Diagnostic performance of a 256-row detector coronary CT angiography in patients with high heart rates within a single cardiac cycle: A preliminary study

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AIM: To evaluate the image quality and diagnostic performance of coronary computed tomography angiography (CCTA) in patients with high heart rate within a single cardiac cycle using a 256-row detector CT system.

MATERIALS AND METHODS: Eighty-four consecutive symptomatic patients (mean age 60.4_9.1 years, 52 men) with suspected coronary artery disease and heart rate _75 beats/min undergoing CCTA and invasive coronary angiography (ICA) were enrolled retrospectively. Prospective electrocardiography (ECG)-triggered volume CCTA within a single cardiac cycle was performed using a 256-row, 16 cm detector CT system (Revolution CT, GE Healthcare) using automated tube voltage selection (kV Assist selecting 100 or 120 kV) and tube current modulation (Smart mA) techniques, with images reconstructed using 50% of adaptive statistical iterative reconstruction-V (ASiR-V). The image quality of coronary artery segments was evaluated by two reviewers using a four-point scale based on 18-segment model. The diagnostic accuracy of CCTA to detect _50% stenosis on ICA was analysed. The sensitivity, specificity, positive predictive value, and negative predictive value of CCTA to detect a _50% diameter stenosis on ICA were calculated from the chi-squared test of the contingency table on a per-segment, per-vessel, and per-patient basis.

RESULTS: The body mass index was 25.6_3.5 kg/m2; the HR was 82.8_7.9 beats/min, and the mean HR variability was 8.3_4.8 beats/min. All of the coronary artery segments, 98.9% (1044/1056) of coronary segments were rated as having diagnostic image quality. The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of CCTA, were 91.5%, 95.6%, 77.7%, and 98.5% on a per-segment basis; 95.2%, 93.5%, 87%, and 97.7% on a pervessel basis; 100%, 85.7%, 93.3%, and 100% on per-patient basis, respectively. The mean effective dose was 1.9_1 mSv.

Keywords: Heart rate, Coronary CT angiography, Diagnostic performance, Image quality, Invasive coronary angiography, Radiation dosage

Introduction

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in both developed countries and developing countries [1-3]. In the past decade, coronary computed tomography angiography (CCTA) has been established as an effective modality for the anatomical evaluation of CAD. As a noninvasive imaging modality, CCTA is an ideal tool for quantifying the degree of stenosis and for characterizing atherosclerotic plaques [4, 5]. One of the limitations of CCTA is the presence of motion-related artifacts due to inadequate temporal resolution, especially in patients with high heart rate (HR) [6, 7]. Although the HR of some patients can be reduced with use of β-blockers, 5-11% of patients have contraindications to β-blockers [8] or higher doses of β- blockers are needed with longer time to wait before the scan can be performed [9]. Attempts have been made to improve the image quality by reducing the gantry rotation time, utilizing dual source acquisition techniques, increasing detector row and using motion correction algorithm such as snapshot freeze (SSF) technique to reduce motion artifacts. Sheta et al [7] reported that SSF reduced the motion artifacts by 30% to 41% in comparison with standard algorithm in patient with low HR. Several studies reported high diagnostic accuracy of CCTA using a dual source CT (DSCT) [8, 10, 11] and 64-detector row CT with SSF [12, 13] in patients with high HR. However, the effective dose was higher than 3.4 mSv. In addition，the radiation-induced cancer associated with CCTA still remains a concern [12, 14].

The latest 256-row detector CT scanner with 160 mm cranial-caudal coverage, fast gantry rotation time of 280 ms with the use of SSF can permit acquisition of the whole heart within a single cardiac cycle, but also results in decreased radiation dose [15]. The diagnostic performance of this single cardiac cycle CCTA in patients with HR≥75 bpm using the 256-row detector CT has not been reported.

The aim of this study was to evaluate the diagnostic performance of CCTA for detection of significant stenosis in patients with HR≥75 bpm using a 256-row detector CT scanner. We hypothesize that CCTA can be performed within a single cardiac cycle even at high HR, and high diagnostic performance can be achieved at low radiation dose.

Materials and methods

Study population

Between October 2015 and May 2016, 560 consecutive patients with symptomatic suspected CAD with HR≥75 bpm undergoing CCTA were retrospectively enrolled in this study. Exclusion criteria for CCTA were contraindications to contrast agent, renal function (estimated glomerular filtration rate<60 ml/min), inability to sustain a 10 sec breath-hold and cardiac arrhythmias (arrhythmia, atrial fibrillation). Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) were excluded from this study group. Inclusion criteria were patients undergoing both CCTA and invasive coronary angiography (ICA) examinations within 4 weeks. In clinical practice, the ICA was determined by the referral doctors according to clinical data including CCTA results. A total of 124 patients underwent both CCTA and ICA. Forty patients were excluded from this study due to the following reasons; history of (CABG in 8 patients, 30 patients with PCI, and 2 patients with time interval between CCTA and ICA more than 4 weeks. Therefore, the final population consisted of 84 patients in this study. The study was approved by the institutional review board and written informed consent was obtained from all patients. Figure 1 is the flowchart showing patient recruitment.

CCTA scanning protocol

All patients were scanned using a 256-row detector CT system (Revolution CT, GE Healthcare, Milwaukee, WI). The system provides 160 mm detector, a gantry rotation speed of 280 ms with motion correction technology. Automatically selected tube voltage was set by kV assist and tube current by Smart-mA based on the scout image of the patients. Prospectively ECG-triggered CCTA with volume acquisition was performed within a single cardiac cycle. The data acquisition window was set at 35%-50% of the R-R interval when HR was 70-90 bpm, and 30%-60% of the R-R interval when HR higher than 90 bpm. Scanning parameters included 256×0.625 mm collimation, and scan coverage was 120 mm, 140 mm or 160 mm with a matrix size of 512×512 pixels and reconstruction slice thickness and slice interval of 0.625 mm. After placing an 18-gauge through an antecubital vein for all patients, contrast agent of 60~70 ml (370 mg iodine/ml, Ultravist, Bayer Schering Pharma, Berlin, Germany) was injected at 4~5 ml/s rate followed by 30~35 ml of normal saline with a dual-head power injector. Coronary artery calcium scoring was not performed prior to the contrast-enhanced studies.

CCTA image reconstruction and analysis

Images were reconstructed using 50% of adaptive statistical iterative reconstruction-v (ASIR-V, GE Healthcare, Milwaukee, WI) algorithm. The cardiac phase to evaluate was selected as the one with minimal coronary motion, and the SSF motion correction algorithm was applied whenever required to further minimize artifacts. SSF uses data from 3 neighboring phases of the same cardiac cycle, with the center phase being the prescribed phase of interest, to estimate and compensate for motion [13, 16]. For image quality analysis, datasets were transferred to a workstation with post-processing software (Advantage Workstation 4.6; GE Healthcare), with analysis performed with both standard formats (axial, multi-planar reformations [MPR], and curved multi-planar reformations [CPR]).The subjective image quality was independently assessed by two experienced radiologists (with 8 and 9years of experience in cardiac CT imaging, respectively) who were blind to ICA results. The 18-segment model of coronary artery tree was used according to the guidelines proposed by the Society of Cardiovascular Computed Tomography [17]. A four-point Likert scale was used to assess the image qualitatively: 1= excellent image quality free of artifacts; 2= good image quality with minor artifacts, but fully evaluable and diagnostic; 3= adequate image quality with moderate artifacts, but acceptable for diagnosis; 4= poor/severe artifacts and non-diagnostic image quality. All segments with 1.5 mm or greater in diameter were evaluated. Evaluable segments were assessed independently by the same two radiologists for the presence or absence of significant coronary artery lumen stenosis, defined as a diameter narrowing ≥50%. Stenosis was evaluated on a per-segment, per-vessel, and per-patient level. Any disagreements on the image scores and stenosis between two radiologists, consensus was reached during a joint reading session. Non-evaluable coronary artery segments were considered as positive findings for diagnostic purposes.

ICA protocol and image analysis

Two experienced interventionists (with 6 and 8 years of experience) who were unaware of the CCTA results analyzed the patients’ ICA images. For assessment of luminal narrowing of ≥50% diameter stenosis, at least two standardized projections of the right coronary artery (RCA) were acquired as well as 4 views of the left coronary artery, and additional views were used if necessary. The coronary angiogram was used as the reference standard for stenosis evaluation. Coronary artery stenosis was also evaluated on a per-segment, per-vessel, and per-patient level using the same standard as that for the CCTA. Any case of disagreements between the interventionists was resolved by discussion.

Radiation dose estimates of CCTA

The estimated parameters of the CT volume dose index (CTDIvol) and dose-length product (DLP) values were obtained from the CT console. Effective dose (ED) of CCTA was calculated with the following formula using a chest-specific conversion coefficient: DLP (mGy×cm)×0.014 (mSv×mGy^{-1}×cm^{-1}) for adults [18]. This value is averaged between male and female models.

Statistical analysis

All statistical analysis was performed using SPSS version 17.0 (SPSS, Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation (SD). Categorical variables were described by frequencies or percentage. The inter-observer agreement of image quality scoring and stenosis assessment was tested by Cohen's kappa. This was interpreted as moderate for $0.4 < \text{kappa} < 0.60$, good for $0.6 < \text{kappa} < 0.80$, and excellent for $\text{kappa} > 0.80$. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CCTA to detect a ≥50% diameter stenosis on ICA were calculated from the chi-squared test of the contingency table on a per-segment, per-vessel, and per-patient level. The area under the receiver–operating-characteristic curve (AUC) analyses was used to compare diagnostic performance. The 95% confidence intervals (95% CI) were also calculated for three level and three coronary arteries. All hypotheses were conducted using the significance level of $P < 0.05$.

Results

Study characteristics

In the present study, the mean age was 60.2±8.9 years (range: 34-77 years), 52 (61.9%) of patients were male. Mean HR during the scan was 82.8±7.9 bpm (range: 75~117 bpm). The median time between CCTA and ICA was 10 days (range 1~26 days). The DLP and ED was 141.8±70.5 mGy×cm and 1.9±1.0 mSv, respectively. Details of clinical characteristics are provided in Table 1. The CT scan parameters and radiation dose are listed in Table 2.

Subjective image quality assessment

A total of 1056 segments were included for evaluation in 84 patients. 98.9% (1044/1056) segments were rated as diagnostic (score 1~3). For all of the coronary segments, 71.4% (754/1056) had excellent image quality (score 1); 22.9% (242/1056) had good image quality (score 2); 4.5% (48/1056) had adequate image quality (score 3); and 1.1% (12/1056) were of non-diagnostic image quality (score 4). Inter-observer agreement for image quality was good for the CCTA image quality assessment, with kappa value of 0.78. Figures 2 and 3 are an example of CCTA examination in two patients with high HR, but with diagnostic image quality showing significant coronary stenosis.

Diagnostic performance of CCTA

In this trial population, there was a high prevalence of CAD (66.7% for ≥50% stenosis at ICA). 3-vessel disease was present in 12 (14.3%) patients, 2-vessel disease in 23 (27.4%) patients, single-vessel disease in 21 (25.0%) patients, and 10 (11.9%) patients had occluded coronary arteries. The diagnostic accuracy of CCTA on per-segment, per-vessel and per-patient level were 95.0%, 94.0% and 95.2% respectively. The diagnostic performance of CCTA for the detection of ≥50% stenosis on per-segment, per-vessel and per-patient level assessment is detailed in Table 3. CCTA overestimated stenosis in 4 patients, including 2 patients with significant coronary artery calcification and 2 patients due to motion artifacts (false positives). Of 336 coronary arteries, 100 (29.8%) were found to have at least one ≥50% stenosis at ICA. There were 15 false-positive and 5 false negative results at per-vessel assessment in CCTA. One hundred and thirty-nine of 1056 (13.2%) segments were noted to have at least ≥50% stenosis at ICA. There were 40 false positive and 13 false negative results at per-segment analysis as assessed at CCTA. Comparison of CCTA with ICA for a coronary stenosis ≥50% for the per-patient level evaluation demonstrated that the AUC was 0.93 (95% CI: 0.84~1.00) (Figure 4). The weighted kappa value for agreement between two independent readers in CCTA was 0.84 and in ICA was 0.93.

Only 4 left main arteries in this group of patients were detected with ≥50% stenosis by CCTA and ICA, and no significant difference was found between CCTA and ICA. We also investigated the CCTA on diagnostic performance of other three main coronary arteries. The findings showed the sensitivity and specificity of 97.8% and 84.2% on left anterior descending (LAD), 95.7% and 93.4% on left circumflex (LCX), 93.8% and 94.2% on RCA, respectively (Table 4). Extensive calcifications and motion artifacts were the main reason for false positive findings in small vessel such as the distal segment of LCX and first diagonal branch. The relative low specificity of 84.2% is due to the high false positive rate with 6 cases reported. The 6 false positive cases are due to extensive calcifications in 5 cases and motion artefact of the first diagonal branch on LAD in one case.

Radiation dose associated with CCTA

The value of CTDIvol and DLP for each scanning technique was shown on the CT console. The DLP and ED of the CCTA was 141.8±70.5 mGy/cm and 1.9±1.0 mSv in 84 patients, respectively (Table 2). Overall, the radiation dose was less than 1.0, 2.0, and 3.0 mSv in 22 (26.2%), 43 (51.2%), and 74 (88.1%) patients, respectively. The mean ED was 2.0 mSv in 15 patients with HR above 90 bpm, which was slight higher than the 1.9 mSv in 69 patients with HR below 90 bpm, because of the wider exposure window.

Discussion

The primary finding of this study is that CCTA using a 256-detector row CT within a single cardiac cycle allows coronary artery imaging with high diagnostic accuracy in patients with HR higher than 75 bpm and lower than 117 bpm, with radiation dose below 3.0 mSv in more than three fourths of the patients.

Impaired image quality due to high HR, and high radiation dose are still recognized as limitations to CCTA [2, 12, 19]. The non-proportional shortening of systole and diastole in patients with high HR is well known, with the length of diastole reducing more than that of systole [20]. Motion artifacts will occur when the motion velocity of the coronary artery in patients with high HR surpasses the temporal resolution of the modern CT scanner [21]. It may decrease the image quality of coronary artery in these patients. To achieve high diagnostic accuracy, high image quality is required. During the last decade, there have been some efforts to improve image quality on hardware such as broaden the detector and increase the gantry rotation speed or use dual source scanning. In addition, SSF is also used to increase the effective temporal resolution, which is motion correction algorithm using software. Authors have compared the diagnostic accuracy between CCTA and ICA in patients with high HR using a 64-slice CT with SSF technique. Andreini et al. [12] evaluated the diagnostic accuracy of CCTA with 98% on per-patient level in 64 patients. The mean HR was 74±8.2 bpm during the scan and the mean ED was 3.42±1.26 mSv. Leipsic et al. [13] also reported the diagnostic accuracy of CCTA with 86% of on per-patient level in 36 patients. The mean HR was 71.8±12.7 bpm, whereas, the ED was 13.2±1.8 mSv, which was relatively high due to the use of retrospectively ECG triggered scanning. The diagnostic accuracy was 95.2% on per-patient level and the ED was 1.9±1.0 mSv in 84 patients in our study, which is consistent with these reports in terms of diagnostic accuracy, but with much lower dose. A similar previous study by Koplay et al. [2] reported that the ED was 1.9±0.3 in 23 patients with HR 70-80 bpm, which was performed on a different scanner (dual source CT), however not all of patients underwent ICA. Li et al. [22] reported similar sensitivity and specificity of LAD, LCX, RCA when compared our study (Table 4), however, they used a 64-row detector CT scanner with SSF technique implemented in 46 patients with mean HR below 70 bpm.

Two studies [23, 24] showed that prospectively ECG-triggered CCTA in a single cardiac cycle can achieve high image quality and accuracy with low radiation dose using wide detector and single source CT scanner, but limited to patients with HR lower than 75 bpm. Detector of 160 mm in combination with gantry rotation speed of 0.28s/r on a latest 256-row detector CT also permits single cardiac cycle acquisitions [9]. In clinical practice, some patients may have contraindications to β-blockers and low HR cannot be achieved. In our study, we enrolled patients with HR≥75 bpm and the highest HR up to 117 bpm, who were performed in a single cardiac cycle using this latest CT scanner. SSF technique was used in most patients in this study (64 of 84 patients, 76.2%) to correct motion artifacts. However, the use of SSF was not directly associated with the HR and target phase, which was determined by the image quality of coronary artery. A recently published study reported similar findings to our results. Latif [9] et al analyzed 439 patients with different HR and body mass index (BMI) using a 256-detector row CT. Their results showed the feasibility of acquiring CCTA images with single cardiac cycle with good images quality. However, authors only assessed the image quality without addressing the diagnostic value of CCTA. Our study fills the gap in the literature by evaluating both image quality and diagnostic performance.

In addition, iterative reconstruction techniques have been reported recently to improve the image quality and reduce radiation dose and improve diagnostic accuracy to some extent [9, 25, 26]. In this study, ASIR-V 50% was used in all patients for image reconstruction; therefore, this could contribute to the high percentage of diagnostic image quality and low radiation dose in this patient group.

Radiation dose is directly related to the scan length, which is the DLP. Generally, scan range starts at the tracheal bifurcation and extends below the cardiac border by scout image [27]. In most cases of this study (80 of 84 patients, 95.2%), the entire heart could be scanned within a 140 mm. The mean ED of 1.9 mSv in this study is higher than that reported in some recent studies with mean ED less than 1.0mSv [28-30]. However, different modes of high-pitch with dual-source CT were used in those studies, also with inclusion of patients with different heart rates. Given the average high HR included in this study, we consider the ED of less than 2 mSv is within acceptable range for diagnostic purpose of CCTA, although further dose reduction would be desirable with more intensive use of dose-lowering techniques.

Our study has several limitations. First, the sample size is relatively small and it represents a clinically based cohort of patients undergoing CCTA and ICA examinations. Thus, the selected study cohort had high prevalence of significant CAD, and this may affect the diagnostic value of CCTA, in particular the specificity. Therefore, our results need to be interpreted with caution. Studies with inclusion of patients with low to intermediate likelihood of CAD but with high HR are needed to determine the diagnostic value of CCTA. Second, since the patients with low HR were not included in this study, we could not compare the diagnostic performance between the patients with different heart rates. Further, this was a single center cross-sectional study. Thus, our results need to be confirmed in a larger series of patients, preferably including patient populations from multiple institutions. Third, although ICA is the reference method for determination of stenotic lesions, it does not provide lesion-specific ischemic changes in the coronary artery. Quantitative angiographic analysis of fractional flow reserve determinations should be employed for either CCTA or ICA in future studies. Finally, we only conducted qualitative assessment of image quality, while quantitative analysis of image quality was not performed, as our focus is to determine the diagnostic value of CCTA in CAD in clinical practice.

In conclusion, our results show that CCTA using a 256-detector row CT with SSF technique can be performed in a single cardiac cycle with acquisition of images with high diagnostic value and low radiation dose in patient with high HR. This scan model will greatly widen the scope of its applications with patients who have contraindication to β-blockers.

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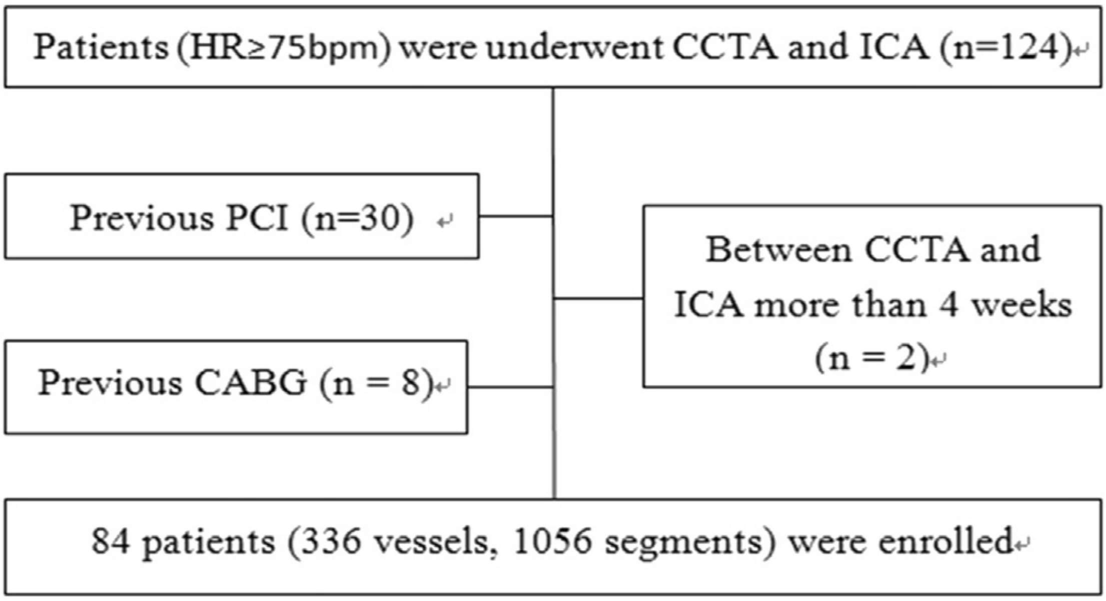

Figure 1. Flow chart shows recruitment of eligible patients in this study. HR, heart rate; CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

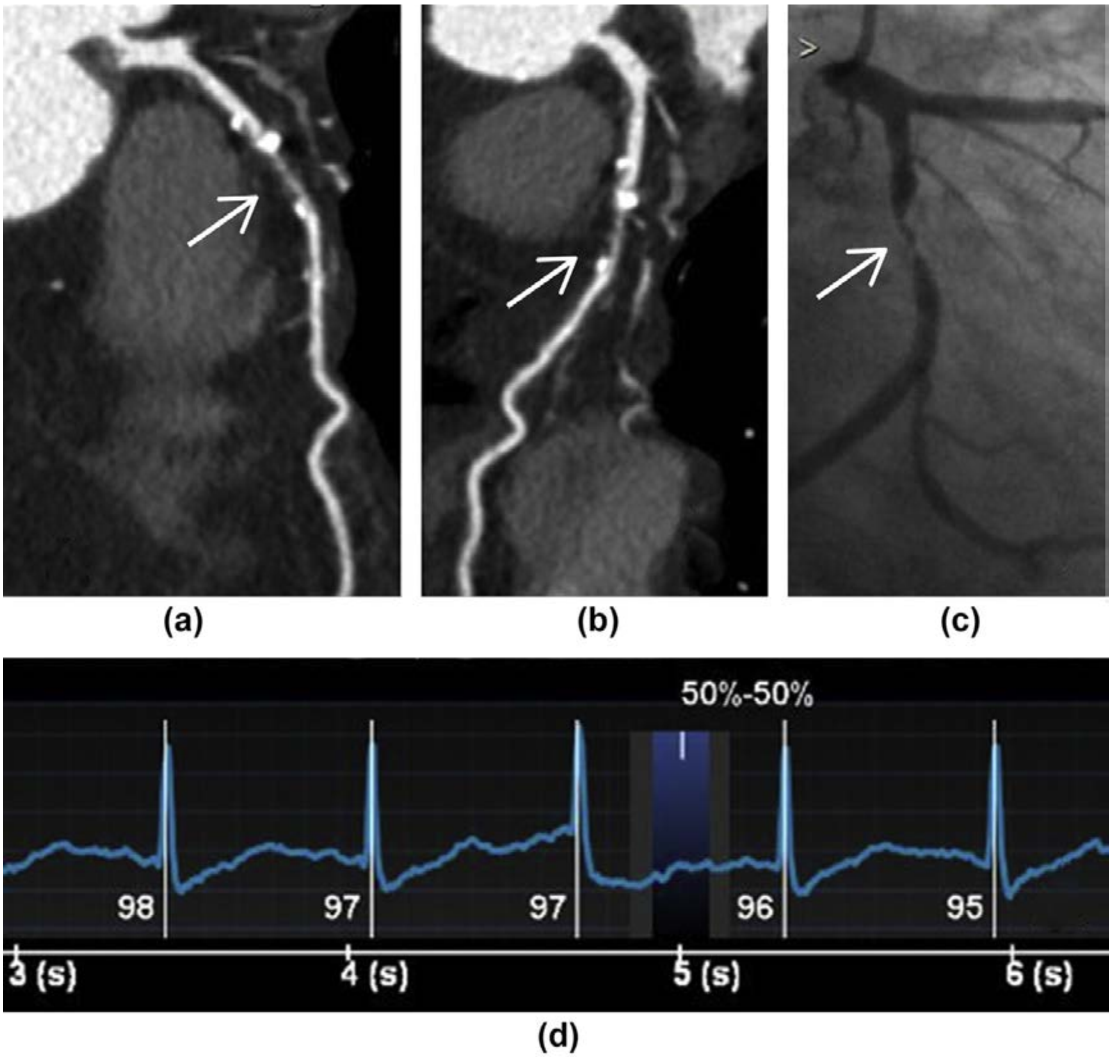

Figure 2 A 58-year-old woman with a BMI of 23.23 kg/m2 was examined. (a,b) Significant stenosis was identified in the mid-segment of LAD artery on curved reformation CT image (arrow), and (c) was confirmed by invasive coronary angiography (arrow). The HR was 90 beats/min during the scan and the reconstruction phase was 50% (d). The effective dose from CCTA was 2.0 mSv.

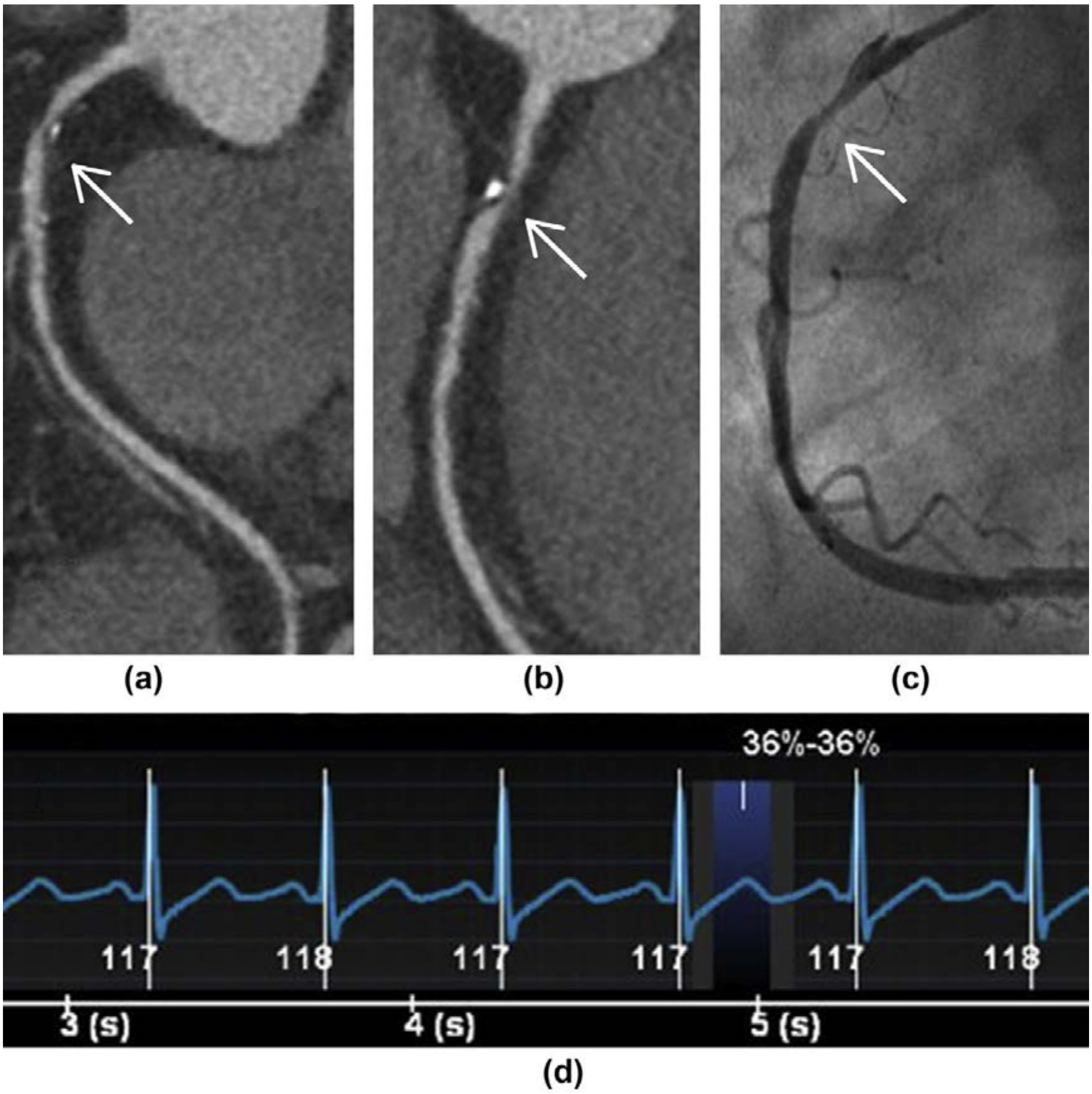

Figure 3 A 60-year-old man with a BMI of 24.34 kg/m$_2$ was examined using 100 kV and 499 mA. (a, b) Significant stenosis was identified in the proximal segment of RCA by CCTA (arrow). (c) The stenosis was confirmed by ICA (arrow). (d) The HR was 117 beats/min during the scan and the reconstruction phase was 36%. The effective dose was 1.81 mSv.

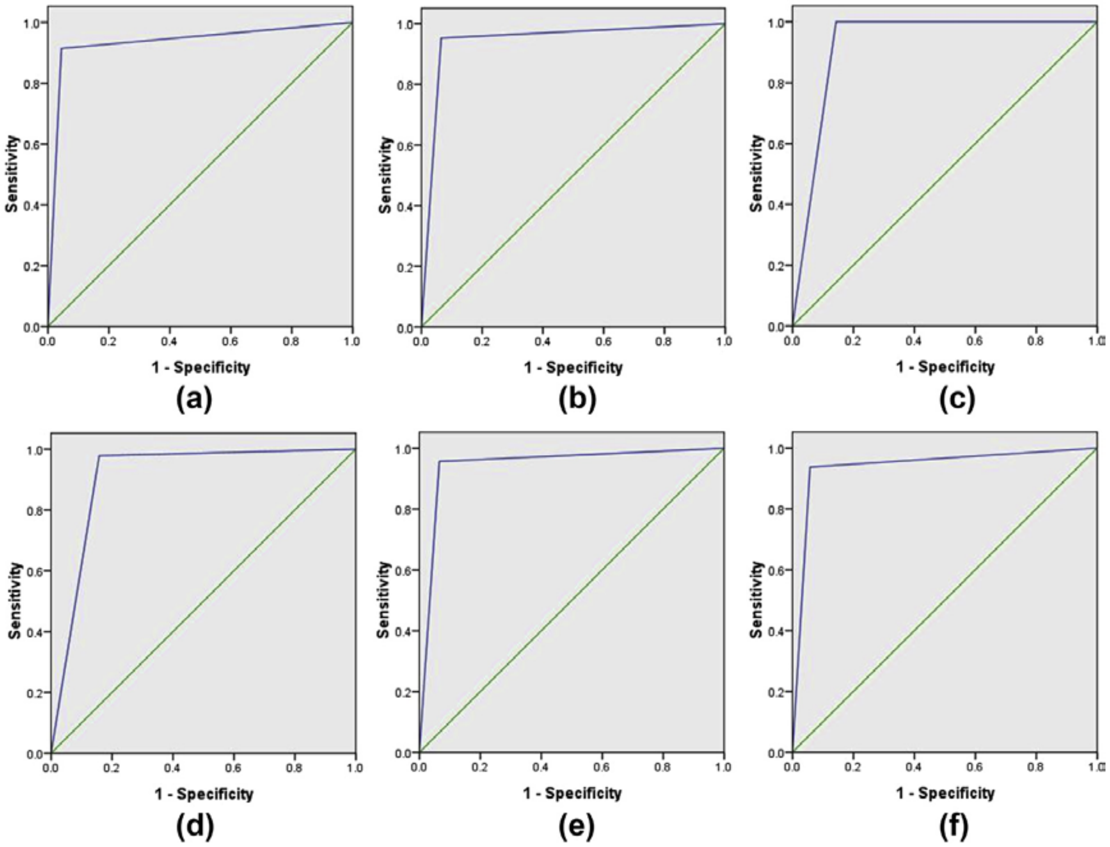

Figure 4 Receiver operating characteristic curves for detection of _50% stenosis on (a) per-segment, (b) per-vessel, (c) per-patient levels, and (d) LAD coronary artery, (e) LCX coronary artery, (f) RCA by artery analysis are demonstrated. The areas under curve were 0.94, 0.94, 0.93, 0.91, 0.95, and 0.94, respectively.

Table 1.

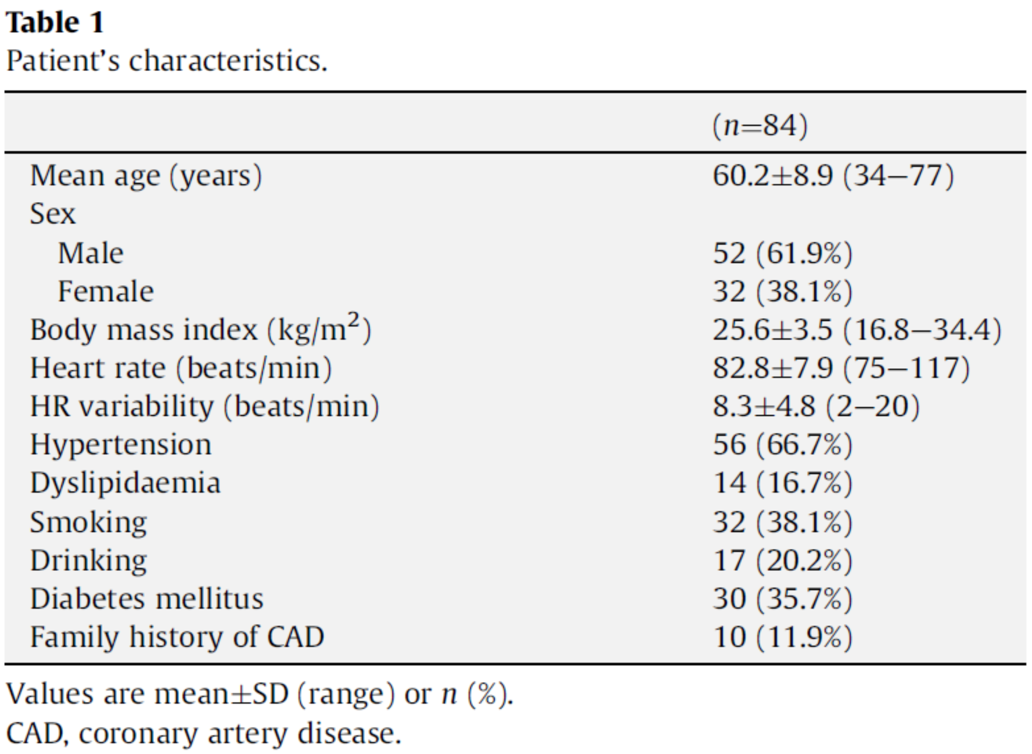

Table 1
Patient's characteristics.

	(n=84)
Mean age (years)	60.2±8.9 (34–77)
Sex	
Male	52 (61.9%)
Female	32 (38.1%)
Body mass index (kg/m^2)	25.6±3.5 (16.8–34.4)
Heart rate (beats/min)	82.8±7.9 (75–117)
HR variability (beats/min)	8.3±4.8 (2–20)
Hypertension	56 (66.7%)
Dyslipidaemia	14 (16.7%)
Smoking	32 (38.1%)
Drinking	17 (20.2%)
Diabetes mellitus	30 (35.7%)
Family history of CAD	10 (11.9%)

Values are mean±SD (range) or *n* (%).
CAD, coronary artery disease.

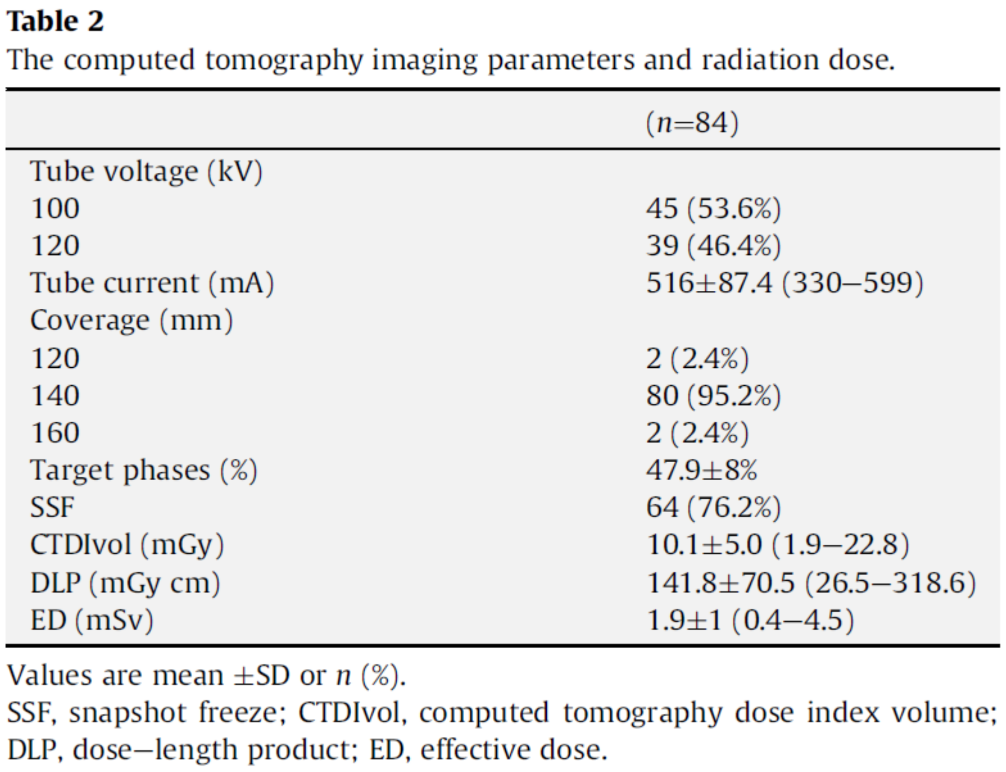

Table 2
The computed tomography imaging parameters and radiation dose.

	(n=84)
Tube voltage (kV)	
100	45 (53.6%)
120	39 (46.4%)
Tube current (mA)	516±87.4 (330–599)
Coverage (mm)	
120	2 (2.4%)
140	80 (95.2%)
160	2 (2.4%)
Target phases (%)	47.9±8%
SSF	64 (76.2%)
CTDIvol (mGy)	10.1±5.0 (1.9–22.8)
DLP (mGy cm)	141.8±70.5 (26.5–318.6)
ED (mSv)	1.9±1 (0.4–4.5)

Values are mean ±SD or *n* (%).
SSF, snapshot freeze; CTDIvol, computed tomography dose index volume; DLP, dose–length product; ED, effective dose.

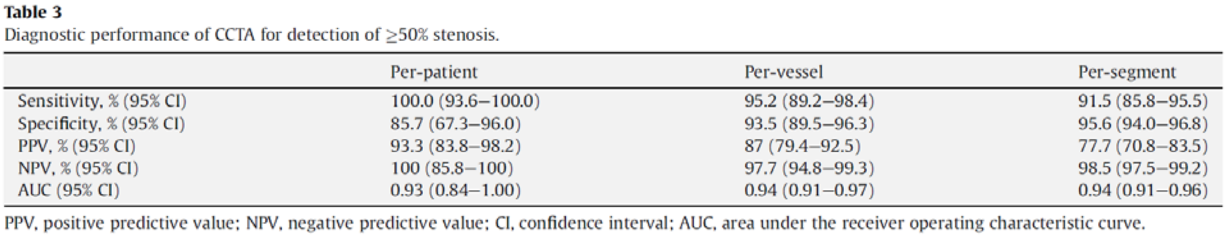

Table 3

Diagnostic performance of CCTA for detection of ≥50% stenosis.

	Per-patient	Per-vessel	Per-segment
Sensitivity, % (95% CI)	100.0 (93.6–100.0)	95.2 (89.2–98.4)	91.5 (85.8–95.5)
Specificity, % (95% CI)	85.7 (67.3–96.0)	93.5 (89.5–96.3)	95.6 (94.0–96.8)
PPV, % (95% CI)	93.3 (83.8–98.2)	87 (79.4–92.5)	77.7 (70.8–83.5)
NPV, % (95% CI)	100 (85.8–100)	97.7 (94.8–99.3)	98.5 (97.5–99.2)
AUC (95% CI)	0.93 (0.84–1.00)	0.94 (0.91–0.97)	0.94 (0.91–0.96)

PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; AUC, area under the receiver operating characteristic curve.

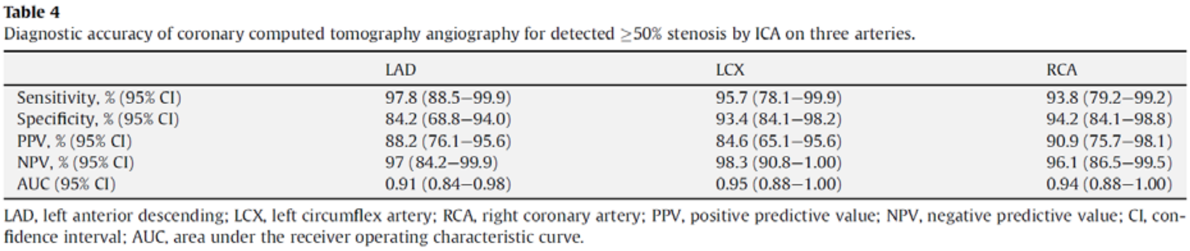

Table 4

Diagnostic accuracy of coronary computed tomography angiography for detected ≥50% stenosis by ICA on three arteries.

	LAD	LCX	RCA
Sensitivity, % (95% CI)	97.8 (88.5–99.9)	95.7 (78.1–99.9)	93.8 (79.2–99.2)
Specificity, % (95% CI)	84.2 (68.8–94.0)	93.4 (84.1–98.2)	94.2 (84.1–98.8)
PPV, % (95% CI)	88.2 (76.1–95.6)	84.6 (65.1–95.6)	90.9 (75.7–98.1)
NPV, % (95% CI)	97 (84.2–99.9)	98.3 (90.8–1.00)	96.1 (86.5–99.5)
AUC (95% CI)	0.91 (0.84–0.98)	0.95 (0.88–1.00)	0.94 (0.88–1.00)

LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; AUC, area under the receiver operating characteristic curve.