Original Article

Comparison between MDCT and Grayscale IVUS in a Quantitative Analysis of Coronary Lumen in Segments with or without Atherosclerotic Plaques

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Abstract

Background: The diagnostic accuracy of 64-slice MDCT in comparison with IVUS has been poorly described and is mainly restricted to reports analyzing segments with documented atherosclerotic plaques.

Objectives: We compared 64-slice multidetector computed tomography (MDCT) with gray scale intravascular ultrasound (IVUS) for the evaluation of coronary lumen dimensions in the context of a comprehensive analysis, including segments with absent or mild disease.

Methods: The 64-slice MDCT was performed within 72 h before the IVUS imaging, which was obtained for at least one coronary, regardless of the presence of luminal stenosis at angiography. A total of 21 patients were included, with 70 imaged vessels (total length 114.6 ± 38.3 mm per patient). A coronary plaque was diagnosed in segments with plaque burden > 40%.

Results: At patient, vessel, and segment levels, average lumen area, minimal lumen area, and minimal lumen diameter were highly correlated between IVUS and 64-slice MDCT ($p < 0.01$). However, 64-slice MDCT tended to underestimate the lumen size with a relatively wide dispersion of the differences. The comparison between 64-slice MDCT and IVUS lumen measurements was not substantially affected by the presence or absence of an underlying plaque. In addition, 64-slice MDCT showed good global accuracy for the detection of IVUS parameters associated with flow-limiting lesions.

Conclusions: In a comprehensive, multi-territory, and whole-artery analysis, the assessment of coronary lumen by 64-slice MDCT compared with coronary IVUS showed a good overall diagnostic ability, regardless of the presence or absence of underlying atherosclerotic plaques. (Arq Bras Cardiol. 2015; 104(4):315-323)

Keywords: Coronary Artery Disease, Plaque, Atherosclerotic / diagnosis; Multidetector Computed Tomography / utilization; Ultrasonography / utilization.

Condensed Abstract

A total of 21 patients (70 vessels; total length 114.6 ± 38.3 mm per patient) underwent 64-slice MDCT and IVUS imaging. At patient, vessel, and segment levels, average lumen area, minimal lumen area, and minimal lumen diameter were highly correlated between IVUS and 64-slice MDCT. The comparison between 64-slice MDCT and IVUS lumen measurements was not substantially affected by the presence or absence of an underlying plaque (defined as IVUS plaque burden > 40%). In addition, 64-slice MDCT showed good global accuracy for the detection of IVUS parameters associated with flow-limiting lesions.

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List of Abbreviations

EEL	External elastic lamina
HU	Hounsfield units
IVUS	Intravascular ultrasound
MDCT	Multidetector computed
ROC	Receiver operating characteristic
CTA	Computed tomography angiography

Introduction

Multidetector computed tomography (MDCT) is a reliable noninvasive method for the detection of coronary luminal stenosis. However, most validation studies have compared

MDCT with catheter-based angiography, a method that is known to have limitations[1,2]. Intravascular ultrasound (IVUS) is currently considered the gold standard for the *in vivo* assessment of coronary luminal dimensions. Compared with quantitative angiography, morphologic data from IVUS imaging have shown a better correlation with coronary flow measurements and noninvasive detection of ischemia[3]. Moreover, IVUS is a valuable prognostic parameter for patients deferred from coronary angioplasty[4].

A number of studies have previously compared MDCT with intravascular ultrasound, indicating a good conformity between these two methods[5,6]. Recent meta-analysis data showed that, compared with IVUS, coronary computed tomography angiography (CTA) appears to be highly accurate for the estimation of luminal area, percentage of area stenosis, plaque volume, and plaque area and for the detection of plaque[7]. However, most studies evaluated specific regions of interest within the coronary tree, restricting the analysis to segments with atherosclerotic plaques by IVUS[5,6,7]. It is important to note that, in clinical practice, MDCT images are commonly analyzed following an all-segment scheme without the aid of a coronary map to focus the assessment on specific regions of interest.

It is important to evaluate the diagnostic performance of MDCT in a comprehensive manner, including both coronary segments with atherosclerosis as well as portions without significant disease. Therefore, the present study compared 64-slice MDCT with IVUS for the quantitative assessment of coronary luminal dimensions following an inclusive, whole-artery analytic strategy.

Methods

Overall Protocol Design and Study Population

The study included patients with known coronary artery disease who were scheduled for elective coronary stent implantation. Intravascular ultrasound examination was performed at the time of the percutaneous procedure, before any therapeutic intervention. At least one major epicardial vessel without previous angioplasty or surgical treatment was examined with IVUS, but operators were strongly encouraged to acquire IVUS images from all three coronary territories. MDCT was performed 72 h prior to the IVUS procedure as part of the study protocol. The study protocol was approved by the local ethics committee, and written informed consent was obtained from each patient.

Ivus Imaging and Analysis

The IVUS examination was carried out after the administration of intracoronary nitrate, utilizing a 20 MHz electronic multi-array 2.9F catheter (Eagle Eye®, Volcano Corporation Inc., San Diego, CA, USA) connected to a dedicated console (InVision Gold®, Volcano Corporation Inc., San Diego, CA, USA). Acquisition was performed during motorized pullback at a constant speed of 0.5 mm/s (R-100® pullback device, Volcano Corporation Inc., San Diego, Ca, USA). Off-line IVUS analyses were performed by operators blinded to other patients' characteristics, using a dedicated software (pcVH 2.2 ®; Volcano Corporation Inc., San Diego, CA, USA) for the measurement of vessels. The luminal and external elastic lamina (EEL) boundaries were traced semi-automatically to obtain area measurements. Total plaque plus media area was calculated as EEL area minus lumen area. Plaque burden was calculated as the plaque plus media area divided by the EEL area, multiplied by 100. A coronary plaque was diagnosed to be present in all segments with plaque burden > 40%. A coronary segment was considered to be free of atherosclerosis or having only mild atherosclerotic plaque when the plaque burden was ≤ 40%.

Multidetector Computer Tomography

Patients with a heart rate greater than 65 bpm received up to 15 mg of intravenous metoprolol before the acquisition of MDCT images, unless contraindicated. Sublingual nitrate was given to all patients prior to the acquisition of MDCT images[8]. All scans were performed utilizing a 64-slice MDCT scanner (Aquillion 64™, Toshiba Medical Systems, Japan). Acquisition protocols were applied as previously described[9]. Patients first underwent calcium scanning performed with prospective electrocardiogram gating and a detector collimation of 64 x 3.0 mm. The trigger delay for prospective gating was adjusted to the heart rate in order to obtain the images during the rest period of the coronary arteries. Only patients with a total calcium score < 600 were included. After calcium scanning, the CT coronary angiography protocol was performed using a 64 x 0.5 mm detector collimation and a minimum gantry rotation time of 400 ms, and the scanner settings including pitch were adjusted according to patient's sex and weight[9]. After the intravenous injection of contrast medium (Iopamidol, 370 mg iodine/ml, Bracco) and after reaching a threshold of 180 Hounsfield units (HU), at the descending aorta, the helical scan for CT coronary angiography was performed.

Quantitative coronary analysis was performed with a dedicated workstation (Vitrea2, v3.9 loaded with the Coronary Vessel Probe and SURE Plaque software; all by Vital Images Inc, Plymouth, MN, USA). All analyses were performed by operators blinded to clinical and IVUS characteristics, following a predefined analytic plan. First, the average lumen attenuation was measured in the ascending aorta (at the level of the coronary ostia) and used as the parameter to set the threshold for the detection of the coronary lumen borders. Then, the lumen and the vessel borders were semiautomatically reconstructed for the measurement of their areas (Figure 1); thus, permitting the calculation of the plaque plus media area (vessel area minus lumen area) and the percent of plaque burden (plaque plus media area divided by the vessel area, multiplied by 100).

IVUS and MDCT Imaging Coregistration and Segment Analysis

Intravascular ultrasound and 64-slice MDCT images were matched by using reproducible vessel landmarks (e.g., aorto-ostial junction, side branches, etc.) as anatomical axial references. Visible landmarks through the target vessel length were annotated for both IVUS and 64-slice MDCT, and all vessel portions were carefully scrutinized to match the exact counterpart (Figure 1). The left main coronary was computed as a separate vessel for analysis. Repeated measurements by the same operators were performed for 27 segments, randomly selected, and correlation coefficients were used to determine intra-observer and inter-observer variability.

Statistical Analysis

The present study is an exploratory analysis without a prior formal sample size calculation. Nevertheless, the chosen sample size of 20 patients would be sufficient to demonstrate a significant correlation of any given continuous parameter with a Pearson coefficient of 0.65at an alfa of 0.05 and a power of 0.9. Statistical analyses were performed with software SPSS 21 (IBM Corp. Released 2012, IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA). Categorical variables are presented as percentages and continuous variables as means and standard deviations. Continuous variables were analyzed for correlation using the Pearson's correlation test. The method proposed by Bland and Altman[10,11] was utilized to evaluate the differences between the measurements of 64-slice MDCT and IVUS for mean lumen area, minimal lumen area, and minimal lumen diameter. In Bland and Altman's method, the average of the two measurements (64-slice MDCT and IVUS) is plotted against the difference between them (64-slice MDCT minus IVUS) with 95% limits of agreement calculated to evaluate the measurement concordance. For all comparison tests, $p < 0.05$ was considered significant.

Results

The study population consisted of 21 patients with 70 imaged vessels (3.3 vessels per patient) and a final total length of 114.6 ± 38.3 mm per patient (ranging from 39.5 mm to 181.0 mm) (Table 1). All patients had coronary artery disease with percutaneous coronary intervention indication. Men were 71% of the study population, and mean

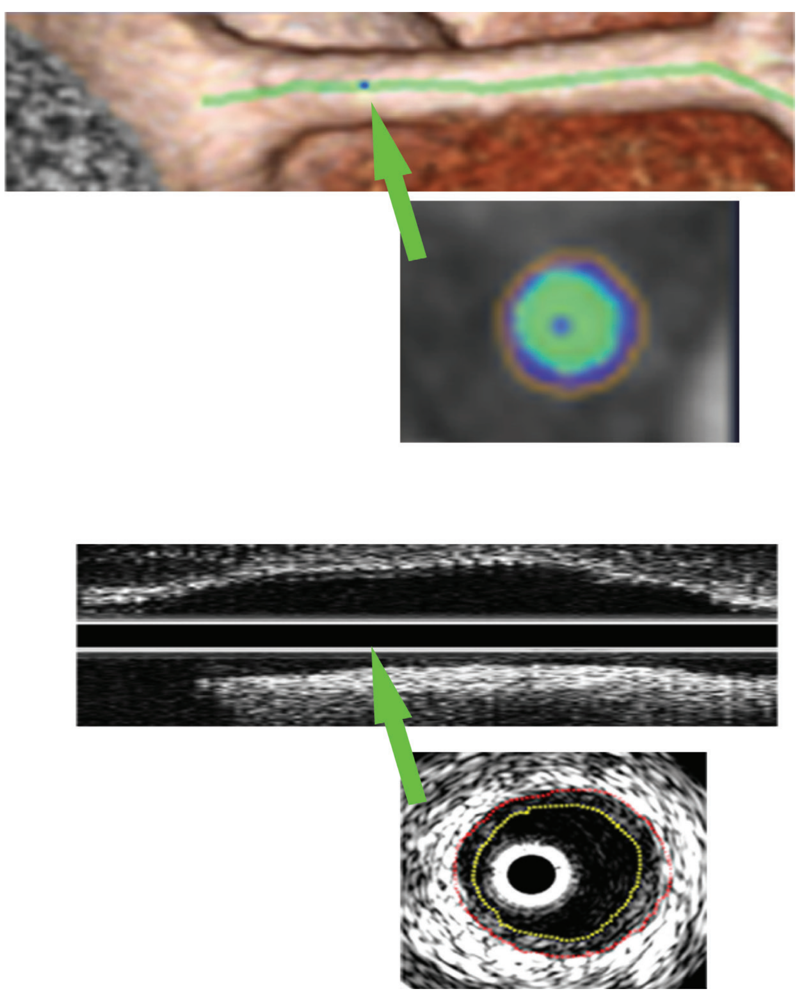

Figure 1 – *Schematic representation of quantitative coronary analysis by 64-slice MDCT (above) and IVUS (below). The upper images show the longitudinal reconstruction for both methods. The lower images show illustrative vessel cross-sections with the outer vessel and lumen (inner) boundaries tracings.*

age was 56 years. There was a high prevalence of diabetes mellitus (48%) and hypertension (71%) (Table 1).

All CT scans were considered of diagnostic quality and all vessel segments > 2 mm were considered for analysis (there were no unevaluable segments). A total of 72 plaques were identified by IVUS (plaque burden > 40%) with 95 remaining coronary segments without plaque or with mild atherosclerotic disease (plaque burden ≤ 40%).

At patient and vessel levels, the measurements of average lumen area and minimal lumen area were highly correlated between IVUS and 64-slice MDCT (correlation coefficient: patient level 0.75 and 0.78, vessel level 0.91 and 0.93, p < 0.01 for all comparisons) (Table 2). At the patient level there was a moderate correlation between minimal lumen diameter measured by IVUS and by 64-slice MDCT (correlation coefficient: 0.64, p = 0.002) (Table 2). At the segment level, the correlation between 64-slice MDCT and IVUS was similar in segments with or without a plaque burden > 40% (Table 2). However, the average absolute difference in measurements tended to be larger among coronary segments without atherosclerotic plaque (Table 2 and Figure 3). Overall, 64-slice MDCT underestimated the lumen size with a relatively wide dispersion of the differences (Table 2 and Figure 2). The correlation coefficients for repeated IVUS and

Table 1 – Patients characteristics (n = 21)

Age, years	56.6 ± 9.5
Male	71.4
Weight, kg	69.2 ± 9.9
Height, cm	161.2 ± 7.3
Diabetes	47.6
Hypertension	71.4
Previous myocardial infarction	38.1
Multivessel disease	38.1
Stable coronary disease	52.3
Total length of analyzed vessels, mm	114.6 ± 38.3
Imaged vessel (n = 70)	
Left main	24.3
Left anterior descending	25.7
Diagonal	1.4
Left circumflex	22.9
Obtuse marginal	1.4
Right coronary	24.3

Numbers are mean ± standard deviation or percentage.

Table 2 – Quantitative coronary lumen parameters by IVUS and by 64-slice MDCT at patient, vessel, and segment levels

	IVUS	64-slice MDCT	Difference	Correlation coefficient	p-value for correlation
Per-patient analysis (n = 21)					
Mean lumen area, mm^2	8.6 ± 2.1	7.8 ± 2.3	-0.7 ± 1.6	0.75	< 0.001
Minimal lumen area, mm^2	3.3 ± 1.3	1.8 ± 1.9	-1.5 ± 1.2	0.78	< 0.001
Minimal lumen diameter, mm	1.8 ± 0.3	1.0 ± 0.6	-0.8 ± 0.5	0.64	0.002
Per-vessel analysis (n = 70)					
Mean lumen area, mm^2	10.1 ± 5.3	9.1 ± 4.8	-1.0 ± 2.2	0.91	< 0.001
Minimal lumen area, mm^2	6.9 ± 5.3	5.3 ± 4.9	-1.5 ± 1.9	0.93	< 0.001
Minimal lumen diameter, mm	2.5 ± 0.9	1.9 ± 1.0	-0.6 ± 0.5	0.87	< 0.001
Per-segment analysis (n = 167)					
Segments with IVUS-PB ≤ 40% (n = 95)					
Mean lumen area, mm^2	10.2 ± 5.2	9.1 ± 4.5	-1.1 ± 2.3	0.89	< 0.001
Minimal lumen area, mm^2	8.1 ± 4.6	6.8 ± 4.1	-1.4 ± 2.3	0.87	< 0.001
Minimal lumen diameter, mm	2.8 ± 0.8	2.4 ± 0.8	-0.5 ± 0.5	0.78	< 0.001
Segments with IVUS-PB > 40% (n = 72)					
Mean lumen area, mm^2	7.1 ± 2.9	7.0 ± 3.3	-0.1 ± 1.8	0.84	< 0.001
Minimal lumen area, mm^2	5.1 ± 2.8	4.3 ± 3.3	-0.9 ± 1.9	0.82	< 0.001
Minimal lumen diameter, mm	2.2 ± 0.5	1.7 ± 0.8	-0.5 ± 0.5	0.76	< 0.001

Numbers are mean ± standard deviation.
IVUS: intravascular ultrasound; MDCT: multidetector computed tomography; PB: plaque burden

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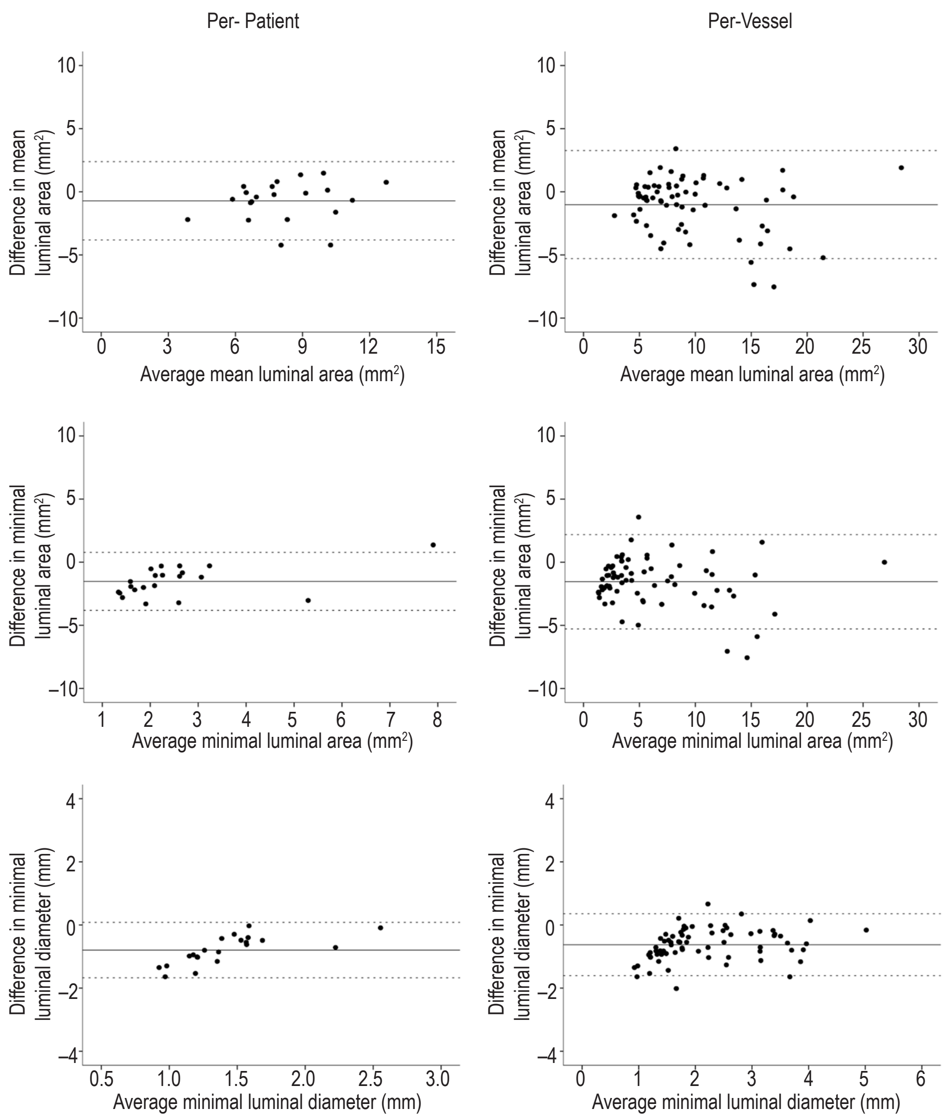

Figure 2 – *Bland-Altman graphs for 64-slice MDCT and IVUS measurements at patient and vessel levels. Mean lumen area (A), minimal lumen area (B), and minimal lumen diameter (C) in per-patient (left) and per-vessel analyses (right). The solid lines represent the mean difference in measurements, and the traced lines represent the upper and lower 95% confidence intervals for the difference in measurements.*

64-slice MDCT lumen area tracings were 0.90 and 0.91, respectively Table 3 shows the diagnostic performance of 64-slice MDCT for detecting luminal areas < 4.0 mm² and lumen diameters < 1.8 mm by IVUS, cutoff values previously shown to be markers of flow-restrictive coronary lesions[3]. Interestingly, the accuracy to detect these IVUS luminal cutoffs was not notably affected by the presence or absence of atherosclerotic plaques (Table 3).

Discussion

Currently, the primary clinical role of 64-slice MDCT is the evaluation of coronary luminal obstructions. This study reports that the assessment of coronary lumen by 64-slice MDCT shows excellent correlation with IVUS, with a good overall diagnostic ability to quantify coronary luminal dimensions regardless of the presence or absence of underlying atherosclerotic plaques.

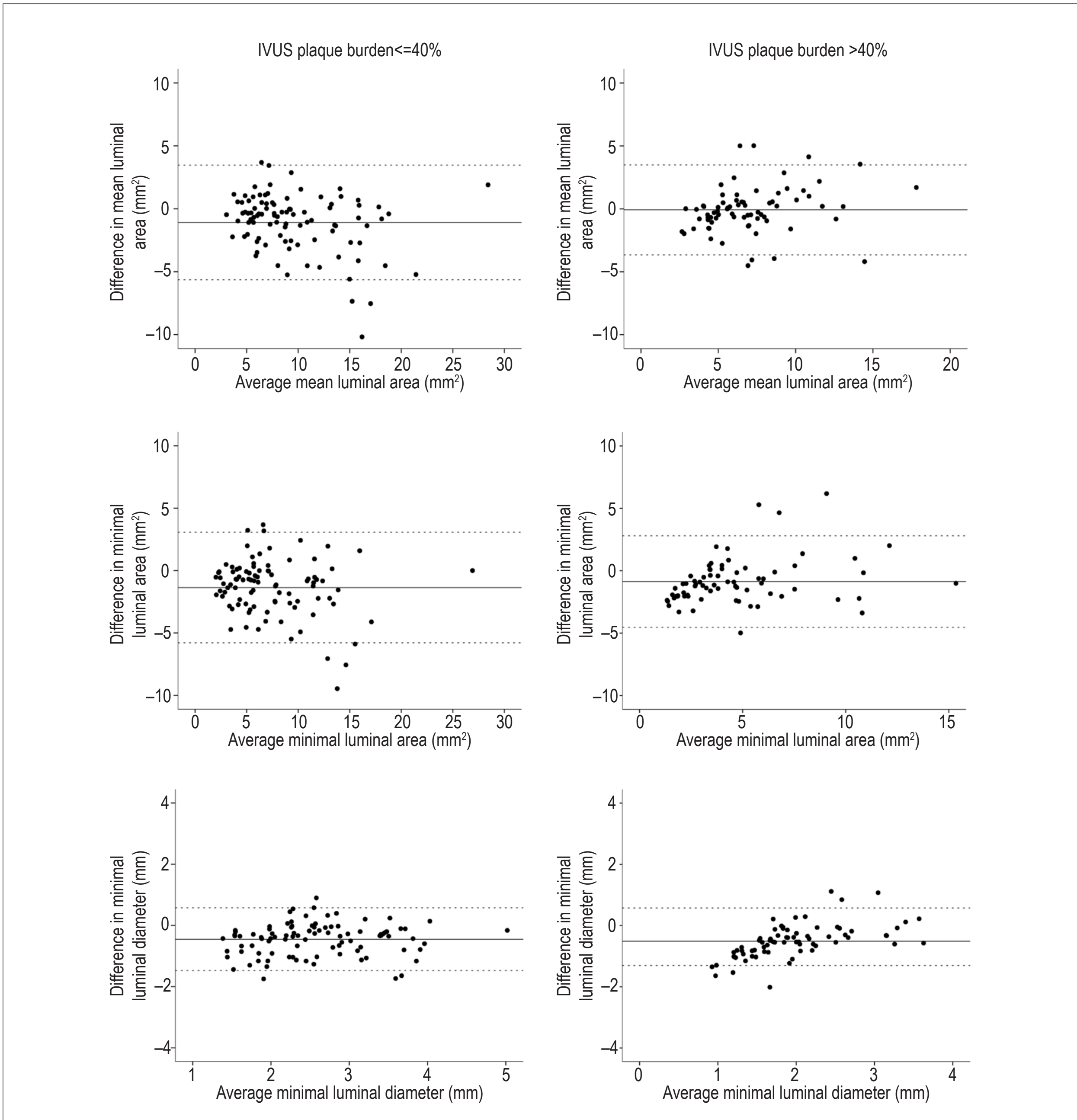

Figure 3 – *Bland-Altman graphs for 64-slice MDCT and IVUS measurements at segment level. Mean lumen area (A), minimal lumen area (B), and minimal lumen diameter (C) for segments without significant plaques (IVUS plaque burden ≤ 40%; left) and for segments with atherosclerotic plaque (IVUS plaque burden > 40%; right). The solid lines represent the mean difference in measurements, and the traced lines represent the upper and lower 95% confidence intervals for the difference in measurements.*

Although significantly correlated with IVUS, the measurements by 64-slice MDCT slightly underestimate the lumen area and the minimal lumen diameter with a relatively wide margin of error. In a previous study, Cademartiri et al. showed that lumen attenuation measured by CTA significantly affected the measured plaque attenuation[12]. The higher the lumen attenuation, the higher the plaque attenuation is. In contrast, calcium attenuation and surrounding fat attenuation were not significantly affected. On the basis of this finding, a semiautomatic tool for tracing coronary lumen and plaque borders based on aortic lumen attenuation could underestimate the luminal area of segments with plaque and reduce the specificity of CTA to identify non-significantly diseased segments by IVUS. Nevertheless, 64-slice MDCT showed a good global predictive accuracy for the detection of an IVUS luminal area < 4.0 mm^2 and an IVUS minimal lumen diameter < 1.8 mm, parameters previously shown to be markers of

Table 3 – 64-slice MDCT sensitivity, specificity, negative predictive value, positive predictive value, and global predictive accuracy* for the detection of luminal area < 4.0 mm² and luminal diameter < 1.8 mm by IVUS†

	Luminal area < 4.0 mm²	Luminal diameter < 1.8 mm
Per-patient analysis (n = 21)		
Prevalence	86%	67%
Sensitivity	100%	100%
Specificity	33%	29%
Negative predictive value	100%	100%
Positive predictive value	90%	73%
Global predictive accuracy	0.82	0.74
Per-vessel analysis (n = 70)		
Prevalence	44%	24%
Sensitivity	90%	94%
Specificity	69%	27%
Negative predictive value	70%	97%
Positive predictive value	70%	41%
Global predictive accuracy	0.90	0.90
Per-segment analysis (n = 167)		
Segments with IVUS-PB ≤ 40% (n = 95)		
Prevalence	14%	6%
Sensitivity	93%	100%
Specificity	83%	77%
Negative predictive value	99%	100%
Positive predictive value	48%	22%
Global predictive accuracy	0.92	0.89
Segments with IVUS-PB > 40% (n = 72)		
Prevalence	49%	21%
Sensitivity	83%	93%
Specificity	69%	49%
Negative predictive value	81%	97%
Positive predictive value	73%	33%
Global predictive accuracy	0.87	0.89

IVUS: intravascular ultrasound; MDCT: multidetector computed tomography; PB: percent plaque burden
** Global predictive accuracy calculated as the area under the receiver operating characteristic curve (C-index)*
† IVUS parameters previously shown to be associated with flow-limiting lesions.(3)

flow-limiting coronary lesions[3]. In particular, 64-slice MDCT showed excellent sensitivity and negative predictive value for the identification of patients or vessels with the above characteristics at the expense of poor specificity and positive predictive value. These findings reinforce the primary clinical role of 64-slice MDCT for screening and ruling out, rather than ruling in, coronary luminal obstruction.

Our findings were obtained in the context of a blinded whole-artery 64-slice MDCT assessment, with no previous indication for focusing on a specific plaque-containing segment. It is important to highlight that this analytic approach emulates the way 64-slice MDCT is interpreted in clinical practice. The fact that the diagnostic performance of 64-slice MDCT for lumen assessment was not substantially different for segments with or without plaques when using IVUS is reassuring and strengthens the value of 64-slice MDCT as a clinical tool. It must be emphasized that the assessment of segments with minimal coronary disease is of clinical relevance, because of the potential impact on future disease progression and acute events and because of the importance of analyzing segments beyond the stenosis site when planning the therapeutic strategy.

Limitations

It must be emphasized that the present study is mainly a methodological analysis with limited immediate clinical application. The main limitation of our study is the relatively small sample size included in the analysis. The patient population analyzed had a relatively high risk profile, which may limit our ability to extrapolate the results of this study to other clinical scenarios. Exclusion of patients with coronary calcium score > 600 could have overestimated the correlation between IVUS and CTA for measurements of coronary lumen area. In a previous study, the presence of calcification was found to be independently correlated to coronary CTA inaccuracy in evaluating coronary lumen area[13]. Each patient contributed with multiple measurements; thus, affecting data independence. Nonetheless, such limitation is a drawback potentially found in every study aiming to evaluate the imaging of coronary atherosclerotic disease.

Conclusion

This study demonstrates that 64-slice MDCT has a good correlation with IVUS for the evaluation of the coronary artery lumen in segments with significant plaques as well as in segments without plaques. Our data suggest that 64-slice MDCT can be used by the clinician to comprehensively define coronary artery anatomy in patients with coronary artery disease, thereby improving clinical risk stratification and facilitating effective clinical care.

Author contributions

Conception and design of the research: Falcão JLAA, Silva ER, Rochitte CE, Lemos PA. Acquisition of data: Falcão JLAA, Falcão BAA, Gurudevan SV, Campos CM, Silva ER, Shiozaki AA, Coelho-Filho OR, Lemos PA. Analysis and interpretation of the data: Falcão JLAA, Falcão BAA, Gurudevan SV, Campos CM, Rochitte CE, Shiozaki AA, Coelho-Filho OR, Lemos PA. Statistical analysis: Falcão JLAA, Rochitte CE, Lemos PA. Obtaining financing: Falcão JLAA, Rochitte CE, Lemos PA. Writing of the manuscript: Falcão JLAA, Kalil Filho R, Lemos PA. Critical revision of the manuscript for intellectual content: Falcão JLAA, Kalil Filho R, Rochitte CE, Lemos PA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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