

European Heart Journal – Cardiovascular Imaging doi:10.1093/ehjci/jeu009

Diagnostic value of coronary CT angiography in comparison with invasive coronary angiography and intravascular ultrasound in patients with intermediate coronary artery stenosis: results from the prospective multicentre FIGURE-OUT (Functional Imaging criteria for GUiding REview of invasive coronary angiOgraphy, intravascular Ultrasound, and coronary computed Tomographic angiography) study

Joon-Hyung Doh<sup>1</sup>, Bon-Kwon Koo<sup>2\*</sup>, Chang-Wook Nam<sup>3</sup>, Ji-Hyun Kim<sup>4</sup>, James K. Min<sup>5</sup>, Ryo Nakazato<sup>5</sup>, Todung Silalahi<sup>6</sup>, Hardjo Prawira<sup>6</sup>, Hyunmin Choi<sup>1</sup>, Sung Yun Lee<sup>1</sup>, June Namgung<sup>1</sup>, Sung Uk Kwon<sup>1</sup>, Jae-Jin Kwak<sup>1</sup>, and Won Ro Lee<sup>1</sup>

<sup>1</sup>Department of Medicine, Inje University Ilsan Paik Hospital, Goyang, Korea; <sup>2</sup>Department of Medicine, Seoul National University Hospital, Seoul, Korea; <sup>3</sup>Department of Medicine, Keimyung University Dongsan Medical Center, Daegu, Korea; <sup>4</sup>Department of Medicine, Dongguk University Ilsan Hospital, Dongguk University Graduate School, Goyang, Korea; <sup>5</sup>Department of Imaging and Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA; and <sup>6</sup>PGI Cikini Hospital, Jakarta, Indonesia

Received 9 July 2013; accepted after revision 6 January 2014

#### **Aims**

The anatomical criteria for the diagnosis of ischaemia referenced by fractional flow reserve (FFR) from non-invasive coronary computed tomographic angiography (CCTA), invasive coronary angiography (ICA), and intravascular ultrasound (IVUS) have not been evaluated contemporarily in a large-scale study. The aim of this study was to assess the diagnostic value of CCTA compared with ICA and IVUS in patients with intermediate coronary stenosis.

## Methods and results

CCTA, ICA, IVUS, and FFR were performed in 181 coronary lesions with intermediate severity. Minimal lumen diameter (MLD) and per cent diameter stenosis (%DS) were determined by CCTA and ICA, whereas minimal lumen area (MLA) was determined by CCTA and IVUS. Inducible ischaemia was defined by FFR  $\leq$ 0.80. Diagnostic performances from noninvasive and invasive methods were compared. FFR  $\leq$ 0.80 was observed in 49 (27.1%) lesions. CCTA MLD was smaller than ICA MLD (1.3  $\pm$  0.5 vs. 1.5  $\pm$  0.4 mm, P < 0.001), CCTA %DS was higher than ICA %DS (54.0  $\pm$  14.0 vs. 50.3  $\pm$  12.8%, P < 0.001), and CCTA MLA was smaller than IVUS MLA (2.2  $\pm$  1.2 vs. 3.2  $\pm$  1.2 mm², P < 0.001). This trend was consistent irrespective of lesion location, lesion severity, and plaque characteristics. For the determination of ischaemia, diagnostic performance of CCTA %DS was lower than ICA %DS [area under the curve (AUC) 0.657 vs. 0.765, P = 0.04], and that of CCTA MLA was lower than IVUS MLA (AUC 0.712 vs. 0.801, P = 0.03).

#### Conclusion

Anatomical criteria for the diagnosis of ischaemia-producing coronary stenosis differ by non-invasive and invasive methods. Compared with invasive methods, CCTA presents overestimation in assessing lesion severity and lower diagnostic performance in assessing ischaemia.

<sup>\*</sup>Corresponding author. Seoul National University College of Medicine, 101 Daehang-ro, Chongno-gu, Seoul 110-744, Korea. Tel: +82 2 2072 2062; Fax: +82 2 3675 0805, Email: bkkoo@snu.ac.kr, bkk1214@gmail.com

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**Keywords** 

coronary computed tomographic angiography • intravascular ultrasound • fractional flow reserve • myocardial ischaemia • coronary disease

#### Introduction

Invasive coronary angiography (ICA) and intravascular ultrasound (IVUS) are regarded as gold standards for the anatomical assessment of coronary artery disease. However, recent advances in noninvasive coronary computed tomographic angiography (CCTA) technology enable anatomical evaluation of the coronary arteries without invasive procedures. <sup>1–5</sup> As CCTA is increasing in utilization for both clinical and research purposes, it is important to understand the relationship between the parameters derived from CCTA and from ICA and IVUS. To date, prior studies have been limited to small patient cohorts. 6-10 Fractional flow reserve (FFR) is an invasive physiologic index to define the presence of ischaemia-generating coronary stenosis. 11 Several studies demonstrated the clinical benefit of FFR-guided percutaneous coronary intervention strategy. 12-15 FFR measurement is now regarded as a gold standard invasive tool to assess the functional significance of coronary stenosis. Previous studies revealed the limitation of anatomical criteria in the prediction of ischaemia-generating coronary stenosis. 16-18 However, there has been no large study which directly compared the diagnostic performance of CCTA with that of ICA and IVUS in various lesion subsets. We performed this study to assess the diagnostic value of CCTA in comparison with ICA and IVUS for the diagnosis of inducible ischaemia in patients with intermediate coronary stenosis.

#### **Methods**

#### **Patient population**

The FIGURE-OUT (Functional Imaging criteria for GUiding REview of invasive coronary angiOgraphy, intravascular Ultrasound and coronary computed Tomographic angiography) study was a prospective multicentre diagnostic performance study conducted at three Korean university hospitals (clinicaltrials.gov NCT01400230). Patients who underwent ICA, IVUS, and FFR measurement for angiographic intermediate stenosis (visually 30–70% stenosis) in major epicardial coronary arteries and available CCTA within 3 months prior to ICA were consecutively enrolled. Patients were excluded for the following criteria: acute coronary syndrome with regional wall motion abnormality; visible thrombus of target vessel segment; additional stenosis (>30% by visual estimation) in the same vessel; lesion length >40 mm; reference vessel diameter of < 2.5 and > 4.0 mm by visual estimation; left ventricular ejection fraction of < 40%; primary myocardial or valvular heart disease; left main stenosis; presence of collateral vessels; and non-diagnostic CCTA. The study protocol was approved by the Institutional Review Boards at each participating centre. Written informed consent was obtained in each patient.

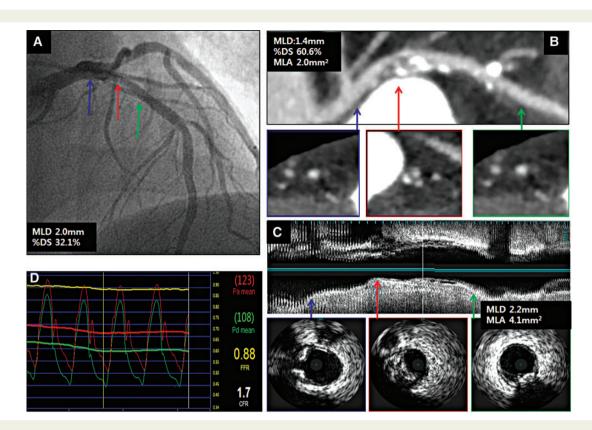
# Protocol for CCTA and quantitative CCTA analysis

Each centre performed CCTA in accordance with the Society of Cardiovascular Computed Tomography (SCCT) performance guidelines using different CT scanner platforms (Somatom® Sensation and Definition CT, Siemens, Forchheim, Germany; Aquilion One<sup>TM</sup> and Aquilion<sup>TM</sup> 64, Toshiba, Otawara, Japan). 19 Oral metoprolol was administered for any patient with a heart rate of  $\geq$  65 bpm and 0.2 mg sublingual nitroglycerin was administered immediately before scanning. CCTA results were analysed in a blinded fashion at the independent core laboratory (Cedars-Sinai Medical Center, Los Angeles, CA, USA) according to the SCCT guidelines on CCTA interpretation. 20 One blinded experienced level-III CT reader interpreted each segment for per cent diameter stenosis (%DS), minimal lumen area (MLA), plaque characteristics, and minimal lumen diameter (MLD) using a three-dimensional CT workstation (AW Advantage<sup>TM</sup> 4.5, GE Healthcare, Waukesha, WI, USA). All measurements were performed using the minimal available slice thickness.<sup>20,21</sup> The MLA was measured using double-oblique short-axis views of the coronary segment at the site of the minimal luminal crosssectional area. %DS was assessed using the most representative long-axis view of the coronary artery using techniques established in prior studies.<sup>21</sup> This was done by measuring the luminal diameter at the site of maximal DS and also by measuring the diameters of proximal and distal reference segments, which were selected to be the most adjacent points to the maximal stenosis in which there was minimal or no plaque (Figure 1). The distance between the proximal and the distal reference sites was measured along a centreline of the artery from the curved multiplanar reformatted images. Plaques were visually classified as noncalcified plaque (plaques containing only non-calcified components with no visible calcium) or calcified plaque (plaques containing any calcium).

## Invasive procedures and quantitative coronary angiography and IVUS analysis

The target coronary artery was engaged using a 5- to 7-Fr guide catheter. Angiographic images were acquired after intracoronary administration of  $100-200~\mu g$  of nitroglycerin. FFR was measured using a 0.014-inch pressure sensor-tipped guide wire (PressureWire $^{TM}$ , St. Jude Medical Systems, St. Paul, MN, USA) as previously described. Hyperaemia was induced with intracoronary bolus administration (80  $\mu g$  in the left coronary artery and 40  $\mu g$  in the right coronary artery) or intravenous continuous infusion (140  $\mu g/kg/min$ ) of adenosine. An FFR value of  $\leq 0.80$  was defined as the diagnostic threshold of myocardial ischaemia. WUS was performed in a standard fashion using an automated motorized pullback system (0.5 mm/s) with commercially available imaging catheters (Boston Scientific/SCIMED, Minneapolis, MN, USA or Volcano Corporation, Rancho Cordova, CA, USA). Intracoronary nitroglycerin (200  $\mu g$ ) was administered before an IVUS run or FFR measurement.

Both quantitative coronary angiography (QCA) and IVUS analyses were performed at an independent core laboratory (Seoul National University Cardiovascular Center, Seoul, Korea). QCA was performed by a single experienced observer, who was blinded to the FFR value and CCTA and IVUS findings. Using the guide catheter for calibration and an edge detection system (CAAS 5.7 QCA system, Pie Medical, Maastricht, the Netherlands), the reference diameter, MLD, and lesion length were measured and the %DS was calculated. Lesion location was determined according to the American Heart Association classification. <sup>22</sup> IVUS analysis was performed by one independent experienced observer blinded to the FFR and QCA information. Quantitative analyses



**Figure I** A representative case demonstrating ICA (A), CCTA (B), IVUS (C), and FFR (D) assessment for the stenosis located in the proximal left anterior descending coronary artery. Blue arrow indicates proximal reference; green arrow, distal reference; and red arrow, minimal lumen site. ICA, invasive coronary angiography; CCTA, coronary computed tomographic angiography; IVUS, intravascular ultrasound; FFR, fractional flow reserve; MLD, minimal lumen diameter; %DS, per cent diameter stenosis; MLA, minimal lumen area.

were performed using the computerized planimetry software (echoPlaque $^{TM}$  3.0, Indec Systems, Inc., Santa Clara, CA, USA) as previously described. <sup>23</sup> MLA was measured at the narrowest luminal cross-section and the per cent plaque burden was calculated as [(100  $\times$  (external elastic membrane area – lumen area)/external elastic membrane area].

#### Statistical analysis

Categorical variables are presented as frequencies and percentages and continuous variables as mean ± standard deviations. Student's t-test was performed to test the difference of continuous variables between two groups divided by FFR. The differences in angiographic and IVUS parameters between invasive and non-invasive methods were assessed by the paired t-test. The agreement between the two parameters was evaluated by Bland-Altman plot analysis. Analysis of discrete variables was performed using the  $\chi^2$  test. The area under the curve (AUC) by the receiver operating characteristic (ROC) curve analysis was calculated to examine the diagnostic performance of CCTA, ICA, and IVUS parameters to define the presence of myocardial ischaemia (FFR  $\leq$ 0.8). AUCs were compared by the DeLong method. The best cut-off value (BCV) was determined by the maximum sum of sensitivity and specificity. Pearson's correlation coefficients were calculated to determine the relationship between FFR and CCTA, ICA and IVUS parameters. A P-value of <0.05 was considered statistically significant. All analyses were performed using SPSS<sup>®</sup>, version 16.0 (IBM Corporation, Armonk, NY, USA) and  $MedCalc^{\text{@}}$ , version 12.3.0 (Medcalc software bvba, Mariakerke, Belgium).

#### Results

Between December 2007 and December 2011, 204 patients with 254 lesions were consecutively enrolled. Seventy-three lesions were excluded and 181 lesions in 151 patients were finally included in this study (see Supplementary data online, Figure S1). Baseline clinical, angiographic, and IVUS characteristics are presented in Tables 1 and 2. Mean FFR was  $0.85 \pm 0.08$  and FFR  $\leq 0.8$  was in 49 (27.1%) lesions. Lesions with FFR  $\leq 0.8$  were located more often in the LAD than those with an FFR value of >0.8. The distribution of FFR was unimodal (Figure 2). Compared with lesions with an FFR value of >0.8, lesions with FFR  $\leq 0.80$  demonstrated smaller lumen measurements and greater plaque burden by CCTA, ICA, and IVUS (Table 2).

# Comparison between CCTA, ICA, and IVUS parameters

CCTA MLD was smaller than ICA MLD (1.3  $\pm$  0.5 vs. 1.5  $\pm$  0.4 mm, P < 0.001), CCTA %DS was greater than ICA %DS (54.0  $\pm$  14.0 vs. 50.3  $\pm$  12.8%, P < 0.001), and CCTA MLA was smaller than IVUS

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MLA ( $2.2\pm1.2$  vs.  $3.2\pm1.2$  mm², P<0.001). This trend was consistent irrespective of lesion location, lesion severity, and plaque characteristics (Table~3 and see Supplementary data online, Figure~52). The relationship between CCTA MLA and MLD was not different between calcified and non-calcified plaques. There was a positive correlation between CCTA MLD and ICA MLD (r=0.492, P<0.001), CCTA %DS and ICA %DS (r=0.445, P<0.001), and CCTA MLA and IVUS MLA (r=0.528, P<0.001). 95% limits of agreement between CCTA MLD and ICA MLD, CCTA %DS and ICA %DS, as well as CCTA MLA and IVUS MLA ranged from -1.1

**Table I** Baseline demographic and clinical characteristics of the study population (N = 151)

Age, years	63.2 ± 9.6
Male	108 (71.5%)
Risk factors	
Hypertension	115 (76.2%)
Diabetes mellitus	50 (34.7%)
Hyperlipidaemia	103 (68.2%)
Clinical diagnosis	
Stable angina	104 (68.9%)
Acute coronary syndrome	42 (27.8%)
Silent ischaemia	5 (3.3%)
Previous myocardial infarction	4 (2.6%)
Previous revascularization	15 (9.9%)
Left ventricular ejection fraction, %	$64.9 \pm 7.6$

Data are presented as mean  $\pm$  SD and n (%).

to 0.7 mm, -24.1 to 31.4%, and -3.3 to 1.3 mm<sup>2</sup>, respectively (Figure 3).

# Diagnostic performance of CCTA, ICA, and IVUS to define the functional significance

There was a weak negative correlation between CCTA %DS and FFR (r = -0.271, P < 0.001) and a weak positive correlation between CCTA MLA and FFR (r = 0.363, P < 0.001). There was a moderate negative correlation between ICA %DS and FFR (r = -0.536, P <0.001) and a moderate positive correlation between IVUS MLA and FFR (r = 0.547, P < 0.001). This trend was consistent irrespective of lesion and plaque characteristics (Table 4). The BCVs of CCTA %DS and ICA %DS to define FFR < 0.80 were 54.0 and 49.6%, and those of CCTA MLA and IVUS MLA were < 1.80 and < 2.82 mm<sup>2</sup>, respectively. Diagnostic accuracy of BCV for CCTA %DS and CCTA MLA to predict the presence of ischaemia was 60.2 and 65.7%, while that of ICA %DS and IVUS MLA was 68.5 and 74.0%, respectively (see Supplementary data online, Figure S3). When the diagnostic performance was compared by AUC differences from ROC curve analysis, CCTA %DS was lower than ICA %DS (area difference of AUC 0.108, P = 0.04) and CCTA MLA was lower than IVUS MLA (area difference of AUC 0.089, P = 0.03) (Figure 4).

#### **Discussion**

The present multicentre prospective study demonstrated that: (i) CCTA presented overestimation of the stenosis severity when compared with ICA and IVUS; (ii) CCTA parameters had weaker correlation with FFR than ICA and IVUS parameters; (iii) these findings were consistent regardless of lesion characteristics; and

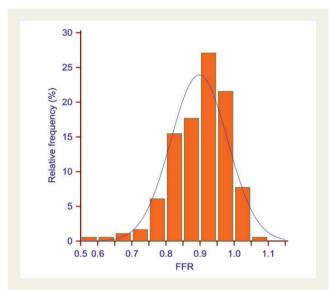
 Table 2
 Angiographic, CCTA, and IVUS parameters of the studied lesions

	All	FFR ≤0.8	FFR >0.8	<i>P</i> -value
N	181	49	132	
FFR	$0.85 \pm 0.08$	$0.74 \pm 0.06$	$0.89 \pm 0.05$	< 0.001
LAD lesion, n (%)	108	38 (77.6%)	70 (53.0%)	0.004
Proximal lesion, n (%)	143	42 (85.7%)	101 (76.5%)	0.220
Angiographic parameters				
Minimal lumen diameter, mm	$1.5 \pm 0.4$	$1.2 \pm 0.3$	$1.7 \pm 0.4$	< 0.001
Reference diameter, mm	$3.1 \pm 0.4$	$3.0 \pm 0.4$	$3.2 \pm 0.4$	0.014
Per cent diameter stenosis, %	$50.3 \pm 12.8$	$58.7 \pm 10.9$	$47.2 \pm 12.1$	< 0.001
Lesion length, mm	16.7 ± 9.1	16.5 ± 9.4	$16.8 \pm 9.0$	0.854
CCTA parameters				
Minimal lumen diameter, mm	$1.3 \pm 0.5$	$1.1 \pm 0.4$	$1.4 \pm 0.5$	< 0.001
Reference diameter, mm	$2.9 \pm 0.5$	$2.8 \pm 0.5$	$2.8 \pm 0.5$ $3.0 \pm 0.5$	
Per cent diameter stenosis, %	$54.0 \pm 14.0$	$59.2 \pm 13.3$ $52.0 \pm 13.7$		0.002
Lesion length, mm	$30.3 \pm 12.5$	$29.3 \pm 13.5$	$30.7 \pm 12.2$	0.517
Minimal lumen area, mm <sup>2</sup>	$2.2 \pm 1.2$	1.7 ± 1.0	2.4 ± 1.2	< 0.001
IVUS parameters				
Minimal lumen area, mm <sup>2</sup>	$3.2 \pm 1.2$	$2.4 \pm 0.8$	$3.5 \pm 1.2$	< 0.001
Per cent plaque burden, %	$72.0 \pm 10.6$	$76.0 \pm 12.3$	$70.6 \pm 9.5$	0.003

 $CCTA, coronary\ computed\ tomographic\ angiography;\ IVUS,\ intravascular\ ultrasound;\ FFR,\ fractional\ flow\ reserve;\ LAD,\ left\ anterior\ descending\ coronary\ artery.$ 

(iv) CCTA's diagnostic performance for the detection of ischaemia-producing stenosis was lower than both ICA and IVUS.

As CCTA is increasing in utilization, it is important to understand the relationship between CCTA, ICA, and IVUS parameters, as well as the diagnostic accuracy of CCTA compared with ICA and IVUS to define the functional significance of coronary stenoses. Although it is well known that CCTA can provide important information on the diagnosis and assessment for patients with coronary artery disease, <sup>1–5</sup> previous studies showed the wide variability of agreement between CCTA and ICA/IVUS parameters. <sup>7–10</sup> However, the degree of over- or underestimation of lesion severity was different among these studies. In a study by Voros *et al.*, <sup>9</sup> MLA by CCTA was larger than IVUS MLA, while there was no systemic over-



**Figure 2** Distributions of FFR values. The distribution of FFR was unimodal.

underestimation between CCTA and ICA/IVUS parameters in studies by Kristensen et al.<sup>7</sup> and by Caussin et al.<sup>6</sup> In contrast, Boogers et al. 10 recently reported that CCTA MLA was smaller than IVUS MLA (3.6 vs. 6.4 mm<sup>2</sup>). These contradictory results may be due to the difference in lesion characteristics, lesion severity, and methodology for CCTA and lesion measurement and small sample size. In our study, only patients with intermediate stenosis for whom decision-making for revascularization is often the most clinically ambiguous were included. Most of the lesions were clinically very relevant as 79% of lesions were located at the proximal part of major epicardial coronary arteries. In those lesions, quantitative CCTA measurements demonstrated overestimated lesion severity compared with ICA and IVUS. The mean differences between CCTA MLD and ICA MLD, and CCTA MLA and IVUS MLA were 0.2 mm, and 1.0 mm<sup>2</sup>, respectively, and this overestimation of CCTA was consistent regardless of vessel size, lesion severity, lesion location, and the presence of calcification. Understanding this difference is clinically relevant especially when the patient is assessed by multiple imaging modalities. Moreover, this information is critical when extrapolating evidence from ICA and IVUS studies to the findings of CCTA in patients with coronary artery disease.

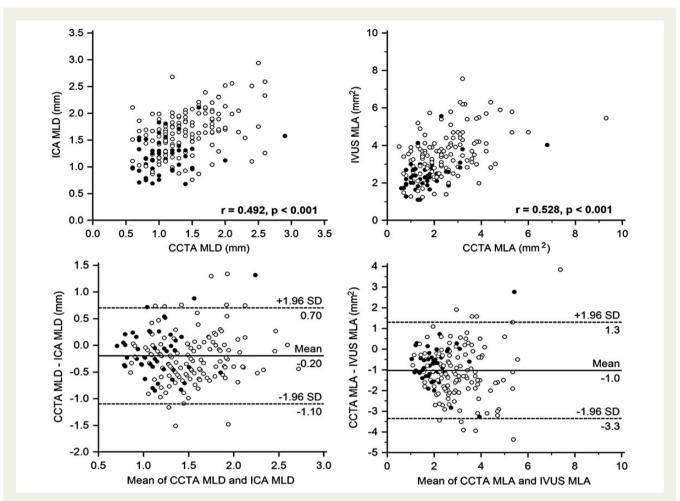
Previous studies showed the limitation of CCTA in the prediction of functional significance of a coronary stenosis. <sup>7,16,24</sup> However, prior studies have been limited to small patient cohorts and examined all lesions, including those of very severe or very mild angiographic stenoses. Moreover, no study has directly compared the diagnostic performance of CCTA, ICA, and IVUS in a large number of patients with intermediate stenosis. In our study, CCTA parameters consistently had weaker correlation with FFR than ICA and IVUS parameters regardless of lesion characteristics, and the diagnostic performance of CCTA %DS and MLA to define the functional significance of a stenosis was inferior to ICA %DS and IVUS MLA, respectively. Owing to the overestimation of lesion severity by CCTA, BCV of CCTA %DS to define the functional significance was higher than ICA %DS (54 vs. 50%) and those of CCTA MLA was smaller than

Table 3 Comparison between CCTA, ICA, and IVUS parameters according to various lesion subsets

	CCTA MLD	ICA MLD	<i>P-</i> value	CCTA MLA	IVUS MLA	<i>P-</i> value
All	1.3 ± 0.5	1.5 ± 0.5	<0.001	2.2 ± 1.2	3.2 <u>+</u> 1.2	< 0.001
Lesion location						
LAD	$1.3 \pm 0.4$	$1.5 \pm 0.4$	< 0.001	$2.0 \pm 1.0$	$3.0 \pm 1.1$	< 0.001
Non-LAD	$1.4 \pm 0.5$	$1.6 \pm 0.5$	< 0.001	$2.5 \pm 1.5$	$3.5 \pm 1.3$	< 0.001
Reference vessel si	ze by ICA (mm)					
≥3.0	$1.4 \pm 0.5$	$1.7 \pm 0.5$	< 0.001	$2.5 \pm 1.3$	$3.5 \pm 1.2$	< 0.001
<3.0	$1.2 \pm 0.4$	$1.4 \pm 0.4$	0.002	1.9 ± 1.0	2.9 ± 1.1	< 0.001
Lumen area by IVU	IS (mm²)					
≥3.0	$1.6 \pm 0.5$	$1.8 \pm 0.4$	< 0.001	$2.7 \pm 1.4$	4.1 ± 1.0	< 0.001
<3.0	$1.1 \pm 0.3$	$1.3 \pm 0.3$	< 0.001	$1.7 \pm 0.7$	$2.3 \pm 0.5$	< 0.001
Calcified vs. NC pla	aque by CCTA					
Calcified	$1.3 \pm 0.4$	$1.5 \pm 0.4$	0.001	$2.3 \pm 1.3$	$3.2 \pm 1.2$	< 0.001
NC	$1.3 \pm 0.5$	$1.5 \pm 0.5$	< 0.001	2.1 ± 1.2	$3.2\pm1.2$	< 0.001

CCTA, coronary computed tomography; ICA, invasive coronary angiography; IVUS, intravascular ultrasound; MLD, minimal lumen diameter; MLA, minimal lumen area; LAD, left anterior descending coronary artery; NC, non-calcified.

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**Figure 3** Scatterplots (upper panels) and Bland–Altman plots (lower panels) of CCTA and invasive parameters. The dots represent lesions with functionally significant stenosis. SD, standard deviation. Other abbreviations as in Figure 1.

IVUS MLA (1.8 vs. 2.8 mm<sup>2</sup>). The reasons for this inferiority can be numerous, but are at least partly inherent to CCTA's modest spatial and temporal resolution at present. This limitation of CCTA may be overcome by novel technologies. 25-28 The latest co-registration system for IVUS and CCTA image data can provide the optimal measurement at the same location. Recently developed CT-derived non-invasive FFR showed better diagnostic accuracy to define the functional significance of a stenosis (84.3 vs. 58.5%) than CCTA %DS by the application of novel computational fluid dynamics technology.<sup>27</sup> As this technology is based on three-dimensional modelling of coronary geometry, development of better CCTA to better estimate the lesion severity can improve the accuracy of this novel technology. Integrated anatomical parameters as aggregated plaque volume from CCTA, proposed by Nakazato et al., could improve its diagnostic performance.<sup>28</sup> However, the results of this study revealed the possible limitation of any technologies dependent on CCTA stenosis severity as current CCTA does not accurately reflect the severity of coronary stenosis.<sup>29</sup>

This study had several limitations. First, although the number of lesions included in this study was larger than previous studies, the exclusive enrolment of individuals with lesions of intermediate stenosis

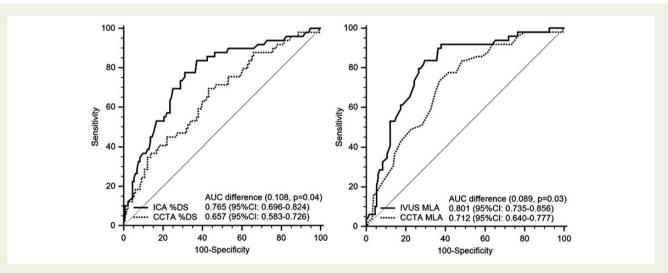
severity by ICA cannot disencumber this study from potential selection biases. However, it may be impractical to perform ICA, IVUS, and FFR in all patients with intermediate stenosis by CCTA. Secondly, quantitative assessment of CCTA by a core laboratory specialist can be different from the more commonly used visual estimation of community-based CCTA interpreters. Thirdly, two different IVUS systems which have different imaging characteristics were used in our study (Boston Scientific system for 66 lesions and Volcano system for 115 lesions). However, this difference may not have influenced on the results of our study as the key IVUS parameters used in our study were lumen and vessel areas. Finally, this study does not provide outcome data. Further studies are needed to assess the clinical implications of the differences between non-invasive CCTA and invasive ICA/IVUS parameters.

In conclusion, anatomical criteria for the diagnosis of ischaemia-producing coronary stenosis differ by non-invasive and invasive methods. Compared with invasive methods, CCTA presents overestimation in assessing lesion severity and lower diagnostic performance in assessing ischaemia. These differences should be appreciated when interpreting CCTA-based lesion severity in patients with coronary artery disease.

Table 4 Correlation between FFR and the parameters of CCTA, ICA and IVUS in different lesion subsets

	<i>N</i> (FFR ≤0.8)	Correlation (r)				
		CCTA %DS	ICA %DS	CCTA MLA	IVUS MLA	
All	181 (49)	-0.27	−0.54	0.36	0.55	
Lesion location						
LAD	108 (38)	-0.27	-0.54	0.35	0.54	
Non-LAD	73 (11)	-0.31	-0.56	0.32	0.51	
Reference vessel siz	e by ICA (mm)					
≥3.0	98 (20)	-0.29	-0.57	0.36	0.53	
<3.0	83 (29)	-0.27	-0.56	0.32	0.54	
Lesion length by ICA	4 (mm)					
≥20	52 (16)	-0.22	-0.54	0.39	0.50	
<20	129 (33)	-0.30	-0.52	0.34	0.56	
Lumen area by IVUS	S (mm <sup>2</sup> )					
≥3.0	93 (8)	-0.09	-0.411	0.19	0.38	
<3.0	88 (41)	-0.18	-0.400	0.26	0.26	
Calcified vs. NC pla	que by CCTA					
Calcified	72 (21)	-0.275	-0.440	0.399	0.564	
NC	109 (28)	-0.266	-0.580	0.363	0.548	

FFR, fractional flow reserve; CCTA, coronary computed tomographic angiography; ICA, invasive coronary angiography; IVUS, intravascular ultrasound; %DS, per cent diameter stenosis; MLA, minimal lumen area; LAD, left anterior descending coronary artery; NC, non-calcified.



**Figure 4** Comparison of diagnostic performance of CCTA and ICA/IVUS parameters by receiver operator characteristics curve analysis. Comparisons between CCTA %DS vs. ICA %DS (left) and CCTA MLA vs. IVUS MLA (right) are shown. AUC, area under the curve; 95% CI, 95% confidence interval. Other abbreviations as in *Figure 1*.

### Supplementary data

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

**Conflict of interest:** J.K.M. is supported by grants from the National Institutes of Health (NIH R01 HL118019 and NIH R01 HL111141) as well as by a generous gift from the Dalio Institute of Cardiovascular Imaging.

#### **Funding**

This work was supported by the Inje Research and Scholarship Foundation in 2008 and by grant Inje University in 2004.

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