



Original Article

## Diagnostic performance of 128-slice computed tomography angiography in patients with suspected coronary artery disease



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### المخلص

**أهداف البحث:** لتحديد الأداء التشخيصي والعوامل المؤثرة في التصوير الوعائي المقطعي المحوسب للشريان التاجي المكون من 128 شريحة مقارنة بتصوير الأوعية التاجية المجتاحة في مرضى الشريان التاجي.

**طريقة البحث:** سجلت دراسة تحليلية مقطعية 139 مريضاً يشتبه في إصابتهم بمرض الشريان التاجي والذين خضعوا لـ 128 شريحة للتصوير المقطعي المحوسب للأوعية وكذلك تصوير الأوعية التاجية المجتاحة.

**النتائج:** أظهر النموذج المعتمد على المريض حساسية عالية بنسبة 93.2% وقيمة تنبؤية إيجابية بنسبة 95.3% للتضيق  $\leq 50\%$ . ومع ذلك، كانت هذه القيم أقل عند تحليلها من خلال النماذج المستندة إلى الشرايين (حساسية عالية بنسبة 85.6% وقيمة تنبؤية إيجابية بنسبة 81.1%) والقطاعات (حساسية عالية بنسبة 73.9% وقيمة تنبؤية إيجابية بنسبة 66.6%). كانت الخصوصية والقيمة التنبؤية السلبية هي الأعلى في النموذج المعتمد على القطعة، وانخفضت في النماذج المستندة إلى الأوعية والمرضى بنسبة 96.4% و 95.4%؛ و 90.5% و 90.0%؛ و 36.4% و 42.1% على التوالي (للتضيق  $\leq 70\%$ ). انخفضت جميع القيم التشخيصية عندما كانت درجة الكالسيوم 400 وحدة أغاتستون.

**الاستنتاجات:** يظهر التصوير الوعائي المقطعي المحوسب للشريان التاجي المكون من 128 شريحة الطريقة المثلى وذات الحد الأدنى من الاجتياح وعالي

الأداء لتشخيص تضيق وتشكل آفات الشريان التاجي. كان الأداء التشخيصي لتصوير الأوعية المقطعي المحوسب للشريان التاجي المكون من 128 شريحة مرتفعاً جداً. لم يؤثر معدل ضربات القلب ومؤشر كتلة الجسم على دقة التشخيص، بينما تم العثور على درجة الكالسيوم البالغة 400 وحدة أغاتستون كعامل يتسبب في انخفاض الأداء التشخيصي.

**الكلمات المفتاحية:** تصوير الأوعية التاجية المقطعي المحوسب؛ مرض الشريان التاجي؛ تصوير الأوعية التاجية المجتاحة؛ الأداء التشخيصي

### Abstract

**Objectives:** To determine the diagnostic performance and influencing factors of 128-slice coronary computed tomography angiography (CCTA) compared with invasive coronary angiography (ICA) in patients with suspected coronary artery disease (CAD).

**Methods:** A cross-sectional analysis study enrolled 139 patients suspected of having CAD, who underwent and received a 128-slice CCTA and ICA.

**Results:** The patient-based model showed high sensitivity and a positive predictive value of 93.2% and 95.3%, respectively (for stenosis  $\geq 50\%$ ). However, these values were lower when analyzed using vessel-based (85.6% and 81.1%) and segment-based (73.9% and 66.6%) models. Specificity and negative predictive value were highest in the segment-based model, decreasing in vessel- and patient-based models at 96.4% and 95.4%, 90.5% and 90.0%, and 36.4% and 42.1%, respectively (for stenosis  $\geq 70\%$ ). All diagnostic values were reduced when the calcium score was  $\geq 400$  Agatston units.

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**Conclusion:** 128-slice CCTA is an optimal, minimally invasive, and high-performance method to diagnose the stenosis and morphology of coronary artery lesions. The diagnostic performance of 128-slice CCTA is very high. Heart rate and body mass index do not affect diagnostic accuracy, whereas a calcium score  $\geq 400$  Agatston units is a factor that causes a decrease in diagnostic performance.

**Keywords:** Coronary artery disease; Coronary computed tomography angiography; Diagnostic performance; Invasive coronary angiography

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## Introduction

Coronary artery disease (CAD) is the most common form of cardiovascular disease (CVD). According to the 2022 American Heart Association (AHA) Annual Report, the prevalence of CAD was 7.2%, causing 382,820 deaths in 2020.<sup>1</sup> The pathology has a long period of stability but will become unstable at any time due to plaque rupture and thrombosis,<sup>2</sup> causing acute and potentially fatal events. The most common CVD event is myocardial infarction, with 805,000 cases annually, of which 20% are silent.<sup>1</sup> Because of the dynamic course of CAD and the complex pathophysiological mechanisms, early detection of severe coronary stenosis is essential to select the appropriate treatment for each individual.

The advent of coronary computed tomography angiography (CCTA) was considered a solution for the early detection of coronary artery lesions. 128-sequence CCTA allows the assessment of coronary stenosis at five levels, in which stenosis  $\geq 50\%$  of the lumen diameter is defined as significant stenosis. The ACCURACY prospective multicenter trial compared 64-slice CCTA with invasive coronary angiography (ICA) in 230 patients with chest pain<sup>3</sup>. The results showed 95% and 94% sensitivity for 50% and 70% stenosis, respectively. In Asia, a study by Meng<sup>4</sup> analyzed patient-, vessel-, and segment-based models, and showed high diagnostic performance of CCTA. However, studies are limited on coronary artery injury visualized with 128-slice CCTA compared with ICA.

Our study was conducted to determine the diagnostic performance and influencing factors of 128-slice CCTA with contrast in patients with CAD.

## Materials and Methods

### Study design and population

We conducted a prospective cross-sectional study of 139 patients with suspected chronic coronary syndrome detected by CCTA and indicated for ICA from April 2020 to August 2021 at Can Tho Stroke International Services (Can Tho Can Tho City, Vietnam). The study was approved by the Ethics Committee in Biomedical Research of Can Tho

University of Medicine and Pharmacy (Decision No. 1026/HDDD-DHYDCT). All participating patients received health benefits from the study. Patients did not pay or receive any monetary compensation from the study. The identities of all research subjects were kept confidential.

Inclusion criteria were: patients suspected of having chronic coronary syndrome with stable angina and/or dyspnea symptoms, and stenosis  $\geq 50\%$  detected by CCTA and indicated for ICA according to the 2019 European Society of Cardiology (ESC) Guidelines.<sup>5</sup> Exclusion criteria were acute coronary syndrome, percutaneous coronary intervention or coronary artery bypass graft, cirrhosis, severe heart failure, chronic kidney disease, CCTA contrast drug allergy or contraindication, atrial fibrillation, or uncontrolled heart rhythm disturbances.<sup>6</sup>

### Study variables

Clinical characteristics included: sex, age, angina, heart rate (HR), blood pressure, and body mass index (BMI). Risk factors included: hypertension (patients with systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg through at least two measurements or on antihypertensive medication according to ESC and the European Society of Hypertension 2018<sup>7</sup>), dyslipidemia according to ESC and European Atherosclerosis Guidelines,<sup>8</sup> overweight/obesity (according to the World Health Organization 1998 guideline for Asians<sup>9</sup>), smoking (never smoked or quit for  $\geq 5$  years), and type 2 diabetes mellitus (T2DM) (according to the 2020 American Diabetes Association recommendations<sup>10</sup>). Blood biochemical characteristics included: glucose, creatinine, triglycerides, cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

Stenosis was defined as  $\geq 50\%$  stenosis in the lumen diameter, and  $\geq 70\%$  was defined as severe stenosis ( $\geq 50\%$  in the left main coronary artery). Coronary artery injury imaging characteristics through CCTA and ICA included: degree of patient-based stenosis (most severe stenosis vessel); number of stenosis vessels per patient; and degree of vessel-based stenosis in left main coronary artery, left anterior descending artery (LAD), right coronary artery (RCA), and left circumflex artery anterior (LCx). Atherosclerotic plaques were assessed by CCTA and consisted of two components (core containing low-density fat  $< 0-100$  Agatston units, and fibrous densities of 40–60 Agatston units) and three types (calcification when the density was 80–250 Agatston units, no calcification when the density was  $< 80$  Agatston units, mixed atheroma when calcified in the core and capsule<sup>11</sup>). The morphology of coronary artery lesions included concentric stenosis, eccentric stenosis (types I and II), and multiple irregularities (according to 2013 ESC Guidelines<sup>12</sup>).

The diagnostic performance of CCTA was compared with ICA using patient-, vessel-, and segment-based models based on the following values: sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and accuracy (Ac). Influencing factors of CCTA included: HR  $> 70$  beats/min<sup>1</sup>, BMI  $\geq 23$  (kg/m<sup>2</sup>),<sup>2</sup> and calcium score  $\geq 400$  Agatston units<sup>3,13</sup>.

### Data collection methods

Enrolled patients were examined for clinical characteristics and risk factors. A biochemistry blood test was performed with 2 mL blood in a tube with heparin anticoagulant (AU-680 clinical chemistry analyzer; Beckman Coulter, Sykesville, MD, USA). The patients underwent CCTA according to the 2013 Ministry of Health of Vietnam Protocol,<sup>14</sup> vessel and segment assessment according to Agatston score, and AHA guidelines<sup>15</sup> (Siemens 128-segment CT Scanner with Sure Exposure 3D Technology, contrast drug: Ultravist or Omnipaque 100 mL, 300–370 mg/mL). Nitrate was placed under the tongue for 15 min before imaging to improve the coronary imaging, electrocardiogram monitoring (before, during, and after imaging), and laser positioning below the diaphragm. Total injection time was <15 s and water removal time was <10 s. Each vessel was analyzed in at least two parallel and perpendicular views. All patients undergoing CCTA underwent ICA by an interventional cardiologist (with ≥10 years of experience), according to invasive angiographic technique and contrast-selective coronary artery assessment<sup>16</sup> (Siemens Axiom Artis FA/BA machine with VB 11 software, processed with quantitative coronary angiography algorithm). ICA was performed according to the Judkins classical technique following the right femoral artery or right radial artery with a full range of positions. Each coronary artery segment was evaluated in at least two orthogonal positions to avoid omissions on coronary artery stenosis. Patients were given 81 mg aspirin and 75 mg clopidogrel at least 5 days before ICA if they not been given 50 UI/kg heparin and 0.5 g aspirin intravenous bolus. The procedure area was disinfected with Betadine. Local anesthetic (lidocaine 2%) was applied and the catheter (sheath) was inserted into the artery. Then the catheter was inserted into the coronary artery (diagnostic catheter: JL, JR or Tig 5F; interventional catheter for intravascular ultrasound: JR4, AL for the right coronary artery and JL4, XB, AL for the left coronary artery). Nitroglycerine 100–200 µg was directly injected into the coronary artery to be imaged, and coronary angiography was performed using conventional imaging angles.

### Bias control methods

All collected data had information bias control (clear and specific definition of study variables, clinical symptoms were collected using a unified medical record form, diagnosis and classification were performed according to uniform standards), and selection bias control (strictly followed the inclusion and exclusion criteria and study protocol, imaging tests were interpreted by independent radiologists and cardiologists, data and statistical processing were conducted by an independent statistician, analyses were conducted twice to compare the results).

Imaging quality evaluation<sup>17</sup> was performed using a four-point grading scale. Score 1: excellent, continuous vascular imaging, no artifacts and surrounding tissue density blur; Score 2: good image, blood vessel wall was slightly blurred, there may be a slight artifact due to movement, but the blood

vessel was still continuous; Score 3: unsatisfactory, blood vessel wall was slightly blurred, artifact segment <5 mm, broken blood vessel (stair shape) < 25% diameter; Score 4: poor image, difficult to distinguish blood vessels from surrounding tissues, artifact segment >5 mm long, broken blood vessel (stair shape) > 25% diameter.

### Data analysis

Data were collected and processed with SPSS Statistics 20.0 software (SPSS Inc., Chicago, IL, USA). Quantitative variables with normal distribution are presented as the mean ± standard deviation, and non-normal distribution variables are presented as the maximum, minimum, and interquartile range (IQR). Qualitative variables are described by the frequency and rate. The difference between the two qualitative variables was determined using the chi-squared test. Analyses of normally distributed variables were conducted with the *t*-test (2 groups) or analysis of variance (≥3 groups), and non-normally distributed variables were analyzed with the Mann–Whitney U test (2 groups) or the Kruskal–Wallis's test (≥3 groups). *P* < 0.05 was considered statistically significant. The gold standard for evaluating the diagnostic performance of CCTA is ICA, which was performed by a cardiologist with ≥10 years of experience. Sensitivity ( $Se = \frac{a}{a+c}$ ), specificity ( $Sp = \frac{d}{b+d}$ ), PPV ( $PPV = \frac{a}{a+b}$ ), NPV ( $NPV = \frac{d}{c+d}$ ), and accuracy ( $Ac = \frac{a+d}{a+b+c+d}$ ) were calculated with formulas, where a is true positive, b is false positive, c is false negative, and d is true negative. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic performance of CCTA; and the cut-off value was defined by the Youden index (J), which selected the optimal sensitivity and specificity values.

## Results

### Baseline characteristics of the study participants

A total of 139 patients who met the criteria were enrolled, of whom 62.6% were male, with a mean age of  $66.31 \pm 9.65$  years. Hypertension was the highest risk factor at 70.5% (Table 1). Eccentric stenosis accounted for the highest rate (89.8%), and atherosclerotic plaque was mainly calcified (60.2%).

**Table 1: Baseline characteristics of the study participants**

Characteristics	n	%
Clinical characteristics		
Sex (%)		
Male	87	62.6
Female	52	37.4
Age (Mean ± SD)	66.31 ± 9.65	
BMI (kg/m <sup>2</sup> )	25.2 ± 2.34	
Angina	77	57.9
HR (beats/min)		
≤70	137	98.6
>70	2	1.4

(continued on next page)

**Table 1** (continued)

Characteristics	n	%
<b>Blood pressure (mmHg)</b>		
<140/90	67	48.2
≥140/90	72	51.8
<b>Risk factors</b>		
Smoking (%)	52	37.4
Alcohol using (%)	31	22.3
T2DM (%)	81	58.3
CAD (%)	29	20.8
Hypertension (%)	98	70.5
Dyslipidemia (%)	62	44.6
Overweight/obesity (%)	13	9.4
Family history of CAD (%)	10	7.2
<b>CCTA imaging</b>		
Calcium score (Agatston units) (Median ± IQR)	300 ± 381.1	
<b>Atherosclerotic plaque (%)</b>		
Calcification	311	60.2
None calcification	70	13.5
Mixed	136	26.3
<b>Coronary artery lesions morphology (%)</b>		
Eccentric stenosis	283	89.8
Concentric stenosis	23	7.3
Multiple irregularities	9	2.9

BMI, Body mass index; CAD, Coronary artery disease; CCTA, Coronary computed tomography angiography; HDLC, High-density lipoprotein cholesterol; LDLc, Low-density lipoprotein cholesterol; HR, Heart rate; IQR, Interquartile range; PCI, Percutaneous coronary intervention; SD, Standard deviation; T2DM, Type 2 diabetes mellitus.

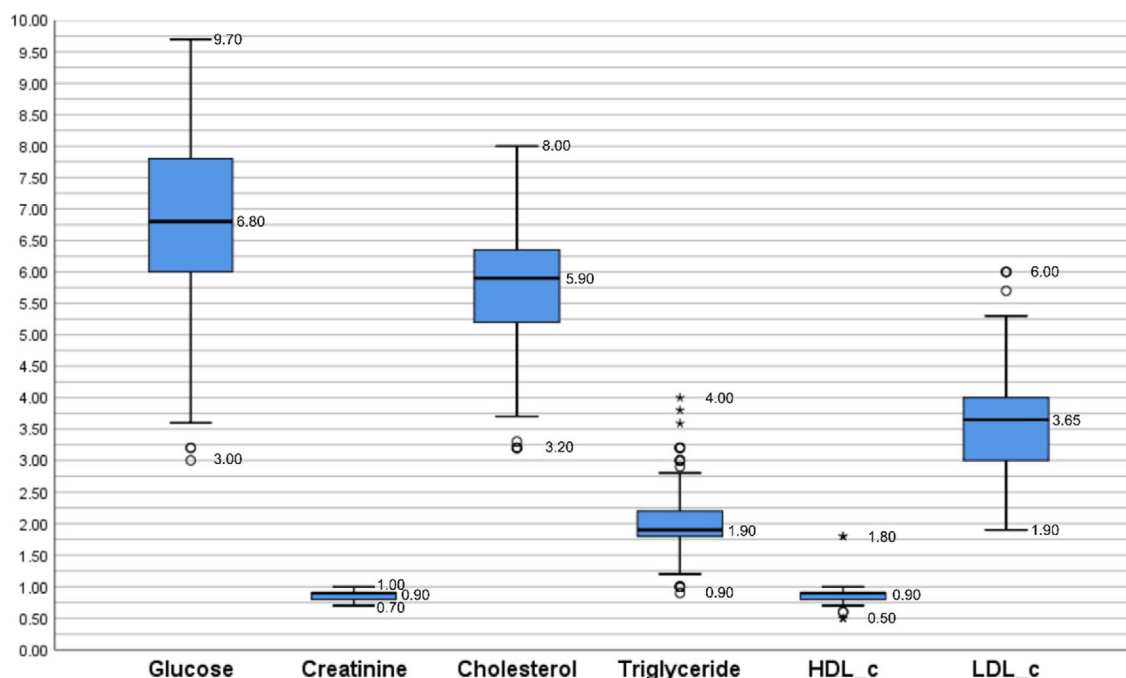
Blood biochemical characteristics are shown in [Figure 1](#), in which the median ± IQR of glucose, creatinine, triglyceride, cholesterol, HDLC, and LDLc was  $6.8 \pm 1.8$  mmol/L,  $0.9 \pm 0.1$  μmol/L,  $5.9 \pm 1.1$  mmol/L,  $1.9 \pm 0.5$  mmol/L,  $0.9 \pm 0.1$  mmol/L, and  $3.65 \pm 1.0$  mmol/L, respectively.

#### CCTA and ICA imaging characteristics

There were 86.3% cases of severe stenosis ( $\geq 70\%$ ) on CCTA and 84.2% on ICA ( $p = 0.001$ ; [Table 2](#)). LAD had the highest stenosis rate; 19.1% (CCTA) and 18.7% (ICA) with stenosis  $\geq 50\%$  ( $p < 0.001$ ), and 16% (CCTA) and 15.6% (ICA) with stenosis  $\geq 70\%$  ( $p < 0.001$ ).

#### Diagnostic performance of CCTA and influencing factors

Most diagnostic values were  $>80\%$ ; there was a slight decrease in Se and PPV at stenosis  $>70\%$  ([Table 3](#)). Our study had a specificity and NPV at stenosis  $>50\%$  through patient-based models at 0.0% due to sampling only in patients with stenosis  $\geq 50\%$  on CCTA or ICA. The ROC curve ([Figure 2](#)) showed a diagnostic performance of CCTA at stenosis  $\geq 50\%$ . The cut-off values of the patient, LAD, RCA, and LCx were 77.5 ( $J = 0.368$ ,  $p = 0.071$ ), 57.5 ( $J = 0.589$ ,  $p = 0.000$ ), 45 ( $J = 0.705$ ,  $p = 0.000$ ), and 45 ( $J = 0.638$ ,  $p = 0.000$ ), respectively. Stenosis  $\geq 70\%$  ([Figure 2](#)) was 65 ( $J = 0.27$ ,  $p = 0.033$ ), 65 ( $J = 0.593$ ,  $p = 0.000$ ), 45 ( $J = 0.534$ ,  $p = 0.000$ ), and 52.5 ( $J = 0.505$ ,  $p = 0.000$ ). The sensitivity in the group with BMI  $<23$  and calcium score

**Figure 1:** Blood biochemical characteristics

**Table 2: CCTA and ICA imaging characteristics**

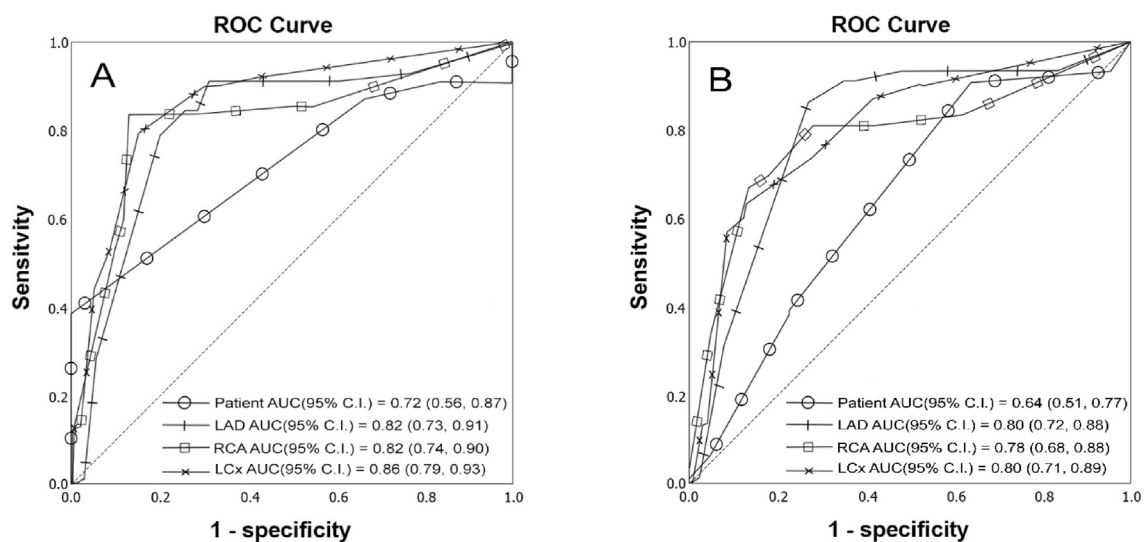
Characteristics		CCTA, n (%)	ICA, n (%)	p*	
Stenosis $\geq 70\%$		120 (86.3)	117 (84.2)	0.001	
Number of stenosis vessels	1	20 (14.7)	27 (19.9)	0.000	
	2	34 (25.0)	41 (30.1)		
	$\geq 3$	82 (60.3)	68 (50.0)		
Vessel-based stenosis degree, (n = 556)	LM	$\geq 50\%$	11 (1.9)	9 (1.6)	0.000
		$\geq 70\%$	3 (0.5)	4 (0.7)	0.001
	LAD	$\geq 50\%$	106 (19.1)	104 (18.7)	0.000
		$\geq 70\%$	89 (16.0)	87 (15.6)	0.000
	LCx	$\geq 50\%$	52 (9.3)	48 (8.6)	0.000
		$\geq 70\%$	26 (4.7)	30 (5.4)	0.000
RCA	$\geq 50\%$	57 (10.2)	55 (9.9)	0.000	
	$\geq 70\%$	37 (6.6)	36 (6.5)	0.000	

CCTA, Coronary computed tomography angiography; ICA, Invasive coronary angiography; LM, Left main coronary artery; LAD, Left anterior descending artery; RCA, Right coronary artery; LCx, Left circumflex artery; \*, Chi-squared test.

**Table 3: Diagnostic performance of CCTA compared to ICA**

Model	Se (%)	Sp (%)	PPV (%)	NPV (%)	Ac (%)
$\geq 50\%$					
Patient-based (n = 139)	93.2	0.0	95.3	0.0	89.2
Vessel-based (n = 556)	85.6	87.9	81.1	90.6	87.0
Segment-based (n = 1946)	73.9	93.7	66.6	95.5	90.9
$\geq 70\%$					
Patient-based (n = 139)	90.5	36.4	88.3	42.1	82.0
Vessel-based (n = 556)	74.5	90.5	75.4	90.0	85.9
Segment-based (n = 1946)	61.2	96.4	67.0	95.4	92.7

Ac, Accuracy; CCTA, Coronary computed tomography angiography; ICA, Invasive coronary angiography; PPV, Positive predictive value; NPV, Negative predictive value; Se, Sensitivity; Sp, Specificity.



**Figure 2:** ROC curve evaluated the diagnostic performance of CCTA compared to ICA at (A) stenosis  $\geq 50\%$ ; (B) stenosis  $\geq 70\%$ . The point of the curve represents stenosis degree from 0–100%. AUC: Area under the curve; CI: Confidence interval; LAD: Left anterior descending artery; RCA: Right coronary artery; LCx: Left circumflex artery.

**Table 4: Influencing factors of coronary computed tomography angiography**

Factor		Se (%)	Sp (%)	PPV (%)	NPV (%)	Ac (%)
HR (beats/min)	≤70	90.4	36.4	88.1	42.1	81.7
	>70	100	100	100	100	100
BMI (kg/m <sup>2</sup> )	<23	94.4	37.5	77.3	75	76.9
	≥23	89.9	35.7	90.8	33.3	83.2
Calcium score (Agatston unit)	<400	92.6	46.2	90.0	54.5	85.2
	≥ 400	87.8	22.2	74.1	25.0	77.6

Comparison in stenosis ≥ 70%; Ac, Accuracy; BMI, Body mass index; HR, Heart rate; PPV, Positive predictive value; NPV, Negative predictive value; Se, Sensitivity; Sp, Specificity.

**Table 5: Diagnostic performance of CCTA compared with other studies**

Author		n	Se (%)	Sp (%)	PPV (%)	NPV (%)	Ac (%)
Patient-based							
Budoff <sup>3</sup>	Stenosis ≥ 50%	245	95	83	64	99	—
	Stenosis ≥ 70%	245	94	83	64	99	—
De Graaf <sup>19</sup>	Stenosis ≥ 50%	53	100	92	79	100	94
Raff <sup>23</sup>	Stenosis ≥ 50%	70	95	90	93	93	—
Meng <sup>21</sup>	Stenosis ≥ 50%	109	98	79	94	91	94
Stolzmann <sup>24</sup>	Stenosis ≥ 50%	100	100	95	93	100	—
Lin <sup>22</sup>	Stenosis ≥ 50%	44	97	45.5	84.2	83.3	—
Our study	Stenosis ≥ 50%	139	93.2	0.0	95.3	0.0	89.2
	Stenosis ≥ 70%	139	90.5	36.4	88.3	42.1	82.0
Vessel-based							
Budoff et al. <sup>3</sup>	Stenosis ≥ 50%	910	84	90	51	99	—
	Stenosis ≥ 70%	910	84	92	36	99	—
Raff <sup>23</sup>	Stenosis ≥ 50%	279	91	92	80	97	—
Meng <sup>21</sup>	Stenosis ≥ 50%	475	97	90	81	98	92
Stolzmann <sup>24</sup>	Stenosis ≥ 50%	300	99	96	94	100	—
Lin <sup>22</sup>	Stenosis ≥ 50%	132	96.6	80.8	80.3	96.7	—
Our study	Stenosis ≥ 50%	556	85.6	87.9	81.1	90.6	87.0
	Stenosis ≥ 70%	556	74.5	90.5	75.4	90.0	85.9
Segment-based							
Sato <sup>17</sup>	Stenosis ≥ 50%	325	92.2	87.5	69.6	97.3	—
Raff <sup>23</sup>	Stenosis ≥ 50%	935	86	95	66	98	—
Meng <sup>21</sup>	Stenosis ≥ 50%	1533	95	91	65	99	92
Stolzmann <sup>24</sup>	Stenosis ≥ 50%	1392	98	99	95	100	—
Lin <sup>22</sup>	Stenosis ≥ 50%	535	66.9	97.8	90.8	89.9	—
Our study	Stenosis ≥ 50%	1946	73.9	93.7	66.6	95.5	90.9
	Stenosis ≥ 70%	1946	61.2	96.4	67.0	95.4	92.7

Ac, Accuracy; PPV, Positive predictive value; NPV, Negative predictive value; Se, Sensitivity; Sp, Specificity.

<400 Agatston units was higher: 94.4% vs. 89.9% and 92.6 vs. 87.8, respectively (Table 4). Diagnostic performance in patients with HR > 70 in our study included only two cases, all of whom had ≥70% stenosis, so the results are not representative.

## Discussion

### Baseline characteristics of the study participants

The prevalence of males with CAD was nearly 1.5 times higher than that of females (62.6%) (Table 1), similar to the study by Sato et al.<sup>18</sup> Males accounted for 85% of the study population, similar to Madhok<sup>19</sup> (90% males). The mean age was 66.31 ± 9.65 years, similar to De Graaf<sup>20</sup> (65 ± 13 years) and Sato et al.<sup>18</sup> (70.7 ± 7.8 years). Madhok et al.<sup>19</sup>

recorded a lower mean age (54.3), as the age of the study population ranged from 51 to 60 years. Our population risk factors were similar to other studies: smoking (37.3%) and obesity (50.7%)<sup>21</sup>; and hypertension (81.0%), T2DM (23.0%), smoking (25.0%), and dyslipidemia (85.0%).<sup>20</sup> Calcified atheroma accounted for the highest percentage (60.2%), similar to Sato et al.<sup>18</sup> with 246/325 (75.7%). Thus, the advantage of CCTA is not only to examine the stenosis of the coronary artery lumen but also to allow the assessment of atherosclerotic plaque characteristics, which is valuable in the prognosis and treatment of patients.

### CCTA and ICA imaging characteristics

The proportion of patients with stenosis in three coronary arteries in our study accounted for the highest rate

(60.3%) (Table 2), which was higher than the rates reported in the studies of De Graaf (2010)<sup>20</sup> (5%); Meng (2009)<sup>4</sup> (10%); Lin (2010)<sup>5</sup> (27.3%). This difference can be attributed to the fact that our study subjects had moderate to severe CAD, resulting in a higher number of patients with three or more coronary stenosis. Of the more than 556 vessels in 139 patients, stenosis in the LAD had the highest prevalence, followed by the RCA and the LCx (Table 2). Similar to Madhok et al.,<sup>19</sup> LAD stenosis accounted for the greatest number of cases. The majority of stenosis cases in the LAD could be seen due to its anterior position in the septum plane and its multi-segment anatomical structure, leading to a change in the local hemodynamic environment and additional sliding effects, as a predisposing factor for atherosclerosis.

#### Diagnostic performance of CCTA and influencing factors

A total of 139 patients were analyzed; the sensitivity, PPV, and accuracy in our study were very high and similar to other studies<sup>3,19,21–24</sup> (Tables 3 and 5). In addition, our study evaluated more at stenosis  $\geq 70\%$  and showed a lower diagnostic performance at higher stenosis levels. This indicated that CCTA had a lower value in predicting the severity of the case. Our study had differences in specificity and PPV because of the high-risk population and stenosis  $\geq 50\%$  on CCTA or ICA in the inclusion criteria, so the NPV was low (stenosis  $\geq 50\%$ , NPV = 0). In addition, it may be due to artifacts, the patient moving during the CT scan, or high coronary calcification. Unlike other studies, our study did not exclude small vascular segments  $< 1.5$  mm in diameter, which might have affected the sensitivity and specificity of the CCTA.

A total of 556 vessels were analyzed in 139 patients (Tables 3 and 5). Our study found that the diagnostic performance of CCTA was mostly high ( $> 80\%$ ), which had a high diagnostic performance for vessel-based lesions. Our study evaluated stenosis  $\geq 70\%$  and recorded a reduced sensitivity value but higher specificity and NPV compared with patient-based models, similar to the study by Budoff et al.<sup>3</sup> However, our NPV was much higher, possibly due to differences in the study population, by Budoff et al.,<sup>3</sup> the prevalence of overweight dyslipidemia was high (with a mean BMI of  $31.4 \pm 6.2$  kg/m<sup>2</sup>, while ours was  $25.2 \pm 2.3$  kg/m<sup>2</sup>). The specificity and NPV when analyzing vessel- and segment-based models were much higher than patient-based models, indicating that the diagnostic performance of CCTA at smaller vessels and segments was relatively good. In addition, it might be due to the small lumen diameter of vessels (3–4 mm) and segments (6–0.8 mm). Therefore, ICA was difficult to identify.

In our study, a total of 1946 segments were analyzed, and our results showed relatively low sensitivity compared to other studies, but the other diagnostic values were high and almost similar to those of other studies, as shown in Tables 3 and 5. The difference in sensitivity may be due to inconsistent anatomical markers between the segments, such as proximal, middle, and distal segments, which may have caused bias in the interpretation of the results. Similar to the study by Budoff et al.,<sup>3</sup> our study also showed a decrease in sensitivity as the stenosis degree

increased, but there was an increase in other diagnostic values. However, the overall accuracy of our study, as evaluated using patient-, vessel-, and segment-based models, was high and similar to that of other studies, indicating the high diagnostic performance of CCTA in CAD patients. The ROC curve showed that the diagnostic performance of CCTA when analyzed patient-based was high on both stenosis  $\geq 50\%$  and  $\geq 70\%$ . The area under the curve was mostly  $> 70\%$  with statistical significance ( $p < 0.05$ ). These values are higher when analyzed in vessel-based models (LAD, RCA, LCx), and the degree of stenosis was  $\geq 50\%$  (Figure 2). The difference may be due to the influence of diagnostic criteria, and the technique of conducting and analyzing the film results.

HR  $< 70$  beats/min as shown in previous studies had a lower diagnostic performance than HR  $> 70$  beats/min.<sup>22,23</sup> Because our study's CCTA protocol had a controlled HR, only two cases with HR  $> 70$  beats/min were recorded and both cases had stenosis  $\geq 70\%$ . BMI  $\geq 23$  (kg/m<sup>2</sup>) had no significant change in diagnostic performance compared with the BMI  $< 23$  (kg/m<sup>2</sup>) group (Table 4). Some other studies also did not record the influence of HR and BMI, such as Budoff et al.<sup>3</sup> and Meng.<sup>4</sup> Others found the elevation of HR and BMI affected the CCTA diagnostic performance such as Raff<sup>23</sup> and Lin.<sup>22</sup> Patients with a calcification score  $\geq 400$  Agatston units had lower diagnostic performance than  $< 400$  Agatston units, which clearly showed the calcification score influence on the diagnostic accuracy of CCTA. When the calcification score was high, the calcified plaques were concentrated into a large plaque that covered the entire coronary lumen and causes image noise (blooming artifact). CCTA can incorrectly assess the degree of coronary stenosis in the regions where heavy calcification plaque is present. In these cases, ICA should be performed. Other studies also found that an increase in Agatston units ( $> 400$ ) caused a decrease in the diagnostic performance of CCTA.<sup>3,4</sup>

The limitation of our study was the low sensitivity of CCTA in vessel- and segment-based models, which clearly showed the difference from other studies. However, these models had high specificity and NPV (mostly  $> 90\%$ ). Therefore, CCTA was valuable in excluding moderate and severe CAD in patients with CVD. In addition, our study was conducted at a single center; thus, a larger multicenter study is required for a clear representation of the population. However, our study showed the high diagnostic performance of CCTA, which could be implemented in clinical practice for screening coronary artery stenosis in patients not indicated for invasive procedures.

#### Conclusions

128-slice CCTA is an optimal, minimally invasive, and high-performance method to diagnose the stenosis and morphology of coronary artery lesions. The diagnostic values of CCTA (sensitivity, specificity, PPV, NPV, and accuracy) are high (mostly  $\geq 80\%$ ). Stenosis  $\geq 50\%$  has a higher diagnostic performance than  $\geq 70\%$ . Sensitivity is higher in the patient-based model, and specificity is higher in the vessel- and segment-based models. HR  $> 70$  beats/

min and BMI  $\geq 23$  (kg/m<sup>2</sup>) do not affect the accuracy of CTTA, while calcification score  $\geq 400$  Agatston units influences the accuracy of CTTA.

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### Conflict of interest

The authors have no conflicts of interest to declare.

### Ethical approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee in Biomedical Research of Can Tho University of Medicine and Pharmacy (No. 1026 dated 5/18/2020).

### Consent

Written informed consent was obtained from all patients involved in the study.

### Authors' contributions

AVT: Conceptualization and original draft preparation; and writing review, and editing. NMN: Conceptualization; methodology; data curation and original draft preparation; and writing review and editing. THN: Methodology; formal analysis; original draft preparation; and writing review, and editing. BLTT: Methodology; software; formal analysis; and writing review and editing. PMN: Data curation; writing review and editing. PTP: Writing review and editing. HTMP: Writing review and editing. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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### Data Availability Statement

Not applicable.

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