Coronary Computed Tomography (CT) Angiography Characteristics of High-Risk Plaque: Correlation with Stress Myocardial Perfusion Imaging in Patients with Moderate Coronary Stenosis

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Data Interpretation **D**
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Background: The aim of this study was to investigate the ability of coronary computed tomographic angiography (CCTA) characteristics of high-risk plaque (HRP) in moderate stenosis to improve differentiation of myocardial ischemia detected by stress CT perfusion (CTP) imaging.

Material/Methods: Sixty-two patients with coronary plaques and moderate stenosis confirmed by invasive coronary angiography (ICA) had stress CTP and 26 of these patients were found to have myocardial ischemia. The other 36 patients without myocardial ischemia were defined as controls. Characteristics of major plaques on CCTA images of the ischemia and non-ischemia groups were analyzed and compared.

Results: Differences between the 2 groups were observed in plaque volume, burden and rough inner surface necrotic core volume, plaque-lipid interface and plaque length. In a multivariable analysis, plaque burden and necrotic core volume were significantly associated with myocardial ischemia: plaque burden odds ratio (OR) was 1.28 (95% confidence interval [CI], 1.12–1.48); necrotic core volume OR was 1.78 (95% CI, 1.03–1.34). Compared with other quantitative measurements, optimized thresholds for plaque burden (area under the curve was 0.852) and necrotic core volume (area under the curve was 0.730) showed significantly higher diagnostic performance for ischemia with threshold values of 60.8% and 11.25 mm^3, respectively.

Conclusions: CCTA characteristics of major plaques may improve the discrimination of ACS patients with myocardial ischemia on stress CTP.

MeSH Keywords: Coronary Artery Disease • Myocardial Ischemia • Tomography Scanners, X-Ray Computed

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Background

Recently suggested degrees of maximal stenosis of coronary arteries confirmed by coronary computed tomographic angiography (CCTA) lack objective validation for moderate stenosis, which may imply obstructive coronary artery disease (CAD) without severe anatomical stenosis [1]. The ROMICAT-I trail showed that more than 50% stenosis is of limited value in the diagnosis of acute coronary syndrome (ACS), as only 46% of patients with CCTA-proven obstructive CAD have matched perfusion abnormalities in stress imaging performed by single-photon emission computed tomography (SPECT). Morphological characteristics of high-risk plaques (HRP) in patients with moderate coronary stenosis are related to acute coronary syndrome (ACS) and offer additional prognostic value over clinical risk factors. Multiple studies have shown that the detection accuracy of combined CCTA+CTP for obstructive CAD and functionally significant CAD exceeds 90% [2,3]. Furthermore, compared with intravenous ultrasound (IVUS), the specific CCTA features of HRP can better improve the diagnostic efficacy of ACS, mainly based on the accurate estimation of stenosis, plaque volume, luminal area, and plaque burden [4,5]. Therefore, we sought to explore whether CCTA characteristics of HRP in moderate stenosis improve discrimination of patients with myocardial ischemia detected by stress CTP.

Material and Methods

The Institutional Review Board of Huadong hospital (Shanghai, China) approved our study (approval no. 2019K072).

Patient selection

From January 2018 to February 2019, we prospectively recruited 153 patients with chest pain clinically suspicion for ACS who were recommended for invasive coronary angiography (ICA). Exclusion criteria mainly included older than 80 years of age, atrial fibrillation, renal insufficiency with glomerular filtration rate lower than 60 mL/min/1.73 m^2, and history of coronary intervention. Moderate stenosis has been defined as one or more coronary artery stenosis with a maximum stenosis of 50% to 69% in diameter [1]. All of the study patients underwent CCTA examination, and if a moderate coronary stenosis was found, stress CTP was followed 30 minutes after the CCTA scan. ICA was performed within 14 days after cardiac CT examination.

Cardiac CT protocols

Before cardiac CT scan, an intravenous line was inserted in the right arm antecubital vein for the delivery of contrast medium, and oral cardio-selective beta-blocker was given to patients with a heart rate >65 beats per minute. Next, all the patients underwent cardiac CT examination using Revolution CT scanner (GE Healthcare, Milwaukee, WI, USA).

Figure 1 shows the cardiac CT acquisition protocol. CCTA was triggered using automated contrast bolus tracking after placing the region of interest (ROI) in the descending aorta automatically at 300 Hounsfield units (HU) in the slice configuration. Scanning parameters were detector collimation, 256×0.625 mm; tube voltage, 120 KV; and tube current, 500 mA. All patients received a 50 mL bolus of iodixanol 320 (Oslo, Norway) at a rate of 5.0 mL/second followed by 50 mL saline solution (5.0 mL/second). After the CCTA scan, images were immediately analyzed by an observer with 10 years of experience in CCTA image post-processing and diagnosis. If moderate coronary stenosis induced by non-calcified plaque (calcific component <50%) was found, another intravenous line would immediately appear in the antecubital vein of left arm for pharmacological stress, which was followed by CTP scan performed 30 minutes after CCTA examination. Adenosine was injected intravenously at a rate of 0.14 mg/kg/minute (over 4 minutes) to induce vasodilation. A single stress CTP scan was performed using the same protocol as CCTA. Then, all datasets were transferred to the post-processing workstation (Advantage Workstation Version 4.7, GE Healthcare) and then evaluated by 2 observers with 10 and 7 years of diagnostic experience in CCTA respectively (Shi KL and Qi L).

Cardiac CT analysis and measurements

CTP images were analyzed by the 2 observers based on the 17-segment myocardial segment model suggested by the American Heart Association [6], where any disagreements were resolved by consensus. A 16-segment model, which was derived from the 17-segment model excluding apex was used for evaluation. Observers were all blinded to medical history, CCTA, and ICA results. Short-axis (basal, mid, and apical reconstructive images) and long-axis (2-, 3- and 4-chamber reconstructive images) views were reformatted and evaluated. Myocardial ischemia was visually assessed on reconstructed CTP images of each segment and determined according to absent or hypoattenuated perfusion defect. Then we obtained the quantitative perfusion ratio (QPR) of the area corresponding to the stenosis, which was defined as the ratio of the mean blood flow (MBF) in the area related to the stenosis to the distal MBF in the region of normal myocardium [7]. Myocardial ischemia was diagnosed when both of the perfusion defect and MBF <1.0 occurred simultaneously. Two radiologists with 5 and 7 years of experience in CTP analysis assessed the CCTA and CTP images independently, and decisions on the diagnosis of myocardial ischemia were reached by consensus.

One patient was excluded for the undiagnostic CCTA image quality (n=1 out of 63). Quantitative plaque analysis was
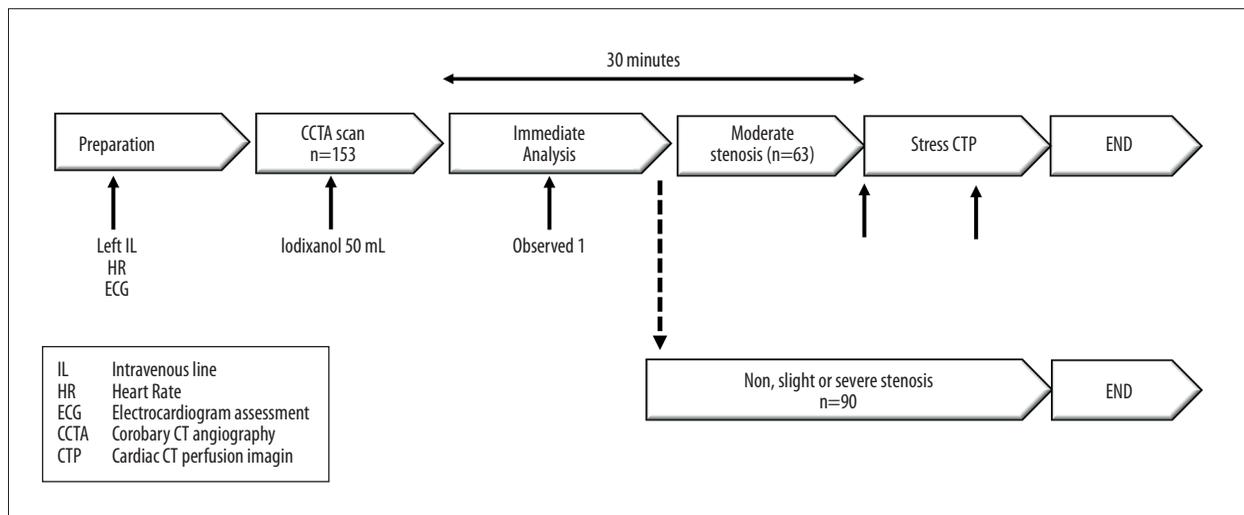
Figure 1. Diagram of comprehensive cardiac CT. After preparation, CCTA scan was performed first. After immediate analysis of CCTA images, stress CTP was performed under adenosine stress of 0.14 mg/kg/min about 30 minutes after CCTA for patients with moderate coronary stenosis. CT – computed tomography; CCTA – coronary computed tomography angiography; CTP – computed tomography perfusion.

performed using software for analysis of coronary plaques (QAngio CT RE 2.0, Medis Medical Imaging Systems B.V., Leiden, the Netherlands). The 2 observers separately identified major non-calcific plaques and analyzed all the parameters to calculate the interobserver variability whilst being blinded to the results of ICA. The quantitative parameters of coronary plaque analysis including plaque length and volume, plaque burden (defined as plaque area of the site of maximum stenosis divided by the outer vessel area), minimum luminal area of the major plaque (MLA), volume of necrotic core (defined as low HU component at <30 HU), and reconstructed index (RI, defined as the ratio of the outer vessel wall area at the position of the maximum stenosis divided by the outer wall area of reference segment) were automatically obtained by the software. The processing steps of the coronary plaque analysis software were as follows: 1) DICOM files of CCTA images were explicitly imported into the application; 2) major plaques were identified in the general viewing interface and the stretched multiplanar reconstruction (MPR) images of the vessels; 3) the coronary arteries of major plaques were automatically or semi-automatically extracted; 4) luminal and outer vessel boundaries were automatically identified and manually corrected by drawing the correct lumen border in the longitudinal cuts; 5) the proximal and distal lesion markers of major plaques were automatically defined as well as the reference markers; 6) quantification results of plaque analysis were exported to Excel files (Figure 2). Morphological features of major plaques were defined as follows: 1) spotty calcification (diameter <3 mm); 2) napkin-ring sign (NRS, higher attenuation rim surrounds the central low zone); 3) unclear plaque-lipid interface (the interface between the major plaque and peri-coronary lipid was blurred); and 4) the inner surface of major plaque (graded as smooth, moderate, and rough).

Statistical analysis

Statistical analysis was carried out by SPSS 25.0 and GraphPad Prism software. Intraclass correlation coefficients (ICCs) and 95% Bland-Altman limits of agreement were used to assess inter-observer variability for the measurements of plaque volume, burden, MLA, necrotic core volume, and remodeling index (RI). Correlation was graded as follows: ICC 0–0.20, poor; ICC 0.21–0.40, fair; ICC 0.41–0.60, moderate; ICC 0.61–0.80, good; and ICC 0.81–1.00, excellent. Values were described with either mean±standard deviation (SD) or median with interquartile range (IQR) after testing the normality of variables using Shapiro-Wilk test. Then the data of the 2 groups were compared using Pearson chi-squared test for categorical variables (gender, cardiovascular risk factors, family history, plaque location, etc.) and independent-sample t-test and Mann-Whitney U test for continuous variables (age, plaque burden, length, MLA, RI, etc.). Receiver operating characteristic (ROC) analysis was used to determine cutoff values of plaque measurements. We used logistic analysis for the univariate analysis and multivariate regression analysis to identify the independent predictors of high-risk plaques inducing myocardial ischemia. A P value of less than 0.05 was considered significant.

Results

Descriptive statistics and CT features of coronary plaques

Finally, 63 participants underwent CTP examination. CCTA images were feasible in all participants. One participant was excluded due to the poor quality of CTP images, leaving a total
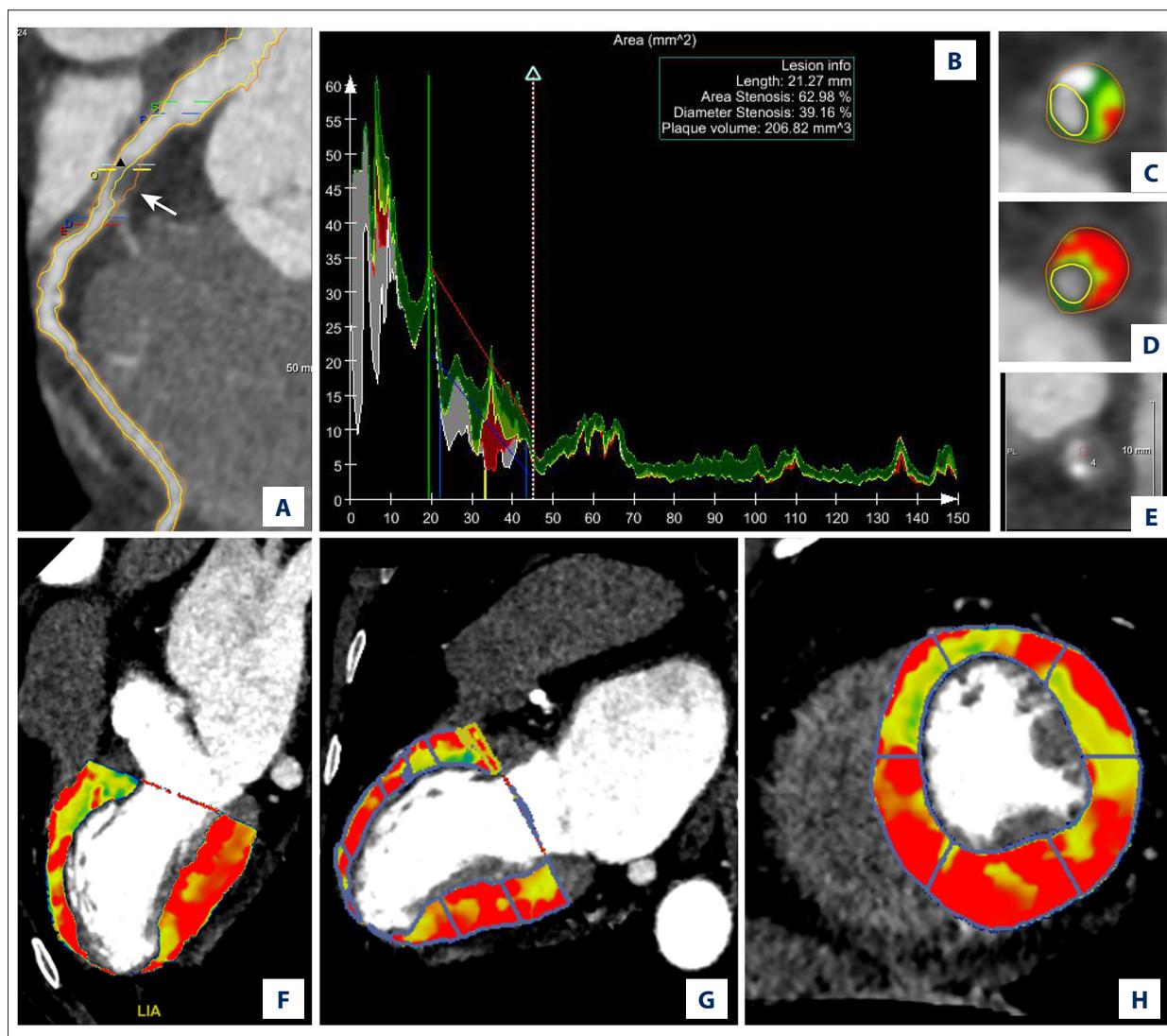
Figure 2. A 56-year male with chest pain suspected of CAD. CCTA and ICA showed moderate coronary stenosis. (**A–E**) Quantitative plaque assessment using (semi) automated software. In a curved multiplanar reconstruction (MPR) of the left anterior descending coronary artery in long axis, luminal and outer vessel boundaries were automatically identified and corrected manually by drawing the correct lumen border in the longitudinal cuts (**A**), showing a major plaque in the mid segment of left anterior descending artery (white arrow) with rough inner surface (black triangle) and unclear plaque-lipid surface (**E**). After defining the proximal and distal region of the major plaque, the software then provides MLA, RI, plaque burden and volume, and volumes of plaque subcomponents (**B–E**). In plaque subcomponent analysis (**C, D**), white color represents the component of dense calcium; red represents necrotic core; light green represents fibrous fatty; deep green represents fibrous. (**F–H**) Visual perfusion assessment of stress CTP identified perfusion defects in anterior wall indicating LAD territory ischemia. CAD – coronary artery disease; CCTA – coronary computed tomographic angiography; ICA – invasive coronary angiography; MPR – multiplanar reconstruction; MLA – minimal luminal area; RI – remodeling index; CTP – computed tomography perfusion; LAD – left anterior descending artery.

of 62 patients who were recruited into the final study (mean age, 65±7.9 years, 69.4% males). Sixty-two primary plaques were determined by CCTA analysis and all of them proved to be moderate stenosis by ICA. Consistency tests for the degree of stenosis induced by non-calcific plaques on CCTA and ICA were excellent (ICC range: 0.852–0.976).

Among the 62 participants, 26 who were shown to have myocardial ischemia by stress CTP were enrolled as the ischemia group, while the remaining 36 patients were placed in non-ischemia group. The descriptive statistics and CT features of coronary plaques are summarized in Table 1. There were no statistical discrepancies between the 2 groups in age, gender, cardiovascular risk factors, plaque location, and number of diseased vessels.

Table 1. Baseline and CT characteristics of patients with moderate coronary stenosis.

Group	Non-ischemia (n=36)		Ischemia (n=26)		F	P-value
Age (years)	67	(62–71)	63	(59–67)	–	0.111
Gender male n [%]	23	(63.9)	20	(76.9)	1.207	0.272
Cardiovascular risk factors [%]						
Hypertension	12	(33.3)	9	(34.6)	0.011	0.916
Diabetes mellitus	3	(8.3)	6	(23.1)	2.645	0.104
Dyslipidemia	7	(19.4)	8	(30.8)	1.056	0.304
Former or current smoker	8	(22.2)	7	(26.9)	0.182	0.67
Family history of CAD	11	(30.6)	7	(26.9)	0.097	0.756
Medication, n [%]						
ACEI/ARB	9	(25)	6	(23.1)	0.03	0.861
CCB	7	(19.4)	5	(19.2)	0.093	0.761
Beta-blockers	2	(5.6)	2	(8.7)	0.034	0.852
Statins	4	(11.1)	5	(19.2)	0.281	0.596
Metformin	3	(8.3)	5	(19.2)	0.773	0.379
Sulfonylurea	2	(5.6)	3	(11.5)	0.145	0.703
Plaque location n [%]					1.025	0.599
LAD	19	(52.8)	17	(65.4)		
LCX	12	(33.3)	6	(23.1)		
RCA	5	(13.9)	3	(11.5)		
No. of diseased vessels					0.911	0.634
1	25	(69.4)	15	(57.7)		
2	10	(27.8)	10	(38.5)		
3	1	(2.8)	1	(3.8)		
Plaque measurements						
MLA (mm)	4.16±1.47		3.68±1.50		0.263	0.610
RI	1.14	(1.00–1.21)	1.08	(1.01–1.20)	–	0.558
Plaque burden (%)	50.05	(46.5–57.4)	67.00	(61.88–71.58)	–	0.000
Plaque length (mm)	12.47±4.08		15.96±6.80		6.857	0.011
Plaque volume (mm³)	181.46±29.83		208.57±57.00		14.153	0.000
<30 HU component volume	14.94±6.84		21.99±9.10		–	0.002
Morphologic features						
Spotty calcification, n [%]	18	(50)	13	(50)	0.000	1.000
Napkin-ring sign, n [%]	7	(19.4)	7	(26.9)	0.483	0.487
Unclear plaque-lipid interface n [%]	2	(5.6)	9	(34.6)	8.736	0.003
In-plaque enhancement n [%]	1	(2.8)	2	(7.7)	0.792	0.374

Table 1 continued. Baseline and CT characteristics of patients with moderate coronary stenosis.

Group	Non-ischemia (n=36)		Ischemia (n=26)		F	P-value
Plaque inner surface n [%]					18.610	0.000
Smooth	20	(55.6)	6	(23.1)		
Moderate	14	(38.9)	6	(23.1)		
Rough	2	(5.6)	14	(53.8)		

CAD – coronary artery disease; ACEI – angiotensin-converting enzyme inhibitor; ARB – angiotensin receptor blocker; CCB – calcium-channel blocker; MLA – minimum luminal area; RI – remodeling index; LAD – left anterior descending artery; LCX – left circumflex artery; RCA – right coronary artery.
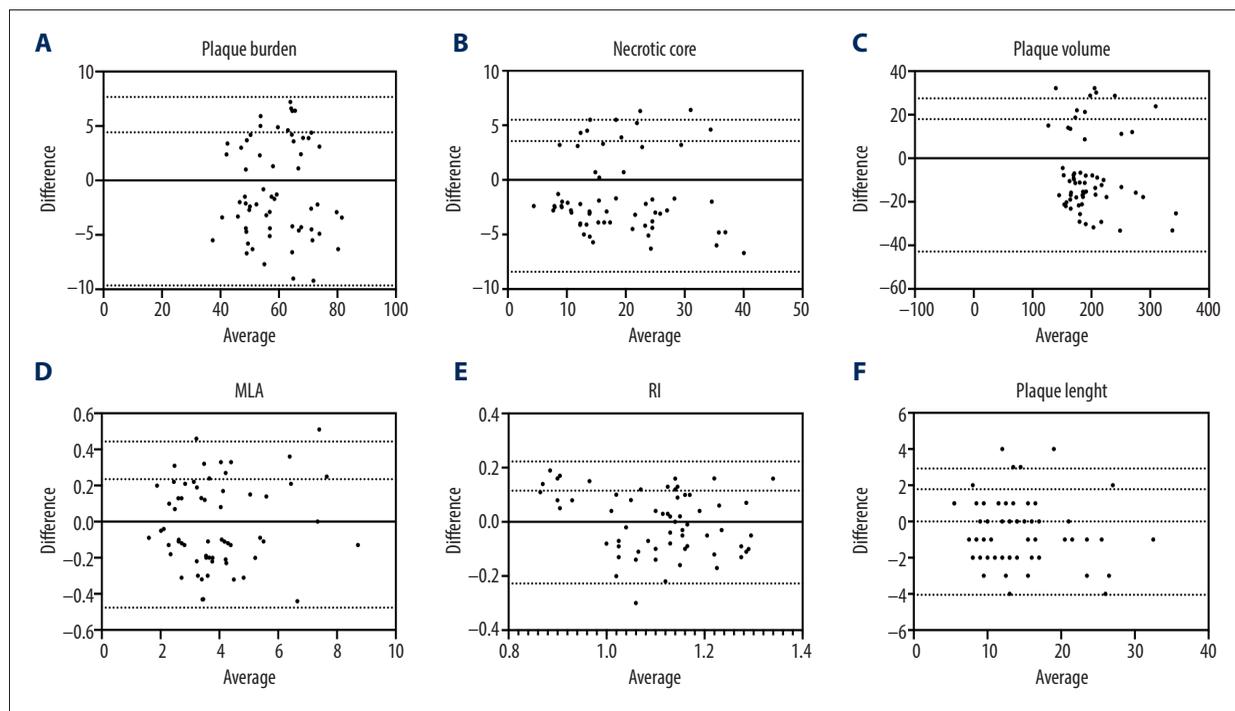

Figure 3. Bland-Altman plots showing inter-observer agreement of measurements of plaque burden (**A**), necrotic core volume (**B**), plaque volume (**C**), MLA (**D**), RI (**E**), plaque length (**F**) of major plaques in patients with ACS and moderate stenosis. X axes show mean measurements, and Y axes show differences between measurements of 2 observers. MLA – minimal luminal area; RI – remodeling index; ACS – acute coronary syndrome.

Inter-observer agreement of thin section computed tomography (TSCT) measurements

Inter-observer agreement was excellent for plaque burden (ICC range: 0.928–0.974), necrotic core volume (ICC range: 0.864–0.948), plaque volume (ICC range: 0.933–0.976), MLA (ICC range: 0.980–0.993) and plaque length (ICC range: 0.921–0.971); and was good for RI (ICC range: 0.697–0.855). Bland-Altman plots with 95% limits of agreement are shown in Figure 3.

Characteristics of coronary plaques inducing myocardial ischemia

We identified 26 coronary plaques with moderate stenosis inducing myocardial ischemia based on stress CTP. The greatest differences between the 2 groups were observed for plaque volume, burden, and rough inner surface (plaque volume, 181.46 mm³ versus 208.57 mm³; plaque burden, 50.05% versus 67.00%; 5.6% versus 53.8%, $P<0.0001$), unclear plaque-lipid interface (2% versus 9%, $P<0.01$), and necrotic core volume (14.94 mm³ versus 21.99 mm³, $P<0.01$). Plaque length also showed significant difference between ischemia and non-ischemia plaques (12.47 mm versus 15.96 mm, $P<0.05$, Figure 4).
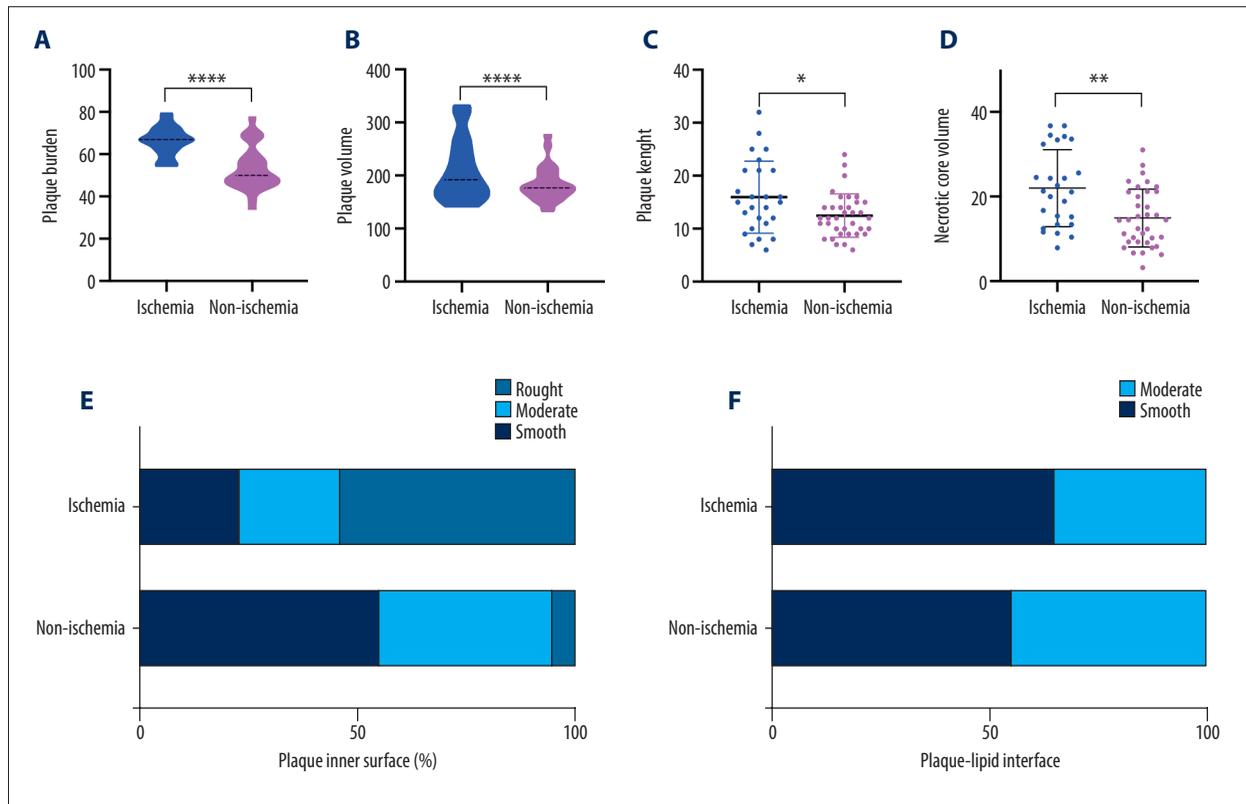
Figure 4. Box and violin figures (**A, B**) show that plaque burden (**A**) and volume (**B**) are significantly increased in moderate stenosis patients with myocardial ischemia on stress CTP. Scatter plot figures (**C, D**) show that plaque length (**C**) and necrotic core volume (**D**) are also increased in ischemia group. (**E, F**) Column bar graphs show that the proportions of rough inner surface and unclear plaque-lipid interface in the ischemia group are significantly increased compared of that in non-ischemia group. (Significant level marks: * $P<0.05$; ** $P<0.01$; *** $P<0.001$; **** $P<0.0001$). CTP – computed tomography perfusion.

Table 2. ROC analysis of plaque measurements on CCTA.

	Area	Std. error	Asymptotic sig. b	Cutoff value			Asymptotic 95% confidence interval	
				Value	Sensitivity (%)	Specificity (%)	Lower bound	Upper bound
MLA (mm)	0.389	0.078	0.138	4.33	30.80	77.80	0.237	0.541
RI	0.456	0.074	0.559	0.94	100.00	11.10	0.311	0.602
Plaque burden (%)	0.852	0.049	0.000	60.80	81.00	83.00	0.756	0.948
Plaque length (mm)	0.653	0.074	0.041	14.50	54.00	75.00	0.508	0.799
Plaque volume (mm³)	0.617	0.076	0.118	195.35	50.00	75.00	0.467	0.767
Necrotic core volume (mm³)	0.730	0.064	0.002	11.25	92.00	61.00	0.604	0.855

MLA – minimum luminal area; RI – remodeling index; ROC – receiver operating characteristic.

Table 3. The results of univariable and multivariable multilevel mixed-effects logistic regression analysis of plaque measurements on CCTA.

	Univariable analysis			Multivariable analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
MLA	0.79	0.54–1.15	0.22	0.44	0.20–0.96	0.05
RI	0.32	0.00–24.42	0.61	0.01	0.00–3.64	0.10
Plaque burden	1.18	1.09–1.28	0.00	1.28	1.12–1.48	0.00
Plaque length	1.13	1.02–1.25	0.02	1.93	0.72–1.22	0.61
Plaque volume	1.02	1.00–1.03	0.03	1.01	0.98–1.03	0.85
Necrotic core volume	1.12	1.04–1.20	0.00	1.78	1.03–1.34	0.01

MLA – minimal luminal area; RI – remodeling index; OR – odds ratio; CI – confidence interval.

Association of plaque features with myocardial ischemia

To determine which CT measurements of coronary plaques with moderate stenosis were related to myocardial ischemia, we used univariable and multivariable multilevel mixed-effects logistic regression analyses (Table 2). In univariable analysis model, independent associations were found for plaque burden (OR, 1.18; 95% confidence interval [CI], 1.09–1.28), length (OR, 1.13; 95% CI, 1.02–1.25), volume (OR, 1.02; 95% CI, 1.00–1.03), and necrotic core (OR, 1.12; 95% CI, 1.04–1.20). In a multivariable analysis, plaque burden and necrotic core volume were significantly associated with present of myocardial ischemia (plaque burden: OR, 1.28; 95% CI, 1.12–1.48; necrotic core volume: OR, 1.78; 95% CI, 1.03–1.34).

The diagnostic performance of plaque measurements for myocardial ischemia

Optimized thresholds showed significantly higher diagnostic performance for plaque burden and necrotic core volume, and borderline significant performance for plaque length, but not for MLA, RI, and plaque volume (Table 3). The optimal threshold of plaque burden for myocardial ischemia was 60.8%, whose sensitivity and specificity were 81% and 83%, and area under ROC curve was 0.852 (*P*<0.001, 95% CI: 0.756–0.948). The optimal threshold of necrotic core volume was more than or equal to 11.25 mm³, and the sensitivity and specificity were 92% and 61%, respectively. The area under the ROC curve was 0.730 (*P*=0.002, 95% CI: 0.604–0.855, Figure 5).

Discussion

CCTA is widely used to exclude obstructive CAD because of its high sensitivity, however, its specificity for identifying ischemia of myocardium is only moderate, which has contributed to a higher rate of resultant ICAs. CTP has been proven to improve
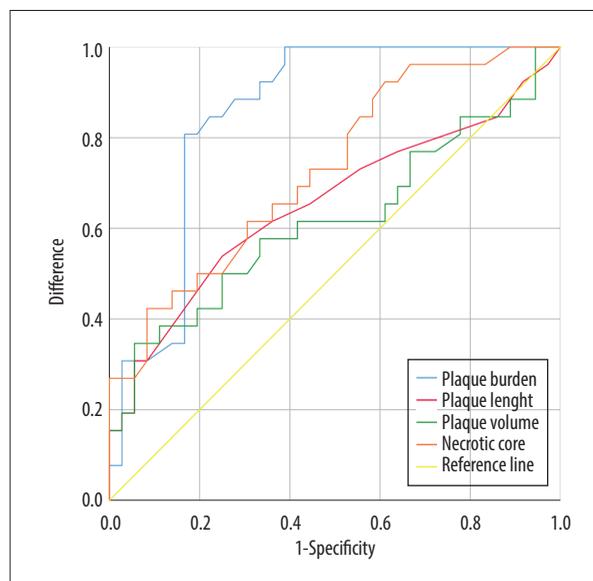

Figure 5. ROC analysis for identifying ischemia in ACS patients with moderate stenosis demonstrated the higher area under the curve for plaque burden (0.852, 95% CI, 0.756–0.948) than necrotic core volume (0.730, 95% CI, 0.604–0.855), plaque length (0.653, 95% CI, 0.508–0.799), and plaque volume (0.617, 95% CI, 0.467–0.767). ROC – receiver operating characteristic; ACS – acute coronary syndrome; CI – confidence interval.

the diagnostic efficiency of CCTA to display ischemic CAD and prior myocardial infarction [8]. For patients with moderate coronary stenosis, the assessment of myocardial ischemia is particularly crucial because the anatomical information is inconclusive to confirm ischemic CAD. Pontone et al. [9] reported that combined CCTA and stress CTP can significantly improve the specificity, positive predictive value (PPV), and diagnostic accuracy in detecting CAD. For both CCTA and ICA, coronary plaques of ≥50% stenosis had to accept a perfusion examination (either CTP or SPECT MPI) to exclude ischemic CAD [10]. Furthermore,

moderate stenosis on CCTA is temporary and requires noninvasive further evaluation including plaque features, presence of myocardial ischemia or not. In patients with moderate stenosis, which usually presents with mild chest pain or stable angina, the relationship between the CT morphologic features of major coronary plaques and myocardial ischemia is rarely reported. Our study is a small prospective cohort study using stress CTP to diagnose ischemic CAD in patients with moderate coronary stenosis as measured by CCTA, and further analyzed the correlation between CT features of major plaques and myocardial ischemia. The results are of economic and clinical value for further CTP to detect myocardial ischemia in patients with moderate coronary stenosis diagnosed by CCTA, so as to avoid excessive cost and radiation [11].

Our results demonstrated that high-risk plaque detected by CCTA improved diagnosis of ACS in patients with acute chest pain who otherwise had no anatomically severe stenosis and evidence of infarction. Puchner et al. [12] reported that one-third of patients with acute chest pain had high-risk plaque. The proportion of high-risk plaques in our cohort was 41.9% (26 out of 62), which is higher than the results of Puchner et al. The reason may be that our patients are all from same center of chest pain, where the proportion of low-risk chest pain (negative cases) is relatively low. Our results, which are consistent with those reported by previous studies, are very relevant since they are not only based on quantitative parameters derived from automated evaluation, but also on some new morphological features such as plaque-lipid interface and inner interface of coronary plaques. Furthermore, all the quantitative parameters were derived from automated evaluation, which were different from the measurements based on subjectively manual methods.

Previous studies [12–14] reported that CCTA-derived plaque features were related to ACS and myocardium ischemia, including positive remodeling (PR), low attenuation plaque (LAP), NRS, and spotty calcification. Motoyama et al. [13] reported that low attenuation plaque (<30 HU) and positive remodeling (RI ≥1.10) on CCTA are related to acute coronary syndrome through mid-term follow-up. We demonstrated that plaque burden, volume, and rough inner surface were strongest predictors for myocardial ischemia in moderate stenosis, followed by unclear plaque-lipid interface, necrotic core volume, and plaque length. In our study, plaque burden >60.8%, plaque length >14.5 mm, plaque volume >195.35 mm^3, and necrotic core volume >11.25 mm^3 were associated with myocardial ischemia on stress CTP. In a multivariable model, only plaque burden and necrotic core volume were found to be independent indicators of ischemia, potentially because of existing collinearities with other plaque characteristics. Our study complements the high-risk plaque features of moderate stenosis with myocardial ischemia, which can provide more diagnostic

information for CCTA and can be combined with stress CTP to improve the diagnostic efficacy of ACS patients. Therefore, cardiologists should consider aggressive medical treatment or ICA on patients with moderate stenosis accompanied by high-risk plaque and myocardial ischemia.

Studies [15,16] have demonstrated that CCTA features of high-risk plaques associated with ACS are NRS, PR, LAP, and spotty calcification. Non-calcified plaque burden is reported as better predictive factor for myocardial ischemia compared to calcium score and the severity of stenosis [1]. Coronary plaques with moderate stenosis can appear as a continuous decrease in pressure along its long axis, which may reduce coronary blood flow reserve and cause myocardial ischemia [17]. In our study, plaque burden and length were best predictors for myocardial ischemia detected on stress CTP in moderate stenosis patients, which is consistent with previous studies.

A histopathologic study confirmed that the best discriminators of vulnerable plaque are the thin fibrous cap, necrotic core, and macrophage infiltration [18]. Shmilovich et al. [19] demonstrated that prediction of myocardial ischemia by lipid core and PR may be helpful in assessing hemodynamic abnormalities of stenotic lesions. We found that necrotic core volume was also associated with myocardial ischemia in moderate stenosis. However, some characteristics such as RI, spotty calcification, and NRS failed to substantially improve determination of myocardial ischemia in patients with moderate coronary stenosis.

The NRS has been reported in ruptured plaques, and is associated with thin-cap fibrous atherosclerosis, which histologically includes enhancement of intraplaque vasa vasorum, intraplaque hemorrhage or thrombus, or plaque microcalcifications [11,20–22]. In our study, NRS failed to predict myocardial ischemia in moderate stenosis patients, which might be that it is more suitable for predicting high-risk plaque in severe stenosis and poor prognosis in ACS patients, and it might not be associated with hemodynamic changes and myocardial ischemia. The study of NRS in patients with moderate disease also require large-scale investigation.

It has been hypothesized that unclear plaque-lipid interface and higher CT density of adjacent adipose might be CT-morphological correlates for inflammation or plaque rupture, which are associated with hemodynamic dysfunction and myocardial ischemia in moderate stenosis patients with ACS [23]. The interplay between high-risk plaque and adjacent adipose density and how these signs are reflected in CT morphology needs to be further investigated. Hedgire et al. [24] demonstrated that detection of perivascular fat stranding may be a useful predictor of culprit lesion for ACS with obvious stenosis. Although atherosclerosis is an intimal lesion in patients

with ACS, inflammation outside the intima, such as increased peripheral fat density, is also considered to be related to myocardial ischemia [25]. In our study, the unclear plaque-lipid interface, which may reflect intimal inflammation, is a potential predictor for myocardial ischemia in ACS patients with moderate coronary stenosis.

Conclusions

In conclusion, CTP examination has incremental value in patients of moderate stenosis detected on CCTA. The plaque characteristics shown by CCTA can help predict myocardial ischemia. The results are of economic and clinical value for further CTP to evaluate myocardial ischemia in moderate stenosis on CCTA, so as to avoid excessive cost and radiation.

Limitations

Firstly, our research lacks follow-up information after ICA, which is why we cannot interpret whether revascularization of moderate stenosis with myocardial ischemia would improve clinical prognosis. This issue is still a gray zone in the decision-making process of ischemic CAD, which needs further investigated. Secondly, the sample size included was small. So, comparative studies with a larger number of series are needed to confirm the results of our research in the future studies. Thirdly, the radiation dose of dynamic cardiac CT scan would be a major concern.

Conflict of interest

None.

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