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Diagnostic accuracy of dual-source coronary computed tomography angiography for detecting coronary artery stenosis without heart rate control comparison with invasive coronary angiography

Dokładność diagnostyczna angiografii dwuźródłowej tomografii komputerowej w wykrywaniu zwężeń tętnic wieńcowych bez kontroli rytmu serca w porównaniu z angiografią wieńcową przeprowadzoną metodą inwazyjną

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Abstract

Introduction. The aim of this study was to assess the diagnostic accuracy of dual-source coronary computed tomography angiography (coronary CTA) for evaluation of coronary artery disease (CAD) in daily practice without heart rate control in comparison with invasive coronary angiography (ICA).

Material and methods. Forty-five consecutive patients underwent both coronary CTA and invasive coronary angiography (ICA). The mean time span between coronary CTA and ICA was 3 ± 13 days. No beta-blockers were administered prior to the scan. All coronary CTA scans were evaluated for the presence of obstructive coronary stenosis by a blinded expert, and the results were compared with ICA.

Results. Coronary CTA with diagnostic image quality in 44 of the overall 45 patients. Two vessels and three segments were non diagnostic on coronary CTA. Therefore, 132 vessels and 608 segments from 45 patients were analysed. In six of seven patients with atrial fibrillation and in all 23 patients with heart rates (HR) > 65 beat per minute, image quality was diagnostic. Mean body mass index was 23.1 ± 6 kg/m^2 (range 15–35 kg/m^2), mean heart rate during DSCT-CA was 70.3 ± 14.2 bpm (range 47–102 bpm), and mean Agatston score was 46 ± 22 (range 0–928). Overall sensitivity, specificity, positive and negative predictive value for evaluating CAD for detect > 50% luminal narrowing were 86.4%, 96.2%, 76%, and 95.6%, respectively, by segment. Moreover, accuracy for detecting > 70% luminal narrowing was excellent by patient, vessel, and segment. The accuracy to detect patients with coronary stenoses > 50% was not significantly different among patients with HR > 65 bpm and < 65 bpm.

Conclusions. Coronary CTA performed by dual-source scanner provides high diagnostic accuracy on per-segment, -vessel and -patient analyses, independent of the HR.

Key words: dual-source computed tomography, coronary computed tomography angiography, heart rate

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Introduction

Recent advances in multi-detector-row computed tomography (MDCT) technology have continuously improved the quality of non-invasive coronary artery imaging. As a result, various studies have demonstrated high accuracy of coronary angiography with 64-slice CT for the diagnosis of coronary artery disease (CAD) [1–3]. In particular, the high negative predictive value has made non-invasive coronary angiography using 64-slice CT a modality that allows significant coronary stenoses to be reliably excluded [1–3]. Consequently, the Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology has recently recommended in their guidelines, that CT coronary angiography should be performed in patients with stable angina, who have a low pre-test probability of CAD, and an inconclusive exercise electrocardiogram (ECG) or stress imaging test [4, 5]. Because of restricted temporal resolution, the clinical utility of MDCT is limited by the frequent occurrence of motion artefacts in patients with HR above 65–70 bpm [6]. Consequently, a negative chronotropic pretreatment is recommended, sometimes complicating the patient management. Because of the high negative predictive value (NPV), MDCT is gaining acceptance as a tool to preclude coronary stenoses [5]. Either intravenous or oral beta-blocker medication for heart rate control has been proposed even for 64-slice CT systems. In most studies, target heart rates for scanning were below 60–65 beats per minute (bpm) [1–3, 6]. The recently introduced dual-source CT (DSCT) scanner is characterised by two X-ray tubes and two corresponding detectors mounted onto the rotating gantry with an angular offset of 90° [7]. Regarding cardiac imaging capabilities, the new scanner system offers a high temporal resolution of 83 ms in a mono-segment reconstruction mode. Temporal resolution is independent of the heart rate, which is a major difference from single-source CT systems that rely on multi-segment reconstruction techniques. The first feasibility studies have shown promising results with coronary computed tomography angiography (coronary CTA) regarding image quality of coronary arteries, cardiac valves, and left ventricular myocardium, independent of the actual heart rate of the patient [8]. The purpose of our study was to determine the efficiency of coronary computed tomography angiography performed by dual-source scanner in diagnosing significant stenoses in comparison to invasive coronary angiography (ICA) without heart rate control.

Materials and methods

Patients

This retrospective study included 45 patients who underwent both invasive coronary angiography (ICA) and coronary computed tomography angiography (coronary CTA) by dual-source scanner, between February, 2012 and September, 2013. The indications for coronary CTA were an abnormal, equivocal or non-diagnostic stress test, atypical chest pain, patients awaiting valvular surgery to detect or exclude associated coronary stenoses, as well as the evaluation of cardiac aetiology of syncope. The above are considered appropriate indications for coronary CT angiography, based on the criteria of the American College of Cardiology (ACC) and the recent American Heart Association Scientific Statement on Cardiac CT [5]. Exclusion criteria for coronary CTA included pregnancy, renal failure, and a history of allergic reaction to iodine-containing contrast agents. The present study was approved by the Ethics Committee of the Faculty of Medicine and informed consent was obtained from all the patients.

Coronary computed tomography angiography protocol

Coronary CTA examinations were performed on a dual-source CT scanner (Definition FLASH, Siemens Healthcare, Forchheim, Germany). The system is equipped with two X-ray tubes and two corresponding detectors mounted on a single gantry with an angular offset of 90° [9]. The coronary CTA was using automatic tube current modulation in x, y, z directions (Care Dose 4D, Siemens Healthcare). The scanner technology enables a prospectively ECG-triggered high-pitch (3.4) spiral acquisition (FLASH Spiral Cardio, Siemens Healthcare, Forchheim, Germany). The coronary CTA scan parameters were as follows: number of X-ray sources = 2, detector collimation 32 × 0.6 mm with double sampling by rapid alteration of the focal spot in the longitudinal direction (Z-flying focal spot) [9], rotation time 330 ms, tube voltage 120 kV. Image acquisition was performed during inspiratory breath-hold. To familiarise the patient with the protocol, breath-holding was practiced before the examination. A contrast agent bolus of 50–80 mL was injected with a mean flow rate of 5 mL/s, followed by a 50 ml saline flush. Circulation time from the antecubital fossa to the aortic root was determined in each patient with administration of a timed bolus of 20 mL of iodinated contrast. The entire volume of the heart was covered during one breath-hold in approximately five seconds with simultaneous recording of the ECG trace. The patients were scanned in the supine position twice, firstly without contrast medium to calculate the calcium score, and secondly after contrast medium injection. Studies were acquired in the cranio-caudal direction from the level of the carina to just below the diaphragm. Irrespective of the individual heart rate and the heart rate variability, no beta-blockers were given prior to the scan.

Coronary computed tomography angiography image reconstruction

A retrospective gating technique was used to synchronise the data reconstruction with the ECG signal. In the first step all reconstructed data sets were evaluated at different ECG-phases for diagnostic image quality and the optimal data set was then chosen for the analysis.

In case of irregular heart rates, the temporal variability in the reconstruction phase was compensated by manual ECG editing. In case of premature heart beats, the temporal window past the premature heart beat was deleted, and the next diastolic window was filled with one to three temporal windows to avoid the data gaps. All ECG editing was performed by one experienced cardiovascular radiologist. All reconstructed images were transferred to a dedicated workstation (Wizard, Siemens Medical Solutions) equipped with dedicated cardiac post-processing software (Syngo Circulation, Siemens Medical Solutions).

Coronary computed tomography angiography data analysis

The mean Agatston score was calculated for each patient from the non-enhanced coronary CTA data with a detection threshold of 130 HU by using semi-automated software (Syngo Calcium Scoring, Siemens Medical Solutions). For analysis of coronary CTA data, coronary arteries were segmented according to the guidelines of the American Heart Association [10]. All reconstructed images were evaluated and classified by two independent readers using axial source images, multi-planar reformations (MPR), and thin-slab maximum intensity projections (MIP) on a per--segment basis. After visually identifying coronary stenoses, a computerised quantitative analysis on the basis of a density-based lumen edge detection algorithm was done. For this purpose, luminal diameters in disease-free proximal and distal reference segments, that were marked by the investigator, were automatically determined and were set into relation to the minimal diameter measured within the stenosis. This approach corresponds to the method used for quantitative coronary angiography (QCA). In the case of vessel calcification, the automatised contour detection was manually edited, in order to exclude calcifications from the lumen contour. The analysis, as well as the manual editing, was based on curved multiplanar reconstructions and cross-sections of the vessel perpendicular to the centreline. Each coronary segment was judged as non-stenosed (no stenosis, < 50%), intermediate stenosis (50–69% diameter reduction), or significant stenosis (≥ 70% diameter reduction). For any disagreement in data analysis, consensus agreement was achieved.

Invasive coronary angiography

The ICA was performed according to standard techniques, and multiple views were stored on a CD-ROM. The angiograms were evaluated by one experienced observer, who was blinded to the results of the coronary CTA. Coronary artery segments were defined according to the same guidelines mentioned above. Each vessel segment was scored as being significantly stenosed, defined as a diameter reduction of > 50% or not. Coronary artery analysis was performed in all vessels with a luminal diameter of at least 1.5 mm, excluding those vessels distal to complete occlusions.

Statistical analysis

Statistical analysis was performed using commercially available software (SPSS 12.0, SPSS, Chicago, IL, USA). Quantitative variables were expressed as mean ± SD and categorical variables as frequencies or percentages. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated from chi-squared tests of contingency, and the 95% confidence intervals (CI) were calculated from binomial expression on a per-segment basis. Because of the interdependencies between different segments, the statistics were also calculated on a per-patient basis (presence of at least one significant coronary artery stenosis or absence of any significant stenosis in each patient). The ICA was considered the standard of reference.

Results

Patient clinical characteristics are presented in Table 1. Forty-five patients (25 men, 20 women; mean age, 55 ± 10 years; range, 25–81 years) were included in this study over a period of 12 months. The mean time interval between coronary CTA and ICA was 3 ± 13 days (range, 0–25 days) and there were no clinical events between the two studies in any patient. The distribution of calcium score of all patients is shown in Table 2.

Coronary CTA revealed ten stenoses ≥ 70% (Figure 1), nine were correctly identified and one was underestimated compared with ICA. Of twelve stenoses with diameter reduction 50 to 69%, eight were correctly classified,

Table 1. Patient characteristics (N = 45)

Characteristic	Value
Age [years], mean ± SD [range]	55 ± 10 (25–81)
Men	25 (55%)
Height [cm], mean ± SD	161.8 ± 13
Weight [kg], mean ± SD	59.8 ± 12
Body mass index [kg/m^2], mean ± SD [range]	23.1 ± 6 (15–35)
Diabetes mellitus	11 (24%)
Hypertension*	21 (46%)
Hypercholesterolaemia**	29 (64%)
Current smoker	11 (24%)
Obesity***	2 (4%)

*Blood pressure > 140/90 mm Hg or treatment for hypertension; **total cholesterol > 180 mg/dL or treatment for hypercholesterolaemia; ***body mass index > 30 kg/m^2

Table 2. Distribution of Agaston calcium score

Total calcium score	N = 45 (%)
0	9 (20)
1–100	10 (22)
101–200	13 (29)
201–300	8 (18)
301–400	3 (7)
> 400	2 (4)

three were overestimated (Figure 2), and one was underestimated by coronary CTA. In 582 of 608 segments, with more than 50% diameter reduction, coronary artery disease was correctly precluded (Tables 3 and 4). In eight of coronary segments where coronary CTA overestimation percentage of stenosis were due to extensive calcification and poor filling due to proximal stenosis or total occlusion. The average HR during scanning was 70.3 ± 14.2 bpm (range 47–102 bpm). Twenty two patients (48.9%) had a heart rate below 65 bpm (mean 59.7 ± 5.9 bpm, range 47–65 bpm), while 23 patients (51.1%) had a heart rate of ≥ 65 bpm or atrial fibrillation (mean 84.2 ± 8.4 bpm, range 72–102 bpm). Accuracy values for the detection of stenoses were not significantly different among the patients with HR > 65 bpm and < 65 bpm as indicated by overlapping confidence intervals and the rate of false ratings was comparable. The data expressing diagnostic accuracy are given in Table 3 and 4.

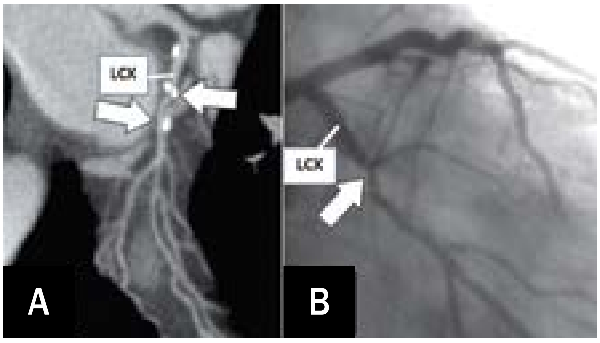

Figure 2A, B. False positive at left circumflex artery (LCX). CCTA curved multiplanar reformation image of the LCX (**A**) showed calcified plaque at proximal LCX (arrows), which identified significant lumen narrowing. Conventional coronary angiogram (**B**) did not identify significant lumen narrowing (arrow)

Discussion

Four main conclusions can be drawn from this study. First, coronary CTA provides a high diagnostic accuracy for the evaluation of coronary artery disease (CAD). Second, this high diagnostic performance of coronary CTA performed by dual-source scanner could be achieved in a patient population with non-zero calcifications and in whom no heart rate (HR) control using beta-blocker medication prior to coronary CTA was performed. Third, false ratings were primarily due to severe vessel wall calcifications rather than motion artefacts. Temporal resolution better

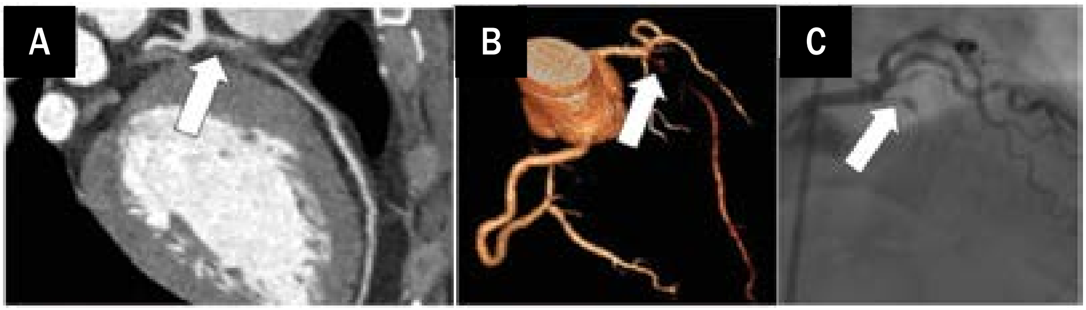

Figure 1A–C. Sample case in individual with stenosed coronary artery: matched positive readings. CCTA curved multiplanar reformation image of the left anterior descending artery (LAD) (**A**) and volume rendering technique image (**B**) showed soft plaque at proximal LAD (arrow) causing significant stenosis (> 70% diameter reduction). Conventional coronary angiogram (**C**) shows significant proximal LAD stenosis

Table 3. Diagnostic accuracy of dual-source computed tomography coronary angiography (DSCT-CA) compared with invasive coronary angiography regarding stenosis severity on a segmental basis

		Invasive coronary angiography		
DSCT-CA	Diameter reduction [%]	< 50%	50–69%	≥ 70%
	< 50	582	1	0
	50–69	3	8	1
	≥ 70	2	3	9

Table 4. Segment-based diagnostic accuracy of diagnostic accuracy of dual-source computed tomography coronary angiography (DSCT-CA) to detect coronary artery stenosis

Diameter reduction	Sensitivity	Specificity	PPV	NPV
All patients (N = 45)				
50–69%	10/12 (83%, 62–99)	582/605 (96%, 95–98)	10/15 (96%, 44–92)	580/582 (99%, 91–100)
≥ 70%	9/10 (90%, 66–99)	604/608 (99%, 89–99)	9/10 (90%, 52–94)	604/608 (93%, 90–98)
> 50%	19/22 (86%, 76–99)	582/605 (96%, 80–95)	19/25 (76%, 58–89)	582/609 (96%, 91–99)
HR > 65 bpm and/or atrial fibrillation (N = 23)				
All > 50%	10/12 (83%, 61–99)	304/306 (99%, 72–99)	10/13 (77%, 45–92)	304/305 (99%, 83–99)
HR < 65 bpm (N = 22)				
All > 50%	9/10 (90%, 66–99)	278/299 (93%, 75–99)	9/12 (75%, 42–94)	278/304 (91%, 87–99)

Data are absolute values used to calculate percentages. Data in parentheses are percentages with 95% confidence intervals; NPV — negative predictive value; PPV — positive predictive value; HR — heart rate

than 100 ms in combination with submillimetre isotropic spatial resolution and examination times no longer than ten seconds are considered prerequisites for successful implementation of coronary CTA into routine clinical algorithms [7]. Dual-source scanners with 0.33-s gantry rotation time and 32 × 0.6 mm collimation in combination with double z-sampling (*i.e.*, simultaneous acquisition of 64 overlapping 0.6-mm slices) fulfil these requirements. Early feasibility studies confirmed the technical capacity of dual-source scanners to provide diagnostic image quality of coronary arteries in patients with high heart rates [9, 11]. In contrast to earlier studies using multidetector-row computed tomography systems with lower temporal resolution [1–3], dual-source technology has demonstrated sufficient clinical robustness even in the presence of arrhythmias and without the usage of negative chronotropic pretreatment in higher heart rate. One important finding of the present study was the fact, that dual-source scanners allows to assess the coronary status in patients with HR exceeding 65 bpm with the same diagnostic accuracy as in lower HR. This fact is a major progress concerning the clinical utility of coronary CTA, because with the current single source CT systems, pharmaceutical HR control or multisegment reconstruction algorithms have to be applied to avoid motion artefacts. Both of these options are affected by several problems [1–3, 12]. Beta-blocker therapy is not effective or is contraindicated in up to 20% of patients [1, 13]. Multisegment reconstruction algorithms that use data of up to four consecutive heart beats offer optimal temporal resolution only in a small HR range. Therefore, even small variations of the HR lead to non-uniform temporal resolution during the scan. Consequently, this approach is prone to artefacts [1–3]. In the present study, we have demonstrated that with constant temporal resolution of 82.5 ms, coronary CTA performed by dual-source scanner can generate artefact-free images independently of the HR. However, post-processing of data acquired at higher HR or atrial fibrillation is more demanding, because different reconstructions for different coronary vessels have to be done. This study is, to the best of our knowledge, the first to demonstrate a high diagnostic accuracy of coronary CTA performed by dual-source scanner for the diagnosis of CAD without heart rate control during scanning in comparison to ICA in Thailand. The results of our study underscore the potential of coronary CTA as a gate keeper diagnostic tool to diagnosis of patients, who suspected coronary artery stenoses. This imaging modality allows to assign patients quickly to different clinical pathways. Patients with significant disease (at least one stenosis > 70%) may be directed to catheter-based intervention, as these high-grade lesions reveal haemodynamic relevance in over 85% of cases. If coronary CTA identifies one or multiple intermediate lesions (50–69%), a stress test to assess the functional relevance (nuclear tests, stress echocardiography, MRI) of these specified lesions should be recommended prior to an invasive procedure and a revascularisation procedure will then only follow if there is evidence for ischaemia. The major strength of the technique is its very high NPV allowing to accurately exclude coronary stenoses. By translating such an algorithm to our study, coronary CTA performed by dual-source scanner allowed to either exclude significant CAD (> 50% stenosis) or to determine severe CAD (> 70% stenosis) with a highly probable need for revascularisation in 72 out of 88 patients without additional testing. Only three patients would have unnecessarily been sent to invasive angiography, in 12 patients additional functional testing would have been recommended, and only one patient with an intermediate lesion would have been missed by coronary CTA.

We acknowledge the following study limitations. First, we included a relatively small group of only 45 patients. Certainly, future studies with larger patient populations are needed to confirm our first experience in Thailand. Second, we did not apply the multisegment reconstruction mode, which possibly may further improve the image quality at elevated heart rates. Third, coronary CTA is associated with substantial irradiation to the patient. However, using the dual-source scanner system allowed the variable use of ECG-pulsing for dose saving purposes in all of our patients [14]. In the protocol applied in this study, the ECG-pulsing window width was chosen according to the mean heart rate during scanning, *i.e.*, a relatively narrow window width at low and a larger window width at higher heart rates.

Finally, the ability to use the two X-ray tubes simultaneously with different voltages to improve plaque composition characterisation [15] and thus potentially to improve the accuracy of stenosis detection has not been investigated.

Conclusion

The present study indicates that coronary CTA performed by dual-source scanner provides high diagnostic accuracy for assessment of CAD without heart rate control. Further studies are needed to confirm our results in appropriate clinical settings with larger patient populations.

What is already known on this topic? Coronary CTA results in good image quality and few non-evaluable coronary artery segments.

What this study adds? This is the first study in Thailand demonstrating a high diagnostic accuracy of coronary CTA performed by dual-source scanner for the diagnosis of CAD without heart rate control during scanning in comparison to ICA. The results of our study underscore the potential of coronary CTA as a gate keeper diagnostic tool to diagnosis of patients who suspected coronary artery stenoses.

Conflict of interest(s)

None.

Streszczenie

Wstęp. Badanie przeprowadzono w celu oceny dokładności angiografii tętnic wieńcowych wykonanej metodą dwuźródłowej tomografii komputerowej (DSCT-CA) w diagnostyce choroby wieńcowej (CAD) w warunkach rzeczywistej praktyki u chorych niestosujących leczenia kontrolującego rytm serca w porównaniu z angiografią wieńcową wykonaną metodą inwazyjną (ICA).

Materiał i metody. U 45 kolejnych pacjentów wykonano angiografię tomografii komputerowej (CTA) tętnic wieńcowych oraz ICA. Średni odstęp czasowy między badaniami wynosił 3 ± 13 dni. Przed badaniem chorzy nie przyjmowali beta-adrenolityków. Wszystkie skany uzyskane w badaniu CTA były oceniane pod kątem obecności istotnych zwężeń w tętnicach wieńcowych przez specjalistę nieznającego danych pacjenta, a następnie porównywano wynik z rezultatem badania ICA.

Wyniki. Diagnostyczną jakość w badaniu CTA tętnic wieńcowych uzyskano u 44 z 45 chorych. Dwa naczynia i 3 segmenty na obrazie CTA tętnic wieńcowych uznano za niediagnostyczne. Ostatecznie do analizy włączono 132 naczynia i 608 segmentów zobrazowanych u 45 chorych. Jakość obrazów była diagnostyczna u 6 spośród 7 chorych z migotaniem przedsionków i u wszystkich 23 chorych z częstotliwością rytmu serca (HR) wynoszącą ponad 65/min. Średni wskaźnik masy ciała wynosił 23,1 ± 6 kg/m^2 (zakres 15–35 kg/m^2), średnia częstotliwość HR w trakcie badania DSCT-CA wynosiła 70,3 ± 14,2/min (zakres 47–102), a średni wskaźnik w skali Agatstona — 46 ± 22 (zakres 0–928). Ogólnie czułość i swoistość oraz dodatnia i ujemna wartość predykcyjna w ocenie CAD w wykrywaniu ponad 50-procentowego zwężenia segmentów tętnicy wieńcowej wynosiły odpowiednio 86,4%, 96,2%, 76% i 95,6%. Ponadto stwierdzono wysoką dokładność w wykrywaniu ponad 70-procentowych zwężeń w odniesieniu do pacjentów, naczyń i segmentów. Dokładność w wykrywaniu pacjentów ze zwężeniami tętnic powyżej 50% nie różniła się istotnie między osobami z HR ponad 65/min a osobami, u których HR wynosiła mniej niż 65/min.

Wnioski. Badanie CTA tętnic wieńcowych przeprowadzone za pomocą aparatu dwuźródłowego zapewnia wysoką dokładność diagnostyczną w wykrywaniu zwężeń w odniesieniu do segmentów, naczyń wieńcowych i pacjentów, niezależnie od HR.

Słowa kluczowe: dwuźródłowa tomografia komputerowa, angiografia wieńcowa tomografii komputerowej, częstotliwość rytmu serca

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