data in 10% R-R period were used for 0-90% reconstruction. There were a total of 10 groups of reconstruction data. Both the slice thickness and the slice distance were 0.5 mm. The 10 groups of data were used for reconstruction of diastolic (75%) phase data. The restructured data were entered into Vitrea fx#TOSHIBA Company#software for analyses of the coronary CTA, left ventricular ejection fraction (LVEF) and left ventricular TPR. For all segments > 1.5 mm, the 16-segment model (except that 17-segment model was applied in the apical segment)\cite{3} was used for recording and analysis. In the workstation, the myocardium was divided into the inner, middle and outer layers. With the 16-segment model, the software automatically calculated the average density (AD) of each cardiac layer and TPR of each segment: \( TPR = \frac{\text{subendocardial AD}}{\text{subepicardial AD}} \). All images and data were analyzed by two CT vascular diagnosticians who were at least associate professors in the field. The mean was calculated.

2.2 Echocardiography examination

Echocardiography examination was applied using GE Vivid E9 echocardiography system#General Electric Company##The probe frequency was 3.0 MHz. The measurements were completed independently by two physicians who were at least associate professors in the Ultrasound division. The main indicator of the left ventricular function, the ejection fraction (EF) was determined (the mean value was calculated). For all patients, the time interval between the cardiac CT examination and the echocardiography examination was no longer than one week.

3. Statistical analysis

The data are expressed as mean ± standard deviation. SPSS17.0#IBM SPSS#was used for statistical analysis. For comparison of the LVEF values determined by CT and echocardiography, paired t test and Pearson correlation analysis were performed. The TPR values in regions with normal coronary blood supply and in regions with coronary artery stenosis in the resting state were compared. The radiation dose of each case was also analyzed.
Results

1. In all 130 cases, good images of the coronary CTA were obtained, including 125 cases of right coronary dominance, 2 cases of balanced coronary dominance, and 3 cases of left coronary dominance. There were 40 cases of normal coronary artery, 9 cases of coronary artery variation (e.g. Figure 1) and 1 cases of coronary artery aneurysm (e.g. Figure 2); in the remaining 80 cases, there existed varying degrees of stenosis in the main coronary arteries (e.g. Figure 3).

2. From the volume data obtained from the 640-slice volume CT data, the computer software automatically calculated the LVEF values (e.g. Figure 4). The mean LVEF value of all 130 patients was 66.6±8.8 (%). The mean LVEF value determined using echocardiography was 65.7±5.0 (%). The two sets of LVEF values showed a certain correlation (r=0.725). The LVEF values obtained using the two methods did not differ significantly (P>0.05)(see Table 1).

Table 1. Comparison of LVEF value obtained from CT and that obtained from echocardiography (n=130, mean±standard deviation)

<table>
<thead>
<tr>
<th>Functional index of the left ventricle</th>
<th>640-slice CT</th>
<th>Echocardiography</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>66.6±8.8</td>
<td>65.7±5.0</td>
<td>0.725</td>
</tr>
</tbody>
</table>

Note: P>0.05 means that the two groups did not differ significantly from each other.

3. The 130 cases of coronary artery CTA were analyzed. The TPR values of 40 normal coronary artery cases served as the control group, and were compared with the TPR values of 80 cases of coronary stenosis (e.g. Figure 5) (patients with coronary artery variations and coronary artery aneurysms were excluded from the TPR analysis). The left anterior descending artery (LAD) blood supply region, the left circumflex artery (LCX) blood supply region and the right coronary artery (RCA) blood supply region of all participants were analyzed. Patients with diseased artery were divided into the mild, moderate and severe stenosis subgroups. In the resting state, the average TPR values of the LAD, LCX and RCA blood supply regions of participants with normal arteries were 1.15±0.08#1.12±0.10 and 1.16±0.15#40#, respectively. The average TPR values of patients with mild, moderate and severe LAD stenosis were 1.17±0.08#29##1.09±0.11#19##1.05±0.13#11#, respectively; the average TPR values of patients with mild, moderate and severe LCX stenosis were 1.12±0.01#24##1.10±0.09#21##1.04±0.16#14#, respectively; the average TPR values of patients with mild, moderate and severe RCA stenosis were 1.13±0.11#28##1.13±0.12#15##1.10±0.12#15#, respectively. The TPR values of the different subgroups were compared with that of the corresponding normal control group using the t test. In the LAD blood supply region, the moderate and severe stenosis
subgroups both showed significantly different TPR values compared to the normal control group (P<0.05), and in the LCX blood supply region the severe stenosis subgroup showed within each group no statistically significant different TPR compared to the normal control group (P>0.05); for all the other comparisons, the differences were not statistically significant (P>0.05). Therefore, severe stenosis of coronary arteries was found to have a relatively large impact on TPR (see Table 2), and the effect of mild stenosis was relatively small.

Table 2. Comparison of TPR in the LAD, LCX and RCA blood supply regions between the normal group and the lesioned group [mean±standard deviation(n)]

<table>
<thead>
<tr>
<th>Group</th>
<th>Normal control group</th>
<th>Mild stenosis group</th>
<th>Moderate stenosis group</th>
<th>Severe stenosis group</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD blood</td>
<td>1.15±0.08#40#</td>
<td>1.17±0.08#29#</td>
<td>1.09±0.11#19#</td>
<td>1.05±0.13#11#</td>
</tr>
<tr>
<td>supply group</td>
<td></td>
<td></td>
<td>* t=2.37</td>
<td>* t=3.17</td>
</tr>
<tr>
<td>LCX blood</td>
<td>1.12±0.10#40#</td>
<td>1.12±0.11#24#</td>
<td>1.10±0.09#21#</td>
<td>1.04±0.16#14#</td>
</tr>
<tr>
<td>supply group</td>
<td></td>
<td></td>
<td>* t=2.18</td>
<td></td>
</tr>
<tr>
<td>RCA blood</td>
<td>1.16±0.15#40#</td>
<td>1.13±0.11#28#</td>
<td>1.13±0.12#15#</td>
<td>1.10±0.12#15#</td>
</tr>
<tr>
<td>supply group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: * means that when the diseased group was compared to the normal control group, P<0.05

4. For each patient, during CT examination the scanner automatically generated CTDI and DLP, and these were recorded. The effective dose (ED) was then calculated using the following formula: ED=DLP×C, where C is the conversion factor; here a value of 0.017, the average chest value proposed by the European guidelines on quality criteria for computed tomography, was used. The mean ED of all 130 participants in the present study was calculated to be 7.04±2.06mSv.
Fig. 1: Coronary variation - high origin of the right coronary artery

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Fig. 2: Coronary aneurysm

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Fig. 3: Coronary stenosis

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Fig. 4: Analysis of left ventricular function

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**Fig. 5:** TPR analysis

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Conclusion

With the development of MSCT and post-processing software in recent years, cardiac and coronary CT examinations have been increasingly applied in clinical practice. The 640-slice dynamic volume CT (DVCT) with a 16 cm wide detector can acquire a full range scan of the heart from the bottom to the apex with only one scan cycle and reconstruct the three-dimensional image of the entire heart in a timely manner within one cardiac cycle. It provides highly detailed images \(^4\), making it possible to apply CT technology for simultaneous qualitative and semi-quantitative assessments on coronary stenosis, cardiac function and myocardial perfusion, thereby achieving one-stop cardiac examination.

1. The characteristics and advantages of 640-slice CT

A 640-slice CT covers a range of 16 cm in the Z-axis. Compared with 64-row CT, which is currently the mainstream technology worldwide, the technical features and benefits of 640-slice CT include the following. First, with only one cardiac cycle, a whole-heart volume scan can be completed. The scan data at different locations are in the same phase, resulting in consistency in the assessment of myocardial perfusion and survival, the characterization of plaques, and evaluation of other imaging data. This avoids the disadvantage of the previous 64-row spiral CT scans, in which accurate assessment of the plaque cannot be ensured due to the fact that the stability of the peak concentration of the contrast agent cannot be guaranteed. Second, in 320-row CT, the improvement of temporal resolution makes it possible to complete the collection of necessary data within 1-2 s, whereas the data acquisition time for 64-row CT is approximately 8-10 s. This not only reduces motion artifacts due to patient breathing, heartbeat and other factors, but also makes 320-row CT applicable for patients with severe heart and lung diseases, who cannot breathe hold for a long period of time, and for patients with arrhythmias, such as atrial fibrillation, and rapid ventricular rate. Therefore, compared to 64-row CT, the clinical examination indications of 320-row CT are expanded \(^5,6\). Third, studies have shown that the ED of 320-row CT is \((6.8±1.4)\text{mSv} \(^7\)\), whereas that of 64-row CT is \((20.0±3.5)\text{mSv} \(^8\)\). In addition, compared to the 64-row CT, in 320-row CT the dose of contrast agent is significantly reduced \(^9\), and this in theory reduces the risk of contrast-induced nephropathy and other clinical complications.

2. The clinical application of 640-slice CT

2.1 Assessment of coronary artery stenosis

The gantry rotation speed of 320-row CT scanner is 350 ms/rotation, making the temporal resolution 175 ms. The spatial resolution is approximately 0.25 mm. Compared to
coronary angiography, of which the spatial resolution is approximately 0.16 mm and the temporal resolution is 33 ms (30 frames/sec), 320-row CT still has poorer spatial and temporal resolution \cite{10}. This limits the application of 320-row CT in assessing distal vessels and small branches, and in these cases it still cannot replace coronary angiography with regards to accurate diagnosis of coronary artery stenosis. However, coronary angiography is an invasive approach that can lead to a variety of surgical complications. In addition, the cost is rather high, and the radiation dose received by the patient is relatively large. Furthermore, a study conducted by Raff et al. \cite{11} revealed that among all patients receiving coronary angiography, less than 45% needed to undergo coronary recanalization and other treatments, resulting in a waste of medical resources. The cost of MSCT for screening for coronary heart disease is much lower than that of coronary angiography, and thus the former is of high value for health economics. Therefore, for patients with suspected coronary artery disease, MSCT has certain advantages in terms of safety and cost. In studies where coronary angiography was used as the diagnostic criteria, it has been found that the sensitivity and specificity of 320-row CT in the diagnosis of coronary artery disease with stenosis > 50% are 100% and 88%, respectively, which are both higher than that of 64-row CT \cite{12}. Thus, 320-CT is considered a noninvasive examination method with relatively high diagnostic value in screening for coronary heart disease. In addition to its good performance in evaluating stenosis, with MSCT the plaque can be characterized according to the CT value of the plaque. Springer et al. \cite{13} showed that MSCT and intravascular ultrasound exhibited consistent results in determining the nature of plaques.

\subsection*{2.2 Assessment of the left ventricular function}

In 320-row CT, coronary artery CTA performs the analysis of the left ventricular function in one cardiac cycle, exhibiting high temporal and spatial resolutions. The examination is completed while the patient breath holds for one time. This reduces the cardiac and respiratory artifacts, and decreases the radiation dose. In 640-slice CT, the heart volume is calculated directly by outlining the endocardium and epicardium at the end of the systolic and diastolic phases from the apex to the bottom of the heart, without making any assumptions \cite{14}, and the indicator of the left ventricular function, LVEF, is directly calculated. From the perspective of data collection, raw CT data are larger in volume than echocardiography data, and with the former the anatomy of the heart can be objectively and clearly displayed. The endocardial and epicardial borders can be clearly identified, which helps with the outlining of the heart and reduces the measurement error. With CT examination, the phases are determined accurately, and the measurement is barely affected by subjectivity of the operator, exhibiting high repeatability. The drawback is that there is a certain X-ray radiation. In the present study, the LVEF values determined using 640-slice CT and that measured by echocardiography showed certain correlation (r = 0.725), and the two sets of LVEF values were not statistically significant (P>0.05). This is consistent with previous relevant studies \cite{15}. Thus, the current study shows that the
LVEF values determined by 640-slice CT are accurate and reliable and can quantitatively assess left ventricular function just like echocardiography.

2.3 Assessment of myocardial perfusion

Myocardial perfusion refers to the process in which the blood flow delivers oxygen and nutrients to the myocardium through the capillary network. Current studies on myocardial perfusion have mainly applied single-photon emission computed tomography (SPECT), MRI and CT. Among these, the applications of SPECT and MRI technologies are predominant. For a long time, CT myocardial perfusion was primarily based on dynamic continuous perfusion and scanning, and the large radiation dose was the main factor limiting its development. With the development of CT equipment, multiple-detector spiral CT of tracheal perfusion is based on the dilution of the contrast agent, so that the concentration of extracellular iodine-containing contrast agent and tissue enhancement show a clear linear relationship with the amount of iodine accumulation. In this way, the CT value directly reflects the concentration of the contrast agent.

Wintersperger et al. [16] reported that local microcirculation damage caused by myocardial infarction could reduce the inflow of the contrast agent. Therefore, after MSCT myocardial perfusion, the ischemic myocardium showed reduced increases in density and reduced rising slope compared to normal myocardial tissue (normal values (31±10) HU and 0.13±0.07, respectively). Thus, CT myocardial perfusion has a broad application prospect, and acquisition of the morphological information of the coronary arteries and the hemodynamic information at the same time has become a trend. For example, with dual-source CT, the myocardial iodine perfusion distribution can be obtained in one scan [17]. George et al. [18] applied 64-row and 256-row CT scans and used data collected in one scan to calculate the perfusion ratio between the endocardial and the epicardial layers, thereby assessing cardiac hemodynamics. In the current study, this method was used. By calculating the TPR values, the impact of different degrees of coronary stenosis on myocardial perfusion was investigated. It has been shown that [19] in the resting state the transmural distribution of blood flow across the wall of the left ventricle is relatively uniform, yet different myocardial layers respond differently to the reduction of coronary blood flow. The endocardium is more sensitive to ischemia than the epicardium. Kohei et al. [20] acquired myocardial perfusion images with a single scan under pressure, and assessed the perfusion of the left ventricular wall by calculating the transmural perfusion gradient (TMPG): TMPG = (average epicardial density - average endocardial density)/the thickness of the left ventricular wall. They defined the condition in which the average endocardial density was lower than the average epicardial density as positive for myocardial ischemia, and showed that with this method the sensitivity, specificity, positive rate and negative rate in the determination of coronary artery stenosis were all higher compared to conventional myocardial perfusion imaging.

In the current study, we found that in resting state the average myocardial TPR values in the LAD blood supply region, LCX blood supply region and the RCA blood supply
region of the normal coronary artery group were 1.15±0.08, 1.12±0.10, and 1.16±0.15, respectively. This was consistent with the blood flow ratio between the endocardial and epicardial layers of normal myocardium determined by Galiuto et al. (1.14±0.17:1) [21]. George et al. [19] applied 320-row CT under pressure and determined the mean TPR of normal myocardium to be 1.13±0.10. In addition, using nuclear myocardial perfusion imaging as the gold standard, the sensitivity, specificity, positive rate and negative rate of the method were determined to be 86%, 85%, 67% and 94%, respectively, thereby demonstrating the reliability of this method and the consistency between this method and other myocardial perfusion methods. Under pressure load, the coronary microvascular resistance is increased. The myocardial blood flow first reaches the myocardium in the epicardial layer during the diastolic phase, and the endocardial layer shows a perfusion delay. In this case, the TPR value will be significantly lower than that in the resting state. Hence, the TPR values measured in the present study were all substantially higher than the myocardium TPR values measured under pressure. Under normal conditions, if there is no coronary artery disease, the extent of subendocardial perfusion is often greater than that of subepicardial perfusion [22], and thus the TPR value of normal myocardium is often > 1. George et al. [19] proposed that a TPR <0.99 indicated myocardial ischemia. In the current study, we also found that severe stenosis of the coronary arteries showed a relatively large impact on TPR (P<0.05), whereas the impact of mild stenosis was rather small. This is consistent with previous relevant reports [23].

3# Radiation dose

The radiation dose has always been the bottleneck limiting the development of MSCT myocardial perfusion. Especially for dynamic scans, selection of a reasonable radiation dose for myocardial perfusion imaging still remains controversial. Recent CT myocardial perfusion studies have mostly controlled the radiation dose to be between 9-15 mSv. For dynamic scanning, the radiation dose is slightly higher, and the highest dose used is 21.9 mSv. In the present study, in the one-stop examination, the morphology of coronary arteries, the physiological cardiac ejection function and the myocardial function were evaluated at the same time, and the ED of the CT was measured to be 7.04±2.06 Sv, notably lower than the standard radiation dose of myocardial perfusion.

4# Future directions

The present study needs to be deepened in the following directions: it is necessary to compare the result with radionuclide or MRI myocardial perfusion experiments; the reliability of the CT perfusion in the resting state needs to be confirmed; the single-scan perfusion method needs to be solidified and further developed; software should be developed so that the mean subendocardial density and subepicardial density can be calculated automatically. In addition, due to the existence of beam hardening artifacts, the false positive rate of the current study was relatively high. Experiments have shown
that this can be solved by choosing the appropriate data acquisition time and increasing the amount injected saline (data not shown).

In short, one-stop cardiac examination using 640-slice volume CT can complete coronary CTA imaging, left ventricular functional analysis and semi-quantitative analysis of myocardial perfusion in one examination, providing a wealth of images for clinical diagnosis of cardiovascular diseases, differential diagnosis and determination of treatment options. It also reduces the scan time and the scan cost, decreases the dose of contrast agent and the radiation dose, and is of high value in the clinical diagnosis of coronary heart disease. With the wide application of 320-row CT in clinical practice, this technique may be further developed to reduce the radiation exposure dose further, establish new indications, expand applications in functional imaging (e.g. evaluation of myocardial viability), and play an even bigger role in the screening and diagnosis of cardiac diseases in the future.
References


