Diagn Interv Radiol 2016; 22:334-340

CARDIOVASCULAR IMAGING

ORIGINAL ARTICLE

Coronary lesion complexity assessed by SYNTAX score in 256-slice dual-source MDCT angiography

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PURPOSE
The SYNTAX Score (SS) has an important role in grading the complexity of coronary artery disease (CAD) in patients undergoing revascularization. Noninvasive determination of SS prior to invasive coronary angiography (ICA) might optimize patient management. We aimed to evaluate the agreement between ICA and multidetector computed tomography (MDCT) while testing the diagnostic effectiveness of SS-MDCT.

METHODS
Our study included 108 consecutive patients who underwent both MDCT angiography with a 256-slice dual-source MDCT system and ICA within 14±3 days. SS was calculated for both ICA and MDCT coronary angiography. Spearman's rank correlation coefficient was used to evaluate the association of SS-MDCT with SS-ICA, and Bland-Altman analysis was performed.

RESULTS
The degree of agreement between SS-ICA and SS-MDCT was moderate. The mean SS-MDCT was 14.5, whereas the mean SS-ICA was 15.9. After dividing SS into three groups (high [≥33], intermediate [23–32], and low [≤22] subgroups), agreement analysis was repeated. There was a significant correlation between SS-MDCT and SS-ICA in the low SS group (r=0.63, $P = 0.043$) but no significant correlation in the high SS group (r=0.036, $P = 0.677$). The inter-test agreement analysis showed at least moderate agreement, whereas thrombotic lesions and the type of bifurcation lesion showed fair agreement.

CONCLUSION
The calculation of SS-MDCT by adapting SS-ICA parameters achieved nearly the same degree of precision as SS-ICA and was better than SS-ICA, especially in the low SS group.

Awareness of the risk of complications before interventional coronary procedures and treatment may lower the rate of these complications. The SYNTAX score (SS) is a scoring system to indicate the complexity of coronary artery disease (CAD), to select the optimal technique for revascularization, and to identify patients at risk of major adverse events following percutaneous coronary intervention (PCI) (1–3). Recently, the reproducibility of angiographic SSs has been shown to be clinically acceptable (4, 5). Angiographic SSs are based on lesions and include parameters such as the dominancy, number, location, and length of the lesion, vessel tortuosity, grade of calcification, presence of thrombus, and branching. The total SS is obtained by multiplying the score for each separate lesion (6). The effectiveness of these scores has brought them in clinical practice to predict long-term prognosis and determine the most convenient treatment procedure for CAD management (4, 7–10).

There have been many reports in the literature related to the high diagnostic accuracy and noninvasive findings of multidetector computed tomography (MDCT) regarding coronary artery anatomy and lesions compared with invasive coronary angiography (ICA) (11). In contrast to ICA, MDCT has no comprehensive scoring system for the assessment of CAD severity (5, 6, 11).

Improvements in MDCT technology have increased MDCT efficiency, specifically in the imaging of coronary artery lesions and in CAD diagnosis. MDCT has been shown to be a reliable technique for the exclusion of suspected CAD patients, with high diagnostic accu-

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Received 21 July 2015; revision requested 17 September 2015; last revision received 5 November 2015; accepted 12 November 2015.

Published online 21 June 2016.
DOI 10.5152/dir.2015.15298

racy and negative predictive levels of over 95% (12, 13). Despite the increasing utilization of coronary computed tomography (CT) angiography in clinical practice, there is no detailed scoring system to note the severity and complexity of CAD. As is known, the lesion-based scoring system for SS was developed using ICA. The applicability of this scoring system for coronary CT angiography has been reported in the literature, which reported a variable correlation between SS-ICA and SS-MDCT (14–17). Similarly, Stahl et al. (6) reported that preprocedural assessment of lesions by MDCT can indicate the complexity of PCI, and prior coronary CT angiography adds important information for planning PCI.

Therefore, the purpose of our study was to investigate the diagnostic performance of SS-MDCT using a 256-slice dual-source MDCT system and to determine the correlation between SS-MDCT and SS-ICA.

Methods

Patients

This prospective study was performed between February 2013 and February 2015. A total of 289 consecutive patients who underwent both MDCT and ICA with negative biomarkers for low-risk acute coronary syndrome, including unstable angina and negative myocardial markers such as troponin I and T or stable CAD, were included in the study. The patients first underwent MDCT and then ICA examination. The mean time interval between MDCT and ICA was 14±3 days, and there were no complications from MDCT or ICA. The exclusion criteria were as follows: no acceptance of informed consent (n=9), patients with inadequate image quality (n=37), history of coronary artery bypass grafting (n=21), and participation in both examinations within a time interval of >30 days (n=114). A total of 108 patients (66 male, 42 female) were included in our study. The study was approved by the institutional review board, and all patients gave informed consent.

Main points

- The SYNTAX score (SS), a scoring system to indicate the complexity of coronary artery disease (CAD), can help select the optimal technique of revascularization.
- MDCT may help to visualize the location of the segment distal to the occlusion and the length of the occlusion better than ICA does, in addition to calcification and tortuosity information.
- The calculation of SS using 256-slice MDCT by adapting SS-ICA parameters reveals a similar degree of precision as the SS-ICA.

Invasive coronary angiography and SYNTAX score

ICA was performed using standard techniques. To determine lesions causing ≥50% stenosis in coronary vessels with a diameter of ≥1.5 mm, at least two orthogonal views were analyzed. For the calculations of SSs, the most recently updated online version of the SS calculator (2.11) was used (18). Using the previously reported parameters (Table 1), SS was calculated for each patient by an experienced cardiologist (I.H.T., five years of experience) who was blinded to the results of the MDCT examinations for the purposes of the study. SSs were classified as follows: high (≥33), intermediate (23–32), and low (≤22). For bifurcation lesions, the Medina classification was used, which is based on the presence of >50% stenosis in the three segments constituting the bifurcation (Table 2). A score of 1 indicates the presence and 0 indicates the absence of >50% stenosis in each sequential segment, i.e., the proximal main vessel, distal main vessel, and side branch.

CT protocol, parameters, and SS-MDCT

MDCT examinations were performed with a 256-slice dual-source MDCT (Somatom Definition Flash, Siemens Healthcare). A single-dose oral β-blocker (metoprolol) was given 1 h before the examination to all patients with a heart rate of above 70 beats/min if there were no contraindications. Iopromide (70 mL, Ultravist 370, 370 mg/mL, Bayer Schering Pharma), followed by 60 mL of saline, was injected at a flow rate of 5 mL/s into the antecubital vein. A bolus tracking technique was used, and the region of interest was located in the left ventricle. Prospective electrocardiography (ECG)-gated or retrospective low-pitch ECG-gated spiral scan mode with ECG pulsing was used, depending on the heart rate. The scanning protocols were conducted as follows: tube voltage, 100 kV or 120 kV for severely obese patients (body mass index [BMI] >30; 23 patients); gantry rotation time, 270 ms; slice acquisition, 2×128×0.625 mm by means of a z-flying focal spot; pitch, 0.23; and tube current, 320 mA. MDCT data sets were reconstructed in the best systolic and best diastolic phases of the R-R interval, with a slice thickness of 0.75 mm and 0.4 mm increments. All image data sets were transferred to an off-line workstation (Syngo Multimodality Workplace Siemens, Siemens) for analysis.

SS-MDCT was calculated by two experienced radiologists (M.K. and U.B. with 10 and five years of experience in MDCT coronary angiography, respectively). In the case of disagreement, a final decision was reached by consensus.

SS-MDCT was classified as low (≤22), intermediate (23–32), and high (≥33). There were no predetermined or accepted criteria for assessment of SS by MDCT. Therefore, the SS-ICA algorithm was used and adapted for the calculation of SS-MDCT (Table 1). SS-MDCT was calculated using the components of SS-ICA, except for thrombus and heavy calcification. Chronic total occlusion (CTO) was defined as a sudden interruption of opacification on images. In the absence of apparent bridging collateral or retrograde collateral flow in the MDCT images, the presence of an opacification distal to the occlusion was accepted as bridging collateral or retrograde collateral flow. The presence of an opacification distal to the occlusion was accepted as collateral flow, and the age of the occlusion was admitted to be >3 months. However, no opacification distal to the occlusion was accepted as the absence of collateral flow and the age of the occlusion was considered to be <3 months.

The interquartile range (IQR) was also determined for the ICA and MDCT SSs. Inter-test agreement analysis was performed to compare ICA and MDCT with regard to the parameters used in calculating SS: coronary dominance, total number of lesions, CTO, and number of bifurcations, trifurcations, aorto-ostial lesions, tortuous lesions, long lesions, heavy calcific lesions, and segments with diffuse small-vessel disease. Because of difficulty in differentiating between subtotal and total lesions on CT angiograms, the presence of calcification on the side of the occlusion, negative remodeling, and an occlusion length of >9 mm were defined as CTO. Inter-test agreement analysis showed at least moderate agreement, whereas thrombotic lesions and the type of bifurcation lesion showed fair agreement (Table 3).

The effective radiation dose was calculated using the dose-length product, which was derived from the patient protocols of the system and a conversion factor of

Table 1. SYNTAX score parameters (adapted from www.syntaxscore.com)

Parameter	Definition for ICA	Definition for MDCT
Number of total lesions	Each coronary lesion with a stenosis diameter of ≥50% in vessels with a diameter of ≥1.5 mm must be scored	Same
Dominance	Right dominance: the posterior descending coronary artery is a branch of the right coronary artery Left dominance: the posterior descending artery is a branch of the left coronary artery. Co-dominance does not exist as an option in the SYNTAX score	Same
Total occlusion	No intra-luminal antegrade flow (TIMI 0) beyond the point of occlusion. However, antegrade flow beyond the total occlusion might be maintained by bridging collaterals and/or ipsicollaterals	Sudden interruption of opacification in the vessel trace. The presence of opacification distal to the occlusion was accepted as collateral flow, and the age of the occlusion was admitted to be >3 months. However, no opacification distal to the occlusion was accepted as the absence of collateral flow, and the age of the occlusion was considered to be <3 months
Trifurcation	A trifurcation is a division of a main branch into three branches of at least 1.5 mm	Same
Bifurcation	A bifurcation is a division of a main parent branch into two daughter branches of at least 1.5 mm. Bifurcation lesions may involve the proximal main vessel, the distal main vessel, and the side branch according to the Medina classification. The smaller of the two daughter branches should be designated as the "side branch." In the case of the main stem, either the left circumflex artery or LAD can be designated as the side branch depending on their respective calibers	Same
Aorto-ostial lesion	A lesion is classified as aorto-ostial when it is located immediately at the origin of the coronary vessels from the aorta	Same
Severe tortuosity	One or more bends of 90° or more, or three or more bends of 45° to 90° proximal to the diseased segment	Same
Length >20 mm	Estimation of the length of the portion of stenosis that has a ≥50% reduction in luminal diameter in the projection in which the lesion appears to be longest. (In the case of a bifurcation lesion, at least one of the branches must have a lesion length of >20 mm)	Same
Heavy calcification	Multiple persisting opacifications of the coronary wall visible in more than one projection surrounding the complete lumen of the coronary artery at the site of the lesion	Presence of calcium occupying >50% of the vessel cross-sectional area within the lesion location
Thrombus	Spherical, ovoid, or irregular intraluminal filling defect or lucency surrounded on three sides by contrast medium observed just distal to or within the coronary stenosis in multiple projections or visible embolization of intraluminal material downstream	Spherical intraluminal filling defect with a low Hounsfield unit value, surrounded on three sides by contrast medium
Diffuse disease/small-vessel disease	Present when at least 75% of the length of any segment(s) proximal to the lesion, at the site of the lesion, or distal to the lesion has a vessel diameter of <2 mm	Same

0.014 mSv/mGy/cm, as recommended by the American Association of Physicists in Medicine Report 96 (19).

Statistical analysis

Continuous variables are expressed as the mean±standard deviation; categorical variables are presented as counts and percentages. Statistical analyses were performed using SPSS 17.0 (SPSS Inc.). Spearman's rank correlation coefficient was used to evaluate the association of SS-MDCT with SS-ICA, and Bland-Altman analysis was performed. The numerical values of SS-MDCT and SS-ICA were compared using the Wilcoxon signed-rank test. The degrees of agreement based on kappa values were as follows: <0 none, 0<slight≤0.20, 0.21<fair≤0.40, 0.41<moderate≤0.60, 0.61<substantial≤0.80, and 0.81<almost perfect≤1.00. A two-sided *P* value of <0.05 was considered to be significant for all tests.

Results

The mean age of the patients was 64.6±6.3 years (range, 47–76 years) and the mean BMI was 25.4±3.7 kg/m^2 (range, 21.4–32.3 kg/m^2) for all patients. In 108 (66 male, 42 female) patients, 18 patients (16.6%) had three-vessel disease, 37 patients (34.2%) had two-vessel disease, 46 patients (42.5%) had one-vessel disease, and seven patients (6.4%) had no significant lesions. The mean heart rate was 61±1.2 beats/min during the MDCT examinations.

In 108 patients, a total of 225 lesions were evaluated in terms of ICA and MDCT scores; 105 lesions (46.6%) were at the left anterior descending (LAD) artery, 64 lesions (28.4%) were at the right coronary artery (RCA), 42 lesions (18.6%) were at the circumflex (Cx) artery, and 14 lesions (6.2%) were at the left main coronary artery.

Table 2. Number and type of bifurcation lesions assessed by ICA and MDCT

Medina classification	ICA n (%)	MDCT n (%)
Type 1.0.0	17 (17.3)	17 (16.7)
Type 1.1.0	10 (10.2)	12 (11.7)
Type 1.1.1	13 (13.3)	16 (15.7)
Type 0.1.0	21 (21.4)	11 (10.8)
Type 0.1.1	11 (11.2)	10 (9.8)
Type 0.0.1	18 (18.4)	25 (24.5)
Type 1.0.1	8 (8.2)	11 (10.8)
Total	98 (100)	102 (100)

"1" indicates the presence and "0" indicates the absence of >50% stenosis for each sequential segment (proximal main vessel, distal main vessel, and side branch).
MDCT, multidetector computed tomography; ICA, invasive coronary angiography.

Table 3. Inter-test agreement between SYNTAX score parameters calculated using ICA and MDCT

	n (%)	Weighted kappa	*P*
Total occlusions	16 (7.1)	0.59 (0.51–0.78)	0.061
Bifurcation lesions	17 (7.6)	0.38 (0.28–0.55)	0.072
Aorto-ostial lesions	9 (4)	0.49 (0.35–0.71)	0.065
Tortuosities	5 (2.2)	0.54 (0.45–0.69)	0.069
Heavy calcific lesions	55 (26.4)	0.59 (0.43–0.72)	0.063
Thrombotic lesions	5 (2.2)	0.37 (0.11–0.74)	0.083
Long lesions	11 (4.9)	0.55 (0.41–0.68)	0.062
Diffuse/small-vessel diseases	14 (6.2)	0.42 (0.18–0.66)	0.073
Patients with right dominance	86 (79.6)	0.78 (0.55–0.82)	0.049

ICA, invasive coronary angiography; MDCT, multidetector computed tomography.

Table 4. Inter-test agreement between SYNTAX score tertiles calculated using ICA and MDCT

		SS-MDCT			
		Low SS (≤22)	Intermediate SS (23–32)	High SS (≥33)	Total n (%)
SS-ICA	Low SS (≤22)	37	8	0	45 (41.6)
	Intermediate SS (23–32)	2	28	2	32 (29.6)
	High SS (≥33)	0	5	26	31 (28.8)
	Total, n (%)	39 (36.1)	41 (37.9)	28 (26)	108 (100)

ICA, invasive coronary angiography; SS, SYNTAX score; MDCT, multidetector computed tomography.

Of 225 lesions, ICA diagnosed 16 CTOs (7.1%); 11 occlusions (68.8%) were located at the middle segment of the RCA, four (25%) at the middle of the LAD artery and one (6.25%) at the Cx artery. Using ICA as the reference standard, MDCT correctly assessed 15 of 16 (93.7%) occlusions; a false-negative lesion was located at the middle segment of the RCA and evaluated as 50%–99% stenosis. The results recorded by ICA and MDCT for the number and type of bifurcation lesions are shown in Fig. 1.

Using ICA, 17 trifurcation lesions (7.5%) and nine aorto-ostial lesions (4%) were diagnosed, whereas 17 trifurcation lesions (7.5%) and 12 aorto-ostial lesions (5.3%) were diagnosed using MDCT. Five tortuosities were detected by both modalities. Using ICA, 55 heavy calcifications were diagnosed (24.4%), whereas 62 calcifications were diagnosed by MDCT (27.5%). Of the five thromboses diagnosed by ICA, MDCT correctly assessed three (Fig. 2). Two false-negative lesions were identified as plaques causing 50%–99% stenosis. Using ICA, 11 long lesions (4.8%) and 14 cases of diffuse small-vessel disease (6.2%) were diagnosed, whereas 12 long lesions (5.3%) and 12 cases of diffuse small-vessel disease (5.3%) were diagnosed by MDCT.

We did not detect any statistical difference between the numerical values of the SS-ICA and SS-MDCT ($P = 0.081$).

In total, there was a statistically significant correlation between SS-MDCT and SS-ICA (r=0.79, $P < 0.001$). The median value of SS-MDCT was 14.5 (IQR, 9–20.1; range, 2–39), whereas the median value of SS-ICA was 15.9 (IQR, 7.3–21.1; range, 3–47) (Fig. 3).

Correlation analysis was performed after dividing the entire population into high (≥33), intermediate (23–32), and low (≤22) subgroups, and agreement analysis was repeated. There was a significant correlation between SS-MDCT and SS-ICA in the low SS group (r=0.63, $P = 0.043$), but no significant correlation in the high SS group (r=0.036, $P = 0.677$) (Table 4).

Inter-test agreement analysis was performed to compare ICA and MDCT with regard to the parameters used in calculating the SS: coronary dominance, total number of lesions, CTO, and number of bifurcations, trifurcations, aorto-ostial lesions, tortuous lesions, long lesions, heavy calcific lesions, and segments with diffuse small-vessel disease. Inter-test agreement analysis showed at least moderate agreement, whereas thrombotic lesions and the type of bifurcation lesion showed fair agreement (Table 3). The average effective radiation dose for MDCT was 15.04±5.2 mSv (range, 5.4–22.6 mSv).

Discussion

In this study, the mean value of SS-ICA was 15.9, whereas in previous ICA studies the mean SS was higher and ranged from 16.2 to 34.1 (15). However, other studies have reported a similar range of SS values (2, 3). A low SS population may not represent the coronary artery bypass surgery group or the SYNTAX trial population. In addition, there was a significant correlation between SS-MDCT and SS-ICA in the low SS group, in contrast to the high SS group.

In our study, we found moderate agreement between SS-ICA and SS-MDCT with regard to both continuous and categorical values of the score. Detailed agreement analysis of the parameters of the SS algorithm revealed that the level of agreement was moderate for all parameters except thrombosis and type of bifurcation lesion. The most probable reason for this agreement between the modalities is the use of an evaluation method based on visual char-

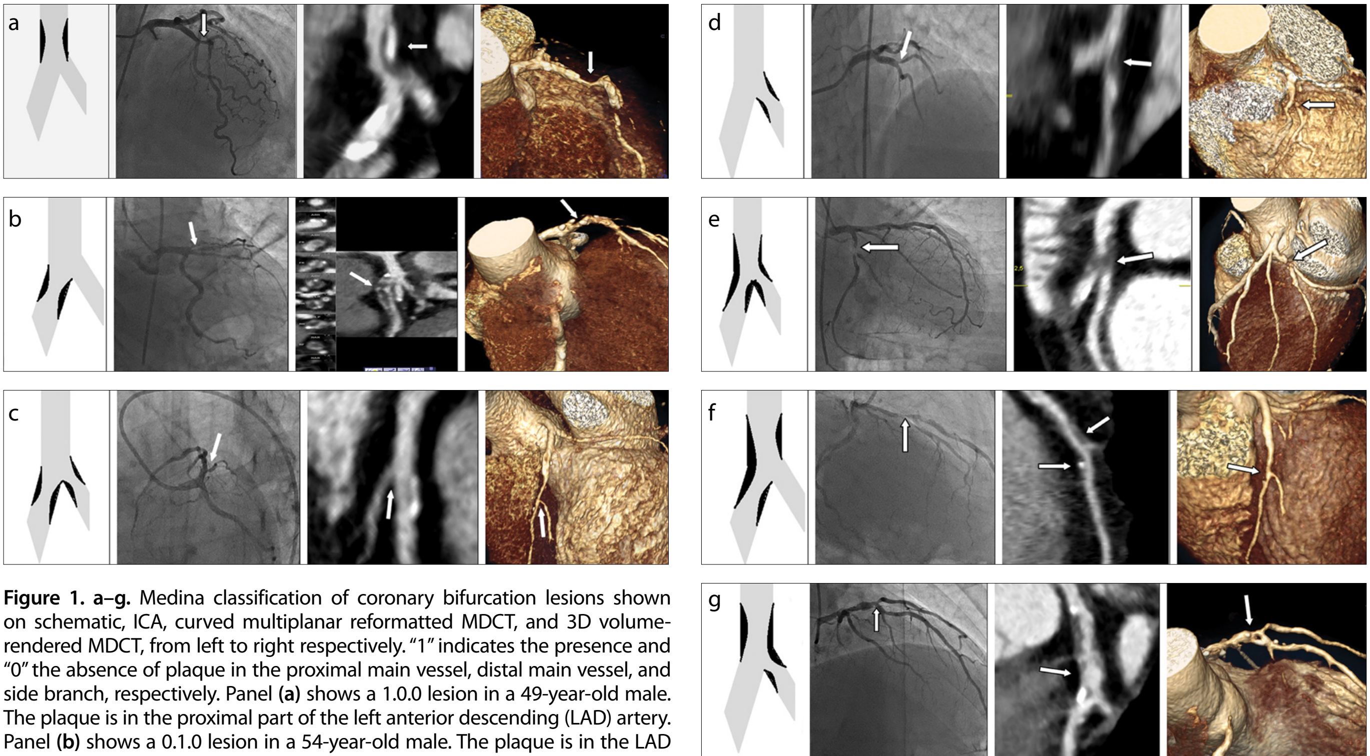

Figure 1. a–g. Medina classification of coronary bifurcation lesions shown on schematic, ICA, curved multiplanar reformatted MDCT, and 3D volume-rendered MDCT, from left to right respectively. "1" indicates the presence and "0" the absence of plaque in the proximal main vessel, distal main vessel, and side branch, respectively. Panel **(a)** shows a 1.0.0 lesion in a 49-year-old male. The plaque is in the proximal part of the left anterior descending (LAD) artery. Panel **(b)** shows a 0.1.0 lesion in a 54-year-old male. The plaque is in the LAD ostium. Panel **(c)** shows a 0.1.1 lesion in a 66-year-old female. The plaque is in the mid-part of the LAD and the proximal part of the diagonal branch. Panel **(d)** shows a 0.0.1 lesion in a 63-year-old male. The plaque is in the proximal part of the diagonal branch. Panel **(e)** shows a 1.1.1 lesion in a 58-year-old male. The plaque is in the proximal and mid-part of the circumflex artery (Cx) and the proximal part of the obtuse marginal branch. Panel **(f)** shows a 1.1.0 lesion in a 61-year-old male. The plaque is in the proximal and mid-part of LAD. Panel **(g)** shows a 1.0.1 lesion in a 60-year-old male. The plaque is in the proximal part of LAD and diagonal branch.

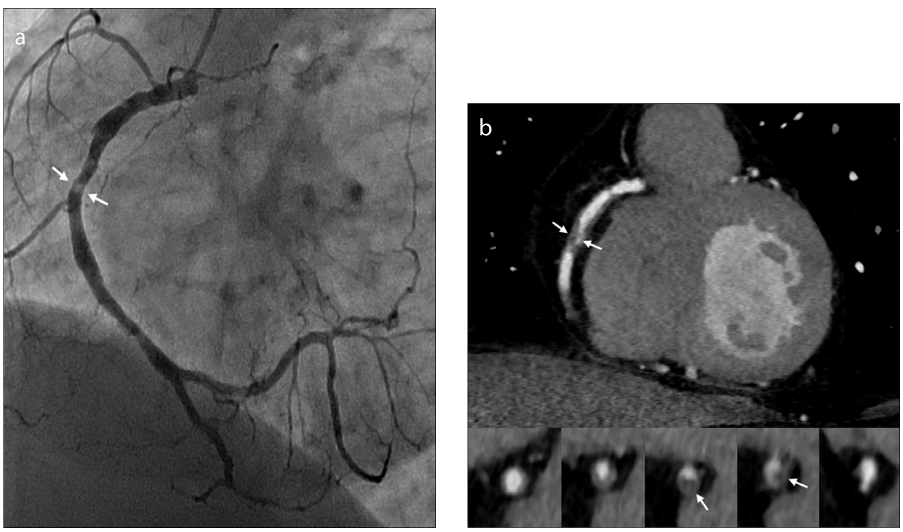

Figure 2. a, b. Thrombus in the right coronary artery (RCA) in a 54-year-old male. Panel **(a)** shows a nonocclusive thrombus *(white arrows)* in the mid-segment of the RCA on invasive right coronary angiogram. Panel **(b)** shows a contrast-filling defect in the mid-segment of the RCA on a maximum-intensity projection image (upper image, *arrows*), a plaque on the second image, which covers the vessel wall and has a higher density, and a thrombus on the fourth image, which is surrounded by contrast medium on three sides and has a lower density, on the reformatted axial vessel section MDCT images (lower images, *arrows*).

acteristics that only allows the inclusion of lesions of a diameter of at least 1.5 mm and ≥50% stenosis. CTOs and some bifurcation lesions are considered as high-risk lesions that have higher restenosis rates and an increased technical failure ratio in PCI (1, 20). This serves to reinforce the importance of appropriate evaluation of these lesions.

The level of agreement was fair for CTO. In MDCT, the presence of anterograde/retrograde collaterals, by allowing opacification of the segments distal to the stenosis, can result in missed or underdiagnosed CTO. However, MDCT may help to visualize the location of the segment distal to the occlusion and the length of the occlusion better than ICA, in addition to information on calcification and tortuosity. The identification of bridging collaterals and retrograde collaterals is not usually possible using previous MDCT systems. It is more feasible to visualize collaterals with new-generation MDCT systems (Fig. 4). In addition, opacification of the segments distal to the stenosis means that there is a collateral, and the presence of bridging collaterals has a small effect on scoring.

There is a discrepancy in the classification and scoring of bifurcation lesions between ICA and MDCT, which is consistent with a previous SYNTAX study (4). In ICA, selected two-dimensional angiographic images and lesion eccentricity provide a limited assessment of bifurcation lesions. Heavy calcification can interfere with the assessment of bifurcation lesions in both ICA and MDCT. In particular, assessment of left main stem lesions by ICA is difficult due to vessel overlap and foreshortening. Importantly, the extension of a lesion that is located in the left main stem may necessitate changing the patient's treatment from PCI to coronary artery bypass grafting (4). Furthermore, the difference in SS between a lesion involving only the left main stem and a distal left main stem lesion extending into the ostium of the LAD artery or the Cx artery is enough to change the score from low to high. Patients with a suspicious lesion in this area can be evaluated using MDCT. Our results were similar to those of other studies (16, 17).

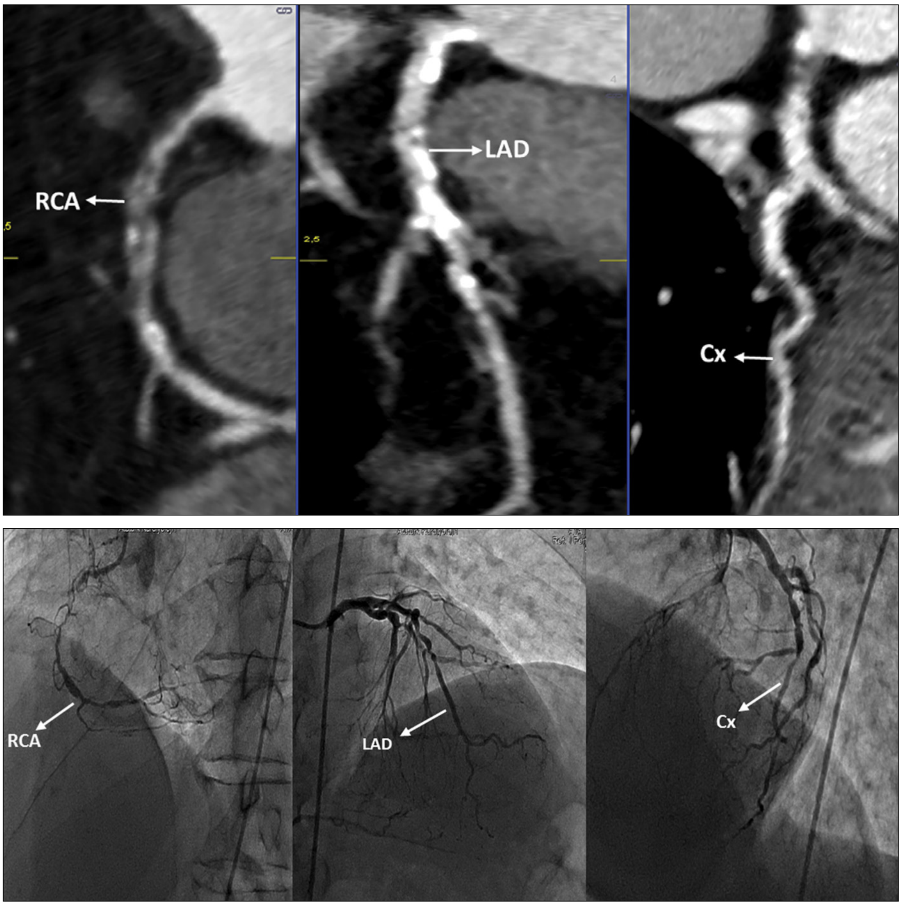

Figure 3. Example of SYNTAX score calculated using ICA and MDCT in a 67-year-old male. SS-MDCT was 34 (upper images, curved multiplanar reformatted MDCT images) and SS-ICA was 28 (lower images, invasive coronary angiograms). RCA, right coronary artery; LAD, left anterior descending; Cx, circumflex artery.

The level of agreement was fair for thrombosis. Although it is difficult to distinguish a thrombus from a plaque, it is possible to visualize lesions with better spatial resolution using the new MDCT systems. Plaques cover the vessel wall and have a higher Hounsfield unit value, whereas thrombi appear as intraluminal filling defects surrounded on three sides by contrast medium and have a lower Hounsfield unit value.

Our study has a few limitations. First, the number and distribution of the patients in our study population are not suitable for comparison with the SYNTAX trial population. Second, neither intraobserver nor interobserver agreement were assessed for the SS-MDCT and SS-ICA. Nevertheless, we believe that this is not particularly relevant for the purposes of this study. Although 20 patients were reviewed for SS-MDCT calculation training, it is natural that operator experience may have a significant influence over the test results. Image quality is an important factor that may affect the agreement level of both MDCT and ICA. However, the diagnostic qualities of ICA or MDCT were not assessed in this study. Failure to evaluate the relationship between the clinical outcomes of the patients and the MDCT-SS results is another limitation of this study.

In conclusion, the SS-MDCT and SS-ICA exhibit moderate agreement. Calculation of SS using 256-slice MDCT by adapting SS-ICA parameters reveals a similar degree of precision to that of the SS-ICA. The standardization of the SS-MDCT may support noninvasive patient management. We recommend that the SS-MDCT should be added to the cardiologic evaluation before invasive procedures. However, further studies such as determining its association with the clinical outcomes of patients should be

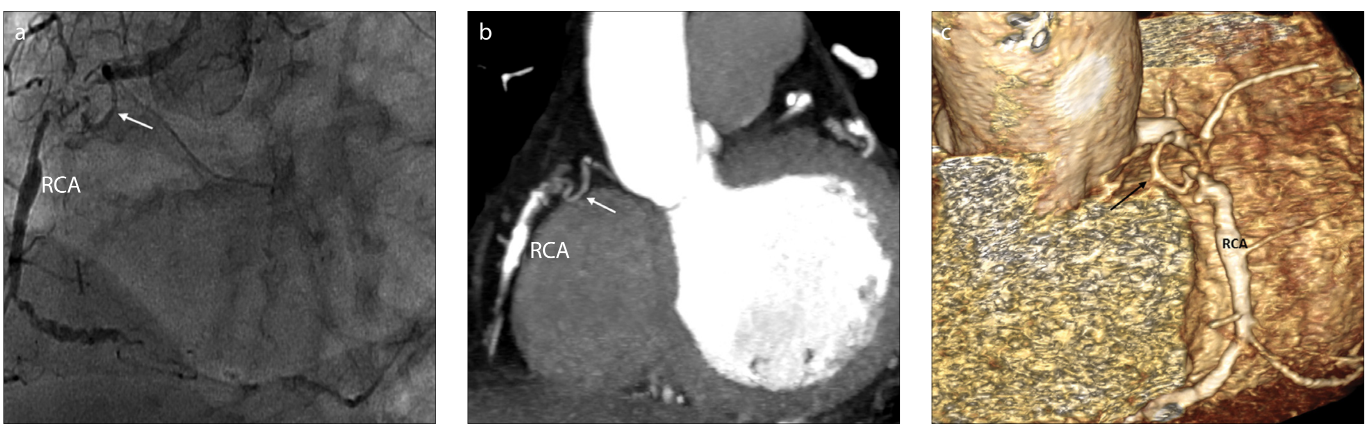

Figure 4. a–c. Bridging collateral in a 65-year-old male. Panel (**a**) shows a bridging collateral of the right coronary artery (RCA) filling the distal part of an occlusion on an invasive coronary angiogram *(arrow)*. Panel (**b**) shows the bridging collateral on a maximum-intensity projection image *(arrow)*. Panel (**c**) shows a 3D volume-rendered image obtained by MDCT *(arrow)*.

performed to evaluate the long-term prognostic role of this scoring system.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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