

Effect of heart rate on the diagnostic accuracy of 256-slice computed tomography angiography in the detection of coronary artery stenosis: ROC curve analysis

GANG WANG¹, YIFEN WU², ZHENTAO ZHANG¹, XIAOLIN ZHENG¹, YULAN ZHANG¹,
MANQIU LIANG¹, HUANCHU YUAN¹, HAIPING SHEN¹ and DEWEI LI¹

Departments of ¹Radiology and ²Oncology, People's Hospital of Dongguan, Dongguan, Guangdong 523000, P.R. China

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Abstract. The aim of the present study was to investigate the effect of heart rate (HR) on the diagnostic accuracy of 256-slice computed tomography angiography (CTA) in the detection of coronary artery stenosis. Coronary imaging was performed using a Philips 256-slice spiral CT, and receiver operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic value of 256-slice CTA in coronary artery stenosis. The HR of the research subjects in the study was within a certain range (39-107 bpm). One hundred patients suspected of coronary heart disease underwent 256-slice CTA examination. The cases were divided into three groups: Low HR (HR <75 bpm), moderate HR (75 ≤ HR <90 bpm) and high HR (HR ≥90 bpm). For the three groups, two observers independently assessed the image quality for all coronary segments on a four-point ordinal scale. An image quality of grades 1-3 was considered diagnostic, while grade 4 was non-diagnostic. A total of 97.76% of the images were diagnostic in the low-HR group, 96.86% in the moderate-HR group and 95.80% in the high-HR group. According to the ROC curve analysis, the specificity of CTA in diagnosing coronary artery stenosis was 98.40, 96.00 and 97.60% in the low-, moderate- and high-HR groups, respectively. In conclusion, 256-slice coronary CTA can be used to clearly show the main segments of the coronary artery and to effectively diagnose coronary artery stenosis. Within the range of HRs investigated, HR was found to have no significant effect on the diagnostic accuracy of 256-slice coronary CTA for coronary artery stenosis.

Introduction

Coronary artery disease (CAD) is an increasingly prevalent threat to human health. The incidence of this disease is associated with the involved coronary arteries, including the degree and number of branches. It is crucial to develop methods to accurately diagnose coronary artery disease, evaluate its severity and ultimately to guide clinical intervention or treatment. Imaging examination methods are crucial; for example, multi-slice spiral computed tomography angiography (CTA), digital subtraction angiography (DSA) and ultrasound examination. Among these techniques, DSA is currently recognized as the gold standard. However, with the continuous development of equipment and technology updates CTA has in certain regards superseded the function of DSA (1-10).

In recent years, CTA has been approved for use in numerous fields and has been increasingly used in the detection and diagnosis of clinical CAD. In particular, the temporal resolution of the latest 64-slice spiral CT has improved considerably, making the imaging of coronary arteries clearer and the diagnosis more accurate (11-21). In general, study reports have evaluated the diagnostic value of coronary CTA by determining the sensitivity and specificity; however, using these two indicators alone tends to ignore the influence of different interpretations by the observers on the results. By contrast, the receiver operating characteristic (ROC) curve method can minimize the possible differences, which makes the diagnostic evaluation more objective. The aim of the present study, therefore, was to investigate the diagnostic accuracy of Philips 256-slice spiral CT for coronary imaging and to perform ROC curve analysis to evaluate the use of 256-slice CTA in coronary artery stenosis.

Patients and methods

Patients. A total of 100 patients underwent coronary CTA and coronary angiography (CAG) checks, with intervals between the two methods of 3-15 days (average, 8 days). According to heart rate (HR), the patients were divided into three groups: Low HR (n=40 patients; HR <75 bpm); moderate HR (n=35 patients; 75 ≤ HR <90 bpm); and high HR (n=25; HR ≥90 bpm). Prior written informed consent was obtained

Correspondence to: Dr Xiaolin Zheng, Department of Radiology, People's Hospital of Dongguan, 3 South Wanda Road, Dongguan, Guangdong 523000, P.R. China
E-mail: xiaolinzheng123@yeah.net

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from the patients and their families. No patient experienced any adverse reaction following the examination. A total of 100 cases of suspected coronary heart disease were collected between May 2011 and June 2012, with the following exclusions: i) Allergy to iodinated contrast agents; ii) respiratory insufficiency or acute decompensated heart function insufficiency; iii) severe hepatic or renal insufficiency; iv) coronary stent or bypass surgery; and v) placement of a permanent pacemaker or following artificial heart valve replacement surgery.

CT examination. CT examinations were performed with prospective electrocardiographic gating using a 256-slice multi-detector CT scanner (Brilliance iCT; Philips Healthcare, Cleveland, OH, USA). The parameters were as follows: Tube potential, 120 kV_p; tube current, 800-1,000 mA; slice thickness, 0.90 mm; increment, 0.45 mm; and matrix, 512x512. The scanning range was from 1 cm below the tracheal bifurcation to the diaphragmatic level. The enhancement scans used high concentrations of iodine-containing non-ionic contrast agent (370 mg I/100 ml; 1.0 ml/kg), saline (30 ml) and an injection rate of 5.0-6.0 ml/sec. Using contrast agent tracking trigger technology, the area of interest was located in the main pulmonary artery window level in the descending aorta. With a triggering threshold of 150 HU, scanning started automatically for the shortest delay time upon reaching the threshold. The patients did not receive β -blockers or other drugs to control HR prior to inspection. At a time of 3-5 min before scanning, the patients were sublingually administered 0.5 mg nitroglycerin (Shanghai Bracco Sine Pharmaceutical Corp., Ltd., Shanghai, China).

CTA image processing. Good-quality images were transferred to the Extended Brilliance Workspace 4.5 (Philips Healthcare) workstation for processing and quality evaluation. The post-coronary CTA image processing methods included volume rendering (VR), maximum intensity projection, multi-planar reconstruction and curved planar reformation (CPR).

Image quality assessment rating scale (1-3). Coronary vessels with a diameter of ≤ 1.5 mm were not analyzed. Images were scored on a four-point ordinal scale (grades 1-4). On grade 1 images (3 points), the blood vessels were continuous and clear, and the axial scanning showed sharp edges with no motion artifacts and a fat density shadow at the edge. No step artifacts could be seen on the VR image. On grade 2 images (2 points), segments of the small parts of the blood vessels showed slightly blurred margins; the axial scanning showed smaller artifacts, and light step artifacts could be seen on the VR image. On grade 3 images (1 point), blood vessels appeared to have more artifacts, a visible profile, bilateral or multilateral findings and partial interruptions or split-levels, although when combined with multi-phase cross-sections of the original image, clear vascular lesions could be seen. On grade 4 images (0 points), the blood vessels had a vague outline and were unclear, making it impossible to distinguish between the blood vessels and the surrounding tissue. Grades 1-3 were diagnostic but grade 4 images could not be used in diagnosis. The degree of coronary artery stenosis was measured using the following equation: Degree of coronary artery stenosis = (average diameter of normal vessel at the proximal and distal ends of the stricture - diameter

of the stricture vessel)/diameter of the normal vessel at the proximal end of the stricture $\times 100\%$. The inner diameter of the coronary artery was measured on the perpendicular to the blood vessel's major axis on the CPR image.

Coronary artery digital subtraction angiography (DSA) and segment evaluation. A Philips FD20 flat panel angiography system (Philips Healthcare) was used and six projection positions were selected (plus other positions when necessary). The left and right coronary angiography procedures were performed through a femoral artery puncture using a non-ionic contrast agent (370 mg I/100 ml). The projection angle for the narrowest of lesion diameters was the basis for the judgment of the degree of stenosis.

According to the American Heart Association definition (12) and the Radiology Heart Coronary Multi-Detector CT Clinical Applications Collaborative Group Consensus (13), the 15-segment classification system was used to evaluate the coronary tree, as follows: Segments 1-3, the right coronary artery proximal, middle and distal segments; segment 4, the posterior descending artery/left ventricular posterior branch; segment 5, the left main coronary artery; segments 6-8, the left anterior descending artery proximal, middle and distal segments; segments 9 and 10, 1-2 diagonal branches; segments 11, 13 and 15, left circumflex artery proximal, middle and distal segments; segments 12 and 14, 1-2 obtuse marginal branches.

Coronary artery CTA and CAG images were independently evaluated by two highly qualified doctors with relevant diagnostic experience. Any disagreements were subject to resolution by discussion.

Statistical analysis. Data are presented as the mean \pm standard deviation. According to the SPSS software package (version 13.0; SPSS, Inc., Chicago, IL, USA), $P < 0.05$ was considered to indicate a statistically significant difference. Count data are expressed as frequency percentages. CAG was used as the 'gold standard' for the control, and an ROC curve was used to analyze 256-slice CTA for the specificity and sensitivity of coronary artery stenosis diagnosis. To compare the diagnostic differences among the different HR groups, one-way analysis of variance was used.

Results

Patient data. The results were selected from 100 patients (63 male and 37 female) aged between 37 and 87 years (average, 64.64 ± 10.64 years) with HRs between 39 and 107 bpm (average, 76.44 ± 13.36 bpm). Among the total 1,500 coronary artery segments, CTA showed 1,447 segments (96.47%). A total of 96.83% of the low-HR group segments were shown, compared with 96.95% of the moderate-HR group segments and 95.20% of the high-HR group segments. The 53 segments not evaluated included segments 2-5, 8-10 and 12-15.

Image quality. Among the 1,500 coronary segments, CTA could be used to evaluate 1,447 coronary segments (96.47%) (Table I). The remaining 53 segments (3.53%) were not shown and included segments 2-5, 8-10 and 12-15; segments 9, 10, 14 and 15 were most frequently not shown. Coronary CTA images

Table I. Coronary computed tomography angiography image quality evaluation of 1,447 segments, n (%).

HR group	3 points	2 points	1 point	0 points	Total
Low	391 (67.30)	154 (26.51)	23 (3.96)	13 (2.23)	581
Moderate	343 (67.39)	121 (23.77)	29 (5.70)	16 (3.14)	509
High	221 (61.90)	93 (26.05)	28 (7.85)	15 (4.20)	357

HR, heart rate.



Figure 1. (A) Computed tomography angiography image of a patient with a low heart rate (64 bpm) showing an eccentric stenosis of the left circumflex artery proximal vessel. (B) Corresponding digital subtraction angiography image. (C) Receiver operating characteristic curve, Az=0.971.

of 1,403 out of the 1,447 segments, accounting for 96.95%, met the diagnostic score (1-3 points).

In the low-HR group, 581 segments from the 40 patients (a total of 600 segments) were shown by CTA, accounting for 96.83%. Images of 568 of these segments (97.76%) met the diagnostic score (1-3 points): 391 (67.30%) were scored 3 points, 154 (26.51%) were scored 2 points and 23 (3.96%) were scored 1 point. In the moderate-HR group of 35 patients (a total of 525 segments), 509 segments (96.95%) were shown by CTA, with images of 493 (96.86%) of these segments meeting the diagnostic score [3 points, 343 (67.39%); 2 points, 121 (23.77%) and 1 point, 29 (5.70%)]. In the high HR group of 25 patients (a total of 375 segments) 357 segments, accounting for 95.20%, were shown by CTA, with images of 342 segments (95.80%) meeting the diagnostic score: 221 (61.90%) were scored 3 points, 93 (26.05%) were scored 2 points and 28 (7.85%) were scored 1 point. The comparison of image quality scores among the different HR groups did not reveal a statistically significant difference ($\chi^2=5.017$, $P=0.081$; $P>0.05$).

Images of the remaining 44 segments were not diagnostic, and those segments were excluded from the coronary artery stenosis assessment. In the low-HR group, 13 segments (2.23%) were excluded, compared with 16 (3.14%) from the moderate-HR group and 15 (4.20%) from the high-HR group. Among these segments, the majority were the middle of right coronary artery (segment 2), accumulated of 10 segments.

Diagnostic accuracy. Using DSA as the 'gold standard', 1,403 segments could be diagnosed with coronary artery stenosis via CTA. The specificity of CTA for the diagnosis

of coronary artery stenosis in the low-HR group was 98.40%, the sensitivity was 95.00% and the area under the ROC curve (Az) value was 0.971. Eight segments were falsely positive and 4 segments were falsely negative (Table II and Fig. 1). In the moderate-HR group, the specificity was 96.00%, the sensitivity was 93.70% and the Az value was 0.955. A total of 14 segments were falsely positive and 9 segments were falsely negative (Table II and Fig. 2). In the high-HR group, the specificity of CTA for the diagnosis of coronary artery stenosis was 97.60%, the sensitivity was 92.20% and the Az value was 0.955. Six segments were falsely positive and 7 segments were falsely negative (Table II, Figs. 3 and 4).

The comparison of the Az values among the three groups did not reveal a statistically significant difference ($F=0.703$, $P=0.516$; $P>0.05$). Among the 1,403 segments that were diagnosed, false positives were found in 28 segments, mainly in segments 1, 2, 5-7 and 11-13; false negatives were found in 20 segments, mainly in segments 9, 10 and 13-15.

Discussion

Numerous studies have reported that multi-slice helical CTA has advantages in diagnosing CAD (21-30). Following the introduction of air-cushion suspension-bearing technology in 256-slice spiral CT, friction and oscillation between objects was dispelled, and this accelerated the rotary speed of the ball tube. The fastest speed is 0.27 sec per circle, reducing the acquisition time of circular cardiac data. Thus, the effect of HR fluctuations and arrhythmia on image quality was reduced. Furthermore, the scan range in the Z-axis direction



Figure 2. (A) Digital subtraction angiography image of a patient with a moderate heart rate (84 bpm) showing a lack of smoothness of the middle right coronary artery walls, local stenosis and dilatation of the vessel. (B) Corresponding computed tomography angiography image. (C) Receiver operating characteristic curve, $A_z=0.955$.

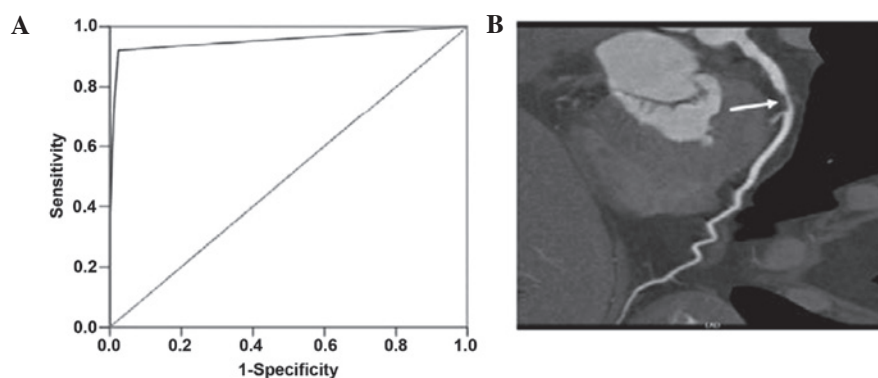


Figure 3. (A) Receiver operating characteristic curve of the high-heart rate group, $A_z=0.955$. The specificity was 97.60% and the sensitivity was 92.20%. (B) Diagnosis of coronary artery stenosis with computed tomography angiography.

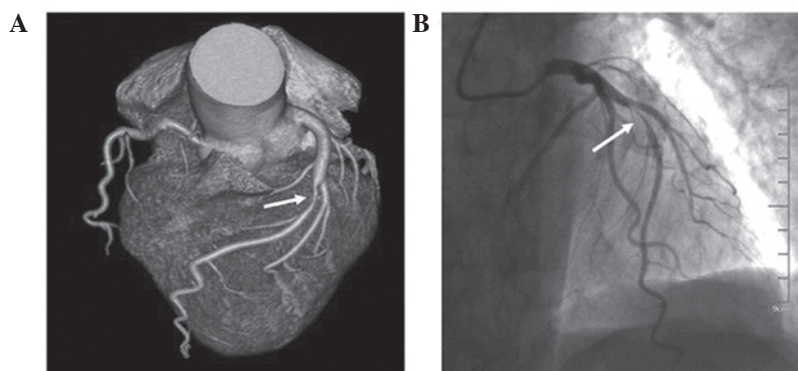


Figure 4. (A) Computed tomography angiography and (B) a digital subtraction angiography images of a patient with a high heart rate (106 bpm) showing local stenosis of the proximal left anterior descending artery. The location, morphology and degree of stenosis are similar.

was increased, which was preferable for the imaging of the coronary artery and the diagnosis of associated diseases.

The results of the present study showed that the display rate of the coronary artery CTA, performed using a 256-slice multi-detector CT scanner, was 96.47%. The display rate in each of the different HR groups was high, and rates were similar among the groups. Certain segments of the coronary artery were not shown by CTA, and this was primarily due to developmental variations or abnormalities. Parts of

the coronary artery branches (circumflex artery or obtuse marginal branch and the second angular branch) were absent or too small and so could not be filled with contrast agent to aid with their visualization. The grading of the images showed that while the number of images with a score of >1 point decreased with increasing HR, the left anterior descending artery, circumflex branch of the left coronary artery and the right coronary artery were still able to be satisfactorily diagnosed. No statistically significant difference was found

Table II. Receiver operating characteristic curve evaluation of the diagnosis of coronary artery stenosis using CTA.

A, Low-HR group						
DSA diagnosis	CTA diagnosis (n)			Specificity, %	Selectivity, %	Az value
	Normal	Coronary stenosis	Total			
Normal	480	8	488	98.40	95.00	0.971
Coronary stenosis	4	76	80			
Total	484	84	568			
B, Moderate-HR group						
DSA diagnosis	CTA diagnosis (n)			Specificity, %	Selectivity, %	Az value
	Normal	Coronary stenosis	Total			
Normal	337	14	351	96.00	93.70	0.955
Coronary stenosis	9	133	142			
Total	346	147	493			
C, High-HR group						
DSA diagnosis	CTA diagnosis (n)			Specificity, %	Selectivity, %	Az value
	Normal	Coronary stenosis	Total			
Normal	246	6	252	97.60	92.20	0.955
Coronary stenosis	7	83	90			
Total	253	89	342			
CTA, computed tomography angiography; DSA, digital subtraction angiography; Az, area under the curve index; HR, heart rate.						

among the groups. The segments in each group can meet the satisfaction of diagnosis, achieving >95%. We therefore believe that 256-slice CTA can show the main segments of the coronary arteries clearly and lead to a satisfactory diagnosis.

Regarding the diagnosis of coronary artery stenosis, the results of the present study showed that the specificity and sensitivity of CTA were high. In each of the HR groups, ROC curve analysis generated an Az value of >0.9, indicating a high efficiency of 256-slice CTA for the diagnosis of coronary artery stenosis. Although the Az value, specificity and sensitivity were different in each group, the differences among the groups were not statistically significant. This indicated that 256-slice CTA was not limited by differences in HR and that imaging could be performed without HR control, leading to a superior effect and a more accurate diagnosis of coronary artery stenosis.

The results of the present study showed that there were false positives in 28 segments and false negatives in 20 segments. A number of reasons for this were considered, based on the results and the literature. Subjective factors are different for the measurement of the narrow center and the normal reference value of the differences between the selected. Objectively, pathological segments of coarse or

diffuse calcification will bring certain of the artifacts. The calcified segments and the area around the formation of parallel linear calcification, a slice of low density, which was easily mistaken form filling defect caused by plaque, and fuzzy edge of the residual lumen (31,32). In particularly tortuous segments, the convolutions in the wall of the coronary artery can cause the edges of those segments to be become blurred, which can result in the degree of stenosis being overestimated. Furthermore, in certain segments, the relatively small lumen means that the scope and extent of any lesions present can be easily underestimated. It is therefore imperative that, in the post-coronary CTA processing, multi-dimensional observations are performed from more than one angle and that the results are combined with a cross-section of the original image, in order to reduce incorrect analyses.

In conclusion, the present study has, to a certain extent, illustrated that HR has no significant effect on the accuracy of 256-slice coronary CTA in the diagnosis of coronary artery stenosis; however, since the HR of all the patients in the present study was within a certain range (39-107 bpm), further study is required to evaluate whether HRs falling outside this range would affect the evaluation of coronary segments using CTA.

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