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Research paper

Quantitative coronary computed tomography assessment for differentiating between total occlusions and severe stenoses

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ABSTRACT

Backgrounds: The impact of quantitative assessment to differentiate total occlusions (TOs) from severe stenoses on coronary computed tomography angiography (CCTA) remains unknown.
Objective: This study investigated whether quantitative characteristics assessed on CCTA could help differentiate a TO from a severe stenosis on invasive coronary angiography (ICA).
Methods: This study is a sub-analysis of the FASTTRACK CABG (NCT04142021) in which both CCTA and ICA were routinely performed. Quantitative analysis was performed with semi-automated CCTA plaque-analysis software. Blinded analysts compared TOs on CCTA, defined as a complete lack of contrast opacification within the coronary occlusion, with corresponding ICA.
Results: Eighty-four TOs were seen on CCTA in 59 of the 114 patients enrolled in the trial. The concordance in diagnosing a TO between ICA and CCTA was 56.0% (n = 47). Compared to severe stenoses, TOs had a significantly longer lesion length (25.1 ± 23.0 mm vs 9.4 ± 11.2 mm, P < 0.001). The best cut-off value to differentiate a TO from severe stenosis was a lesion length of 5.5 mm (area under the curve 0.77, 95% CI: 0.66–0.87), with a 91.1% sensitivity and 61.1% specificity. Dense calcium percentage atheroma volume (PAV) was significantly higher in TOs compared to severe stenoses (18.7 ± 19.6% vs. 6.6 ± 13.0%, P < 0.001), whilst the opposite was seen for fibro-fatty PAV (31.3 ± 14.2% vs. 19.5 ± 10.5%, P < 0.001). On a multivariable logistic regression analysis, lesion length (>5.5 mm) was the only parameter associated with differentiating a TO from a severe stenosis.
Conclusion: In quantitative CCTA analysis, a lesion length >5.5 mm was the only independent predictor differentiating a TO from a severe stenosis.
NCT registration number: NCT04142021.

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CTO, chronic total occlusion; ICA, invasive coronary angiography; PAV, percentage atheroma volume; PCI, percutaneous coronary intervention.

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1. Introduction

Chronic total occlusions (CTOs) of coronary arteries, which are defined as a complete interruption of antegrade blood flow for more than three months,[1] are seen in approximately 20–25% of patients undergoing invasive coronary angiography (ICA). Coronary computed tomography angiography (CCTA) has grown to become one of the primary non-invasive imaging tools to diagnose coronary artery disease (CAD), and can assist in decision-making.[2] Advancements in technology now also enable CCTA to assess additional quantitative characteristics such as the presence and constituents of atherosclerotic plaques, even in the presence of flow-limiting lesions.[3–5] In clinical practice, discordance between ICA and CCTA in the diagnosis of total occlusions (TOs) is frequently encountered, and whilst CCTA has excellent specificity in detecting TOs, its sensitivity is poor.[6] Overall, compared to ICA, the pitfall of CCTA is its limited spatial resolution which can lead to inaccuracy in differentiating a TO from a severe stenosis, and the inability to visualize collateral arteries,[7] despite good opacification of the epicardial bed distal to the occlusion.

Few studies conducted on the factors that may predict discordance between CCTA and ICA in the diagnosis of TOs have concluded that lesion length is the main factor differentiating TOs, defined as TIMI (Thrombolysis in Myocardial Infarction) grade 0 flow on ICA, from severe stenoses.[8,9] However, these conclusions were based on CT-technology from more than a decade ago. Importantly other factors that are assumed to be involved such as lesion characteristics and quantitative assessment could also not be assessed, highlighting the need for reevaluation using contemporary technology. The present study aimed to assess novel CCTA parameters differentiating TOs from severe stenoses when comparing ICA and CCTA.

2. Methods

2.1. Patients population

This study is a sub-study of the FASTTRACK CABG trial (NCT04142021),[10] which in brief was an investigator-initiated single-arm, multicenter, prospective, proof-of-concept, and first-in-man study with feasibility and safety analysis in patients with three-vessel disease with or without left main coronary artery disease (LMCAD) referred for coronary artery bypass graft (CABG) surgery. The surgical revascularization strategy and treatment planning were solely based on CCTA and fractional flow reserve derived from computed tomography (FFR_{CT}) which can provide an accurate physiological assessment in patients with multivessel CAD.[11]

The ICA was used in the treatment decision-making process (e.g. percutaneous vs. surgical revascularization) by a 'Conventional Heart Team' which was not involved in the 'CCTA Planning and Operating Heart Team' or the actual surgical treatment. The flow chart of the original study is shown in Supplemental Fig. 1.

Clinical data were adjudicated by an independent Clinical Events Committee. Safety monitoring was performed by a Data Safety Monitoring Board (DSMB). Each patient provided written informed consent as approved by the Ethical Committee of the respective clinical site. The study was performed in accordance with the Declaration of Helsinki.

2.2. CCTA acquisition protocol

According to the study protocol, a CCTA scan was performed one month before enrollment for the assessment of multivessel CAD with or without LMCAD. All CCTA images were obtained using a 256-slice scanner (Healthcare Revolution CT, GE Healthcare, USA) that had a nominal spatial resolution of 230 μm along the X-Y planes, a rotational speed of 0.28 s, and a Z-plane coverage of 16 cm enabling imaging of the whole heart in one heartbeat.[12,13] The protocol mandated the use of nitrates before CT acquisition and beta-blockers when heart rate was>65 bpm.

2.3. Morphological assessment

For all TOs with a vessel diameter ≥1.5 mm, lesion characteristics such as stump morphology (blunt or not), presence of bridging collaterals, heavy calcification, side branches, and bifurcation lesions were evaluated based on the SYNTAX score algorithm.[14] A calcified lesion on CCTA equated to a calcified area involving >50% of the vessel's cross-sectional area.[15] Positive remodeling was defined by a remodeling index of ≥1.1, which is calculated by the vessel size at the site of the maximal remodeling divided by the vessel size of the reference site. The J-CTO (Multicenter CTO Registry of Japan) and The Computed Tomography Registry of Chronic Total Occlusion Revascularization (CT-RECTOR) scores were calculated according to previous reports.[15,16]

2.4. Definition of TOs and quantitative assessment

Well-trained corelab analysts reviewed CCTA of all patients enrolled in the FASTRACK CABG trial to identify those with TOs, defined by a complete lack of contrast opacification within the coronary occlusion on multiplanar reformation.[17,18] The ICA of these patients were then reviewed by the blinded core-lab analysts to stratify patients as concordant if a TO, defined as the absence of antegrade flow through the lesion (TIMI 0) was confirmed on ICA or discordant if a TO was not seen. ICA was regarded as the gold standard for comparison. All the datasets were analyzed by using semiautomated plaque analysis software (QAngioCT Research Edition version 2.0.5, Medical Imaging Systems [MEDIS], Leiden, the Netherlands). The coronary tree, including vessel and lumen contours, was generated automatically. However, if this could not be done, analysts generated them manually. The complete absence of contrast in the arterial lumen was identified as a TO. The software automatically calculated quantitative parameters, such as lesion length, total plaque volume, and the volume of plaque components. If necessary, manual corrections were done by well-trained observers.

The percentage of atheroma volume (PAV) was defined as the proportion of the total plaque volume occupied by the four components of plaque defined according to their Hounsfield unit (HU) value as dense calcium (>351 HU), fibrous (131–350 HU), fibro-fatty (76–130 HU), and necrotic core (NC) (−30 to 75 HU) tissue.[19] As previously described, the settings for window level and width were fixed at 740 HU and 220 HU.[19,20] To reduce the influence of blooming artifacts for evaluating a calcified plaque in a TO, the settings for the window level and window width were adjusted to 1500 HU and 300 HU respectively.[21]

2.5. Reproducibility of quantitative assessment

All the quantitative parameters, such as plaque volume and the volume of each tissue component (fibrous, fibro-fatty, necrotic core, and dense calcium) were extracted and analyzed. Inter-observer agreement among 25 randomly selected TOs was analyzed by two well-trained corelab analysts (S.K, P.R) blinded to ICA results. Intra-observer agreement was evaluated at least four weeks or longer intervals after the initial assessment.

2.6. Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), or median [interquartile range (IQR)], and Student's t-test was used to compare groups when normally distributed and the Mann-Whitney *U* test when not normally distributed. Categorical variables were expressed as percentages with frequency and were compared with the chi-square test or Fisher's exact test as appropriate. Sensitivity, specificity, positive predictive value, and negative predictive value analysis in identifying TO using ICA as the gold standard was calculated and expressed with a 95% confidence interval (CI) of the mean. Univariable logistic regression analysis was performed to investigate the association between all the quantitative variables and the TO and identify the independent predictor

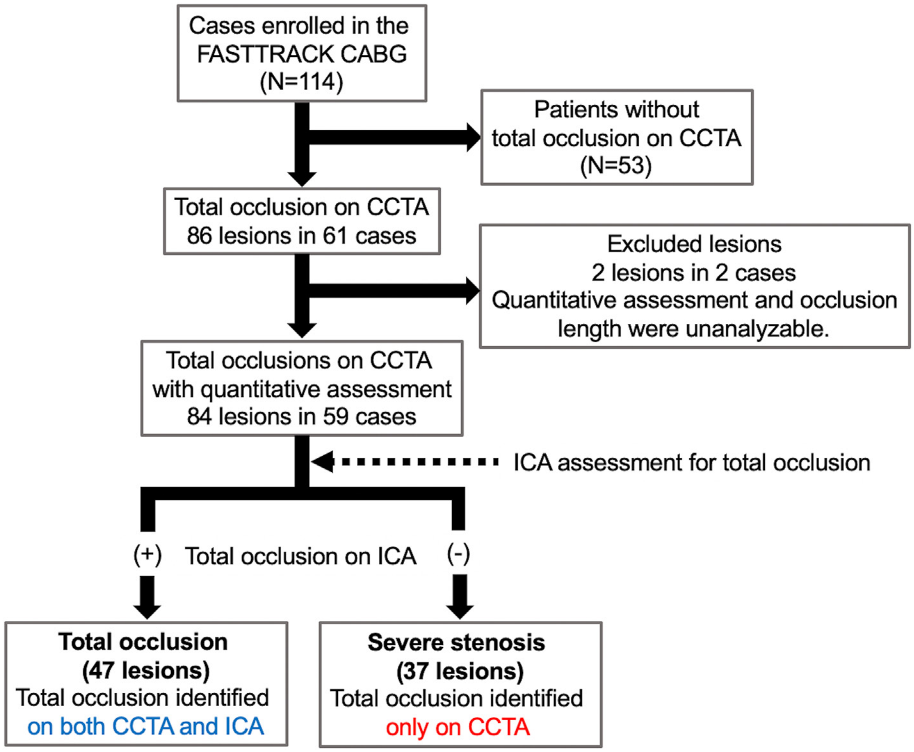

Fig. 1. Flow-chart of the study. **Abbreviations**: CABG: coronary artery bypass grafts; CCTA; coronary computed tomography angiography, ICA; invasive coronary angiography.

of TO amongst the quantitative variables. Multivariable logistic regression analysis was performed adjusting for the following cardiovascular risk factors (age, gender, hypertension, dyslipidemia, current smoking, and diabetes mellitus), and quantitative and qualitative lesion characteristics. The best cut-off for continuous variables was determined using the receiver operating characteristic (ROC) curve analysis.[22] The intraclass correlation coefficient (ICC) was used for comparing inter- and intra-observer variability. Statistical significance was defined as a two-tailed p-value of less than 0.05. All the statistical analyses were performed with SPSS (Version 27.0, SPSS Inc., Chicago, IL).

3. Results

CCTA identified 86 TOs in 61 of the 114 patients enrolled in the study. However, quantitative analysis was only possible in 84 lesions with two occlusions not suitable for analysis. In one case, there was diffuse vessel disease with a distal segment reference diameter ≤1.5 mm, whilst in the other, the end of the occlusion was difficult to visualize on the CCTA. Of the 84 lesions, 47 lesions were TOs on both CCTA and ICA (concordant group), while the remaining 37 lesions which were categorized as TOs by CCTA were not TOs on ICA (discordant group) and were classified as severe stenoses. The study flow chart is shown in Fig. 1.

3.1. Patient and lesion characteristics

Clinical characteristics are summarized in Table 1. Overall, the mean age was 64.2 ± 8.6 years, and 53 (89.8%) patients were male. Six (10.2%) patients had a prior history of myocardial infarction.

Lesion characteristics of TOs seen on CCTA are shown in Table 2. The right coronary artery (RCA; n = 41, 48.8%) was the commonest occluded vessel, followed by the left anterior descending (LAD; n = 23; 27.4%) artery and then the left circumflex (LCX; n = 20, 23.8%). The anatomic lesion distribution was comparable between the TO and severe stenosis groups (P = 0.362). Half (50.0%) of the cohort had a lesion length of ≥20 mm. The presence of any calcification, curvature (≥45°), and lesion length (≥20 mm) were significantly higher in the TO versus the severe stenosis group. The J-CTO score was significantly higher in TOs compared to severe stenoses (P = 0.003), whereas, there was no between-group difference in the CT-RECTOR score (P = 0.084).

Table 1
Baseline patient characteristics.

Characteristics (%, n)	N = 59 patients
Age (years), mean ± SD	64.2 ± 8.6
Male	89.8% (53)
BMI (kg/m^2), mean ± SD	26.6 ± 4.0
COPD	8.5% (5)
PVD	8.5% (5)
DM	30.5% (18)
Current smoking	25.4% (15)
Previous stroke	1.7% (1)
Previous MI	10.2% (6)
Hypertension	83.1% (49)
Dyslipidemia	78.0% (46)
Family history of CAD	30.5% (18)
Previous CABG	0.0% (0)
Chronic kidney disease	5.1% (3)
Previous heart failure	3.4% (2)
LVEF (%), mean ± SD	54.6 ± 8.6

Abbreviations: BMI: body mass index; CAD: coronary artery disease; CABG: coronary artery bypass grafts; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; LVEF: left ventricular ejection fraction; PVD: peripheral vascular disease; SD: standard deviation.

3.2. Quantitative CCTA assessment

The quantitative assessment is summarized in Table 3. Lesion length in the TO group was significantly longer than in the severe stenosis group (25.1 mm vs. 9.4 mm, P < 0.001). TOs had significantly higher total plaque volume, which was inherently related to longer lesion length. The fibro-fatty PAV was significantly larger in severe stenoses than in TOs

Table 2
Lesion characteristics of total occlusions and severe stenoses on coronary computed tomography angiography.

Characteristics (%, n)	All (N = 84)	Total occlusion (N = 47)	Severe stenosis (N = 37)	P value
Lesion location				0.362
RCA	41 (48.8)	26 (55.3)	15 (40.5)	
LAD	23 (27.4)	12 (25.5)	11 (29.7)	
LCX	20 (23.8)	9 (19.1)	11 (29.7)	
Blunt stump	19 (22.6)	13 (27.7)	6 (16.2)	0.213
Any calcification	53 (63.1)	34 (72.3)	13 (35.1)	0.048
Bending (>45°)	12 (14.3)	11 (23.4)	1 (2.7)	0.007
Occlusion length (≥20 mm)	42 (50.0)	31 (66.0)	16 (43.2)	<0.001
Bridging collateral	6 (7.1)	4 (8.5)	2 (5.4)	0.583
Trifurcation lesion	6 (7.1)	2 (4.4)	4 (10.8)	0.247
Bifurcation lesion	17 (20.2)	9 (19.1)	8 (21.6)	0.779
Aorto-ostial lesion	6 (7.1)	4 (8.5)	2 (5.4)	0.583
Multiple occlusion	10 (11.9)	8 (17.0)	2 (5.4)	0.103
J-CTO score				0.003
0	18 (21.4)	5 (10.6)	13 (35.1)	
1	23 (27.4)	9 (19.1)	14 (37.8)	
2	27 (32.1)	20 (42.6)	7 (18.9)	
3	15 (17.9)	12 (25.5)	3 (8.1)	
4	1 (1.2)	1 (2.1)	0 (0.0)	
CT-RECTOR score				0.084
1	50 (59.5)	23 (48.9)	27 (73.0)	
2	22 (26.2)	14 (29.8)	8 (21.6)	
3	9 (10.7)	7 (14.9)	2 (5.4)	
4	3 (6.4)	3 (6.4)	0 (0.0)	

Abbreviations: CT: computed tomography; CTO: chronic total occlusion; CT-RECTOR: Computed Tomography Registry of Chronic Total Occlusion Revascularization; RCA: right coronary artery; LAD: left anterior descending; LCX: left circumflex artery.

Table 3
Lesion length and quantitative coronary computed tomography angiography analysis.

Characteristics	All (N = 84)	Total occlusion (N = 47)	Severe stenosis (N = 37)	P value
Lesion length, mm	18.2 ± 20.2	25.1 ± 23.0	9.4 ± 11.2	<0.001
Vessel volume, mm^3	205.2 ± 316.5	307.9 ± 377.4	74.8 ± 133.1	<0.001
Total plaque volume, mm^3	204.1 ± 316.1	306.5 ± 377.0	74.0 ± 132.9	<0.001
Dense calcium volume, mm^3	41.6 ± 83.3	65.4 ± 98.8	11.0 ± 42.8	0.001
Fibrous plaque volume, mm^3	52.6 ± 85.2	76.4 ± 96.6	22.4 ± 56.1	0.002
Fibrous-fatty plaque volume, mm^3	36.8 ± 61.9	15.6 ± 20.5	53.5 ± 77.1	0.002
Necrotic core, volume, mm^3	63.8 ± 126.7	96.7 ± 158.6	22.2 ± 40.4	0.003
Dense calcium PAV, %	13.4 ± 17.9	18.7 ± 19.6	6.6 ± 13.0	0.001
Fibrous PAV, %	27.1 ± 16.6	26.7 ± 14.2	27.6 ± 19.5	0.824
Fibro-fatty PAV, %	24.7 ± 13.6	19.5 ± 10.5	31.3 ± 14.2	<0.001
Necrotic core, PAV, %	32.6 ± 20.8	32.4 ± 20.6	32.9 ± 21.1	0.911
Remodeling index	1.07 ± 0.22	1.07 ± 0.22	1.06 ± 0.22	0.724

Abbreviations: PAV: percent atheroma volume.

(53.5 ± 77.1%, vs. 15.6 ± 20.5%, P = 0.002), with the opposite seen for dense calcium PAV (6.6 ± 13.0% vs. 18.7 ± 19.6%, P < 0.001). The remodeling index was comparable between the two (1.07 ± 0.22 vs. 1.06 ± 0.22, P = 0.776). A representative case of quantitative CCTA assessment is displayed in Supplementary Fig. 2.

3.3. Intra- and inter-observer variability of quantitative coronary plaque analysis

The intra-observer reproducibility between the first and second evaluations for 25 selected lesions was excellent: vessel volume, ICC 0.999; plaque volume, ICC 0.998; necrotic core plaque volume, ICC 0.994; fibro-fatty plaque volume, ICC 0.995; fibrous plaque volume, ICC 0.999; and dense calcium volume, ICC 0.999. The inter-observer reproducibility between two corelab analysts was also high: vessel volume, ICC 0.999; plaque volume, ICC 0.993; necrotic core plaque volume, ICC 0.995; fibro-fatty plaque volume, ICC 0.991; fibrous plaque volume, ICC 0.997; and dense calcium volume, ICC 0.998.

3.4. The cut-off value for lesion length on CCTA to predict a TO on ICA

ROC analysis demonstrated that the best cut-off value to predict a TO on ICA was 5.5 mm with an area under the curve of 0.77 (95% CI: 0.66–0.87), a sensitivity of 91.1%, a specificity of 61.1%, a positive predictive value of 74.8%, and a negative predictive value of 84.4% (Fig. 2). Representative cases with short and long TO lengths are shown in Fig. 3, whilst a representative case with severe stenosis illustrating the discordance between ICA and CCTA in diagnosing a is shown in Fig. 4.

3.5. Association of quantitative CCTA characteristics with TO on ICA

The results of the logistic regression analysis are shown in Table 4. Univariable logistic regression analysis demonstrated that a lesion length >5.5 mm, a large fibro-fatty PAV, and dense calcium PAV were independent predictors for TO. Multivariable logistic regression analysis showed that occlusion length >5.5 mm was the only predictor of concordance between ICA and CCTA for TOs after adjusting for the influence of potential risk factors (odds ratio 9.847: 95% IC 2.294–42.265, P < 0.002).

4. Discussion

The main findings of our study are;

1. The concordance between ICA and CCTA in the diagnosis of TO was 56.0% (n = 47/84 lesions).

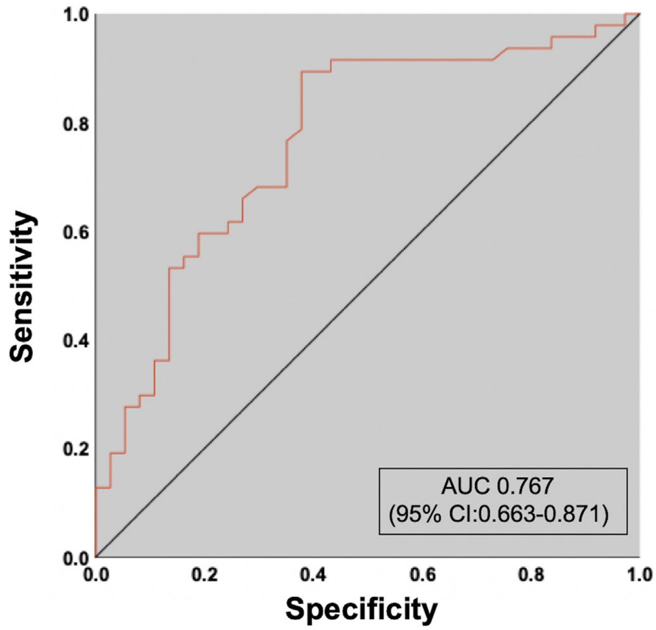

Fig. 2. Receiver-operating characteristic analysis to determine the cut-off value for predicting total occlusion on invasive coronary angiography. The best cut-off value to predict total occlusion on invasive coronary angiography is 5.47 mm. The area under the curve is 0.77 (95% CI: 0.66–0.87), with 91.1% sensitivity and 61.1% specificity. **Abbreviations:** AUC: area under the receiver-operating characteristic curve; CI: confidential interval.

2. Lesion length was significantly longer for TOs compared to severe stenoses (mean value 25.1 mm vs. 9.4 mm, $P < 0.001$). The ROC analysis showed that an occlusion length of 5.5 mm on CCTA was the best cut-off value to differentiate between a TO on CCTA and a severe stenosis on ICA.
3. The plaque type differed significantly between TOs and severe stenoses. Fibro-fatty PAV was significantly higher in severe stenoses as compared to TOs, where the dense calcium PAV was predominant.
4. In the multivariable analysis, an occlusion length of ≥5.5 mm on CCTA was the only independent predictor to differentiate a TO on CCTA from a severe stenosis on ICA.

Compared to conventional ICA, CCTA is a useful imaging tool that can provide a wealth of information including plaque tissue composition, vessel size, degree of remodeling, and luminal contours when the vessel is patent.[23] Pre-procedural assessment of the morphologic characteristics differentiating TOs on CCTA from severe stenoses on ICA helps plan revascularization since these anatomical lesion types may influence the modality of revascularization, as indicated by their impact on anatomical SYNTAX scores.[24] Therefore, a precise assessment of the lesion characteristics affecting this discordance needs to be evaluated with contemporary CT technology.

Several clinical studies have investigated the diagnostic accuracy of CCTA and ICA in diagnosing TOs and have assessed the parameters that differentiate them from severe stenoses. Lee et al. investigated the de novo diagnostic efficacy of CCTA in the assessment of CTOs before ICA and reported that CCTA has excellent specificity (96.8%) but poor sensitivity (57.1%) an observation corroborated by the present study. J. von Erffa et al. investigated the differentiation of TOs from high-grade stenoses in CCTA among 40 patients and reported a diagnostic accuracy for the detection of TOs of 50%. An occlusion length of ≥9 mm was the only parameter they identified to differentiate complete occlusions from high-grade stenoses with 100% specificity (95% CI 0.80–1.0).[8] In addition, Minghua et al. showed that the combination of the reverse attenuation gradient (TAG) sign, which is defined as a reverse intraluminal opacification gradient of the vessel distal to the occlusive lesion, and a lesion length of more than 14.3 mm, were highly specific for a CTO and helps to differentiate it from severe stenosis.[9] In our study, the best cut-off value for differentiating TOs from severe stenoses was a lesion length of 5.5 mm, suggesting that contemporary CT technology might be able to discriminate between the two, even if the lesion is short.

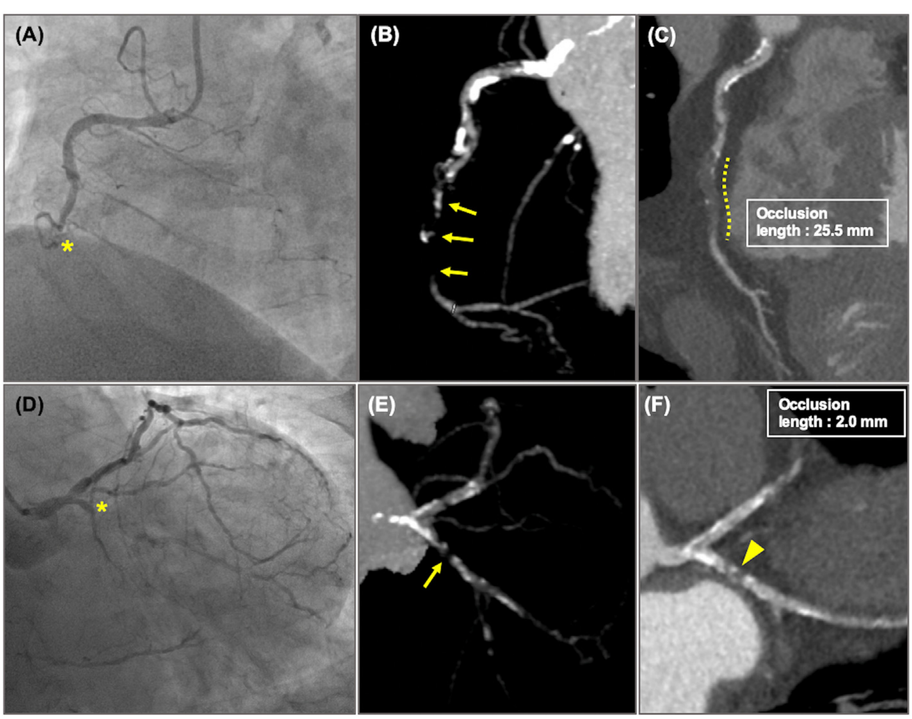

Fig. 3. Representative cases of total occlusion comparing invasive coronary angiography and coronary computed tomography angiography. Representative cases of long (≥20 mm) **(A-C)**, and short total occlusions **(D-F)**. A) Invasive coronary angiography (ICA) demonstrating complete lack of contrast opacification (yellow asterisk) of the mid right coronary artery.[28] B) The maximum intensity projection (MIP) in the same angulation of the ICA confirms complete lack of contrast opacification (yellow arrows). C) The curved multi-planar reconstruction (MPR) shows an occlusion length of 25.5 mm (yellow dotted line). The distal vessel beyond the occlusion is visible by contrast filling from collateral vessels. D) ICA demonstrates complete occlusion of the proximal left circumflex artery (yellow asterisk). The distal vessel beyond the occlusion is visible by contrast filling from collateral vessels. E) The MIP shows a complete interruption (yellow arrow) of the LCX proximal segment in the same angulation of the ICA. F) The curved MPR shows an occlusion with a lesion length of 2.0 mm (yellow arrowhead). **Abbreviations**: CCTA: coronary computed tomography angiography, ICA: invasive coronary angiography, RCA: right coronary artery, LCX: left circumflex. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

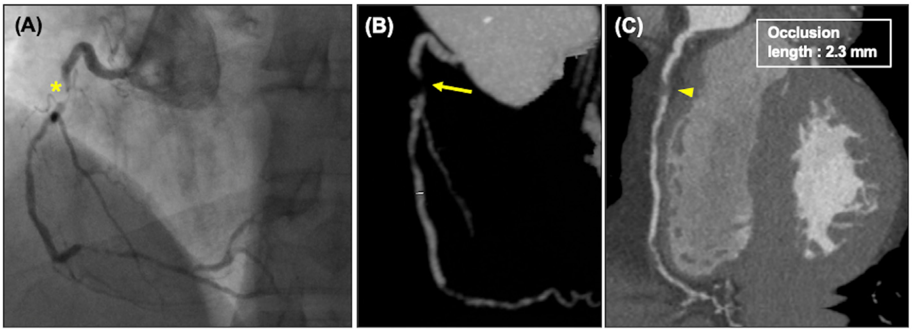

Fig. 4. Representative case of diagnosis discordance between invasive coronary angiography and coronary computed tomography angiography. A) Invasive coronary angiography (ICA) demonstrating a 99% stenosis of proximal right coronary artery (yellow asterisk). B) The maximum intensity projection in the same angulation of the ICA shows complete interruption at the proximal segment (yellow arrow). C) The curved multi-planar reconstruction shows 2.3-mm vessel occlusion with positive remodeling (yellow arrowhead). **Abbreviations**: ICA: invasive coronary angiography. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Univariable and multivariable logistic regression analysis between quantitative characteristics and total occlusions.

Characteristics	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
LL (>5.5 mm)	11.226 (3.797–33.194)	<0.001	9.847 (2.294–42.265)	0.002
Fibrous PAV, %	0.997 (0.971–1.023)	0.815	0.945 (0.844–1.059)	0.945
FF PAV, %	0.926 (0.888–0.965)	<0.001	0.901 (0.812–1.000)	0.901
NC PAV, %	0.999 (0.978–1.020)	0.999	0.962 (0.852–1.086)	0.962
DC PAV, %	1.048 (1.015–1.082)	0.005	0.970 (0.860–1.0839)	0.970
Positive remodeling	1.060 (0.445–2.526)	0.895	0.321 (0.084–1.225)	0.096

Multivariable analysis adjusted for the following traditional cardiovascular risk factors: age, gender, dyslipidemia, hypertension, diabetes mellitus, and current smoking.
Abbreviations: DC: dense calcium, FF: fibrofatty; LL: lesion length, NC: necrotic core, PAV: percentage of atheroma volume, OR: odds ratio, CI: confidence interval.

Previous studies were performed with a 64- or 128-slice CT, whereas our study was performed with a 256-slice CT according to the acquisition protocol. These observations may be explained by improved spatial resolution and partial volume effects. It is suggested that the reduced acquisition time may have reduced the impact of heart rate variability on image quality and may have been involved in reducing the blooming effect in calcified lesions. Furthermore, in the scenario of TO where antegrade coronary flow is blocked, retrograde contrast filling to the distal part of the occlusion is important to identify the site of occlusion. It is This is mainly defined by the degree of collateral arteries. In the present study, 43 of 47 lesions (93.6%) with ICA-diagnosed TOs had Rentrop grade II or III collateral arteries.[25] Suggested that in a population with a high proportion of preserved retrograde flow, the contrast effect of the distal part of the occlusion may be clearer in more cases and the lesion length may be measured more accurately and shorter.

In this study, we also tried to demonstrate the clinical impact of quantitative plaque parameters in the process of differentiating between a TO on CCTA and a severe stenosis on ICA. A previous clinical study showed that the angiographic characteristics of a CTO could be summarized by a long-occluded segment between adjacent side branches, blunt proximal stump, and collateral vessels flowing into the distal segment or side branches.[26] In addition, one previous study assessed the mean attenuation measured within the lesion and reported that there were comparable results between TOs and severe stenoses, indicating that the main plaque composition was equivalent to fibro-fatty plaques according to the current definition.[19] However, no previous quantitative assessments have been performed between the two lesion types.

In our results, all plaque volumes were significantly greater in TOs, due to their significantly longer lesion length compared to severe stenoses. The plaque composition also somewhat differed. Indeed, TOs had a larger calcified PAV, and less fibro-fatty PAV compared to those with severe stenoses. These findings are partially similar to prior studies - wherein the quantitative assessment was not formally assessed - and support our results.[26] Importantly, the multivariable analysis demonstrated that except for the lesion length (>5.5 mm), other quantitative parameters were not independent predictors capable of differentiating TOs from severe stenoses. Therefore, the clinical use of quantitative assessment is limited to an ancillary role in visual lesion morphological assessment.

4.1. Study limitations

Our study has several limitations. First, this was a sub-study of the FASTTRACK CABG in which all patients were referred for surgical revascularization, therefore there might be a specific patient selection bias since the cut-off value that differentiates TOs from severe stenoses might vary depending on the patient's age and CAD complexity. Furthermore, there was variability in patient background. Female sex included only 10.2%, and the proportion of the patients with high body mass index (i.e. >35 kg/m^2) was low. The current 256-slice multidetector CT scanner provides high diagnostic accuracy in both non-obese and obese patients and there are no significant differences in diagnostic accuracy between male and female populations[27,28]; however, further studies will be required with larger sample sizes.

Second, in the FASTTRACK CABG trial, only one type of CT scanner (256-slice GE Healthcare REVOLUTION CT) was used by experimental operators and this may raise the potential issue of generalizability of our results to clinical practice with less CT expertise and usage of lower-quality CT scanners.

Third, quantitative assessment could not be performed in two lesions in which the occlusion length could not be evaluated due to diffuse disease of the distal vessel.

Finally, information in terms of collateral vessels was lacking. Although, there is currently no uniform definition to assess them on CCTA, related parameters (e.g. transluminal attenuation gradient) were not evaluated. Furthermore, corrected coronary attenuation reported as a helpful parameter for coronary artery stenosis was also not assessed. Further studies are needed to include such parameters.

5. Conclusion

Despite differences in atheroma volume and plaque composition, only an occlusion length of >5.5 mm on CCTA predicted a corresponding TO on ICA.

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Declaration of competing interest

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Appendix A. Supplementary data

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