Clinical Investigation

Quantitative Evaluation of Coronary Plaque Progression by Computed Tomographic Angiography

Xiujian Liu, PhD
Guanghui Wu, MD
Chuangye Xu, PhD
Yuna He, MD
Lixia Shu, PhD
Yuyang Liu, PhD
Nan Zhang, MD
Changyan Lin, PhD

Understanding plaque formation in patients at risk for coronary artery disease—the leading cause of morbidity and death in the world—enables physicians to better determine whether and how to treat these individuals. We used computed tomographic angiography to quantitatively evaluate the progression of nonculprit coronary plaques along the full length of the right coronary artery in 21 patients with acute coronary syndrome. Each right coronary artery was analyzed in sequential, 3-mm-long segments, and the minimum luminal area, plaque burden, and plaque volume within each segment were evaluated at baseline and at 12-month follow-up. Serial remodeling of the right coronary artery was also evaluated. In total, 625 arterial segments were analyzed. At 12-month follow-up, the plaque burden had increased slightly by 0.34% (interquartile range [IQR], –4.32% to 6.35%; P=0.02), and the plaque volume was not significantly changed (0.33 mm^3; IQR, –3.05 to 3.54; P=0.213). The minimum luminal area decreased 0.05 mm^2 (IQR, –1.33 to 0.87 mm^2; P=0.012), and this was accompanied by vessel reduction, as evidenced by negative remodeling in 43% of the 625 segments. We conclude that serial computed tomographic angiography can be used to quantitatively evaluate the morphologic progression of coronary plaques. **(Tex Heart Inst J 2017;44(5):312-9)**

Key words: *Coronary angiography/methods; coronary artery disease/diagnostic imaging/physiopathology; models, cardiovascular; plaque, atherosclerotic/diagnostic imaging; observer variation; predictive value of tests; retrospective studies; tomography, x-ray computed/methods*

From: *Departments of Biomedical Engineering (Drs. He, Lin, X. Liu, Shu, Wu, and Xu), Cardiology (Dr. Y. Liu), and Radiology (Dr. Zhang), Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, People's Republic of China*

This study was supported by the National Science Foundation of China (81670371) and the Capital Public Health Project (Z161100000116086).

Address for reprints: *Changyan Lin, MD, Department of Biomedical Engineering, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Rd., Chaoyang District, Beijing 100029, PRC*

E-mail: *llbl@sina.com*

Coronary artery disease (CAD), which causes more than 20 million deaths each year, is the world's leading cause of morbidity and death.[1,2] Most patients with CAD have many coronary obstructions that are in varying degrees of progression and that pose different risks.[3-6] Therefore, understanding the progression of coronary plaque would help physicians make more informed decisions about whether and how to treat patients at risk for CAD.

In clinical studies, intravascular ultrasound (IVUS) has traditionally been used to investigate the composition and progression of coronary plaques in the proximal or mid segments of one or 2 major coronary vessels.[7,8] However, it is not appropriate for routine serial evaluations because it carries a small risk of severe procedural complications. In contrast, computed tomographic angiography (CTA) is less expensive and noninvasive. Advances in computed tomographic (CT) technology and post-image-processing techniques have made it possible not only to detect stenosis with coronary CTA, but also to use it to quantitatively analyze coronary plaques.[9-13] In recent years, a few serial studies with CTA have appeared in the literature,[14-17] but most of them have focused on lesions in diseased segments of the coronary tree. Our objective in this study was to use CTA to examine the natural history of coronary atherosclerosis along the full length of the right coronary artery (RCA) tree and to investigate serial changes in the minimum luminal area (MLA), plaque burden (PB), plaque volume (PV), and arterial remodeling.

Patients and Methods

Twenty-one patients treated at Beijing Anzhen Hospital from 2010 through 2013 were studied retrospectively (Table I). Inclusion criteria were as follows: age >18 years, availability of 2 coronary CTA scans taken >6 months apart, and diagnosis of acute coronary syndrome (ACS) during the initial physical examination. Exclusion criteria included previous percutaneous coronary intervention (PCI) to the RCA or coronary artery bypass grafting, severe valvular heart disease, irregular heart rhythm, renal fail-

ure, and severe hematologic disease. The institutional review board of our hospital approved the study, and all patients gave informed consent before participation.

Image Acquisition and Quantitative Measurement

In accordance with the coronary CTA Guide provided by the Society of Cardiovascular Computed Tomography,[18] coronary CTAs of the RCA tree were obtained at baseline and follow-up, with either a SOMATOM® Definition 64-slice dual-source CT (Siemens Healthcare GmbH; Erlangen, Germany) or an Aquilion ONE™ 320-slice CT (Toshiba Medical Systems Corporation; Tochigi, Japan). Before examination, all patients were given nitroglycerin sublingually. Patients with a heart rate >65 beats/min were given β-blockers. During scanning, a 70- to 90-mL bolus of intravenous contrast agent was injected. The scanning settings included collimations of 0.625 mm for 64-slice CT and 0.5 to 0.75 mm for 320-slice CT, a pitch factor of 0.2 to 0.26, a reconstruction slice thickness of 0.4 mm, a tube voltage of 120 kV, and a tube current of 300 to 650 mAs. During inspection, slice thicknesses of 0.5 to 0.75 mm—measured in 0.3- to 0.4-mm increments—and moderately smooth convolution kernels were used to rebuild axial images. Scanning was performed in the middle or at the end of diastole, when coronary artery movement was relatively slow.

Quantitative measurement and analysis of the coronary CTAs were conducted by an experienced specialist who used OsiriX 6.0 image-processing software (Pixmeo SARL; Bernex, Switzerland). To ensure the reliability of the results, we used a blinding method to hide the time at which each CTA was obtained. During analysis, a centerline originating from the ostium was obtained manually and was used as the reference for generating curved and straightened multiplanar reformatted images. Then, starting from the ostium, contiguous, cross-sectional reconstructions of the RCA

TABLE I. Baseline Characteristics of the 21 Patients

Variable	Value
Age (yr)	55 (49–63)
Male	15 (71)
Body mass index (kg/m^2)	25.2 (24.8–26.2)
History of unstable angina	16 (76)
Myocardial infarction	5 (24)
Previous PCI	8 (38)
Hypertension	19 (90)
Diabetes mellitus	9 (43)
Triglycerides (mmol/L)	1.38 (1.21–1.69)
Total cholesterol (mmol/L)	4.24 (3.29–5.09)
HDL cholesterol (mmol/L)	1.07 (1.02–1.31)
LDL cholesterol (mmol/L)	2.48 (1.83–3.54)

HDL = low-density-lipoprotein; LDL = high-density-lipoprotein; PCI = percutaneous coronary intervention

Data are presented as number and percentage or as median and interquartile range.

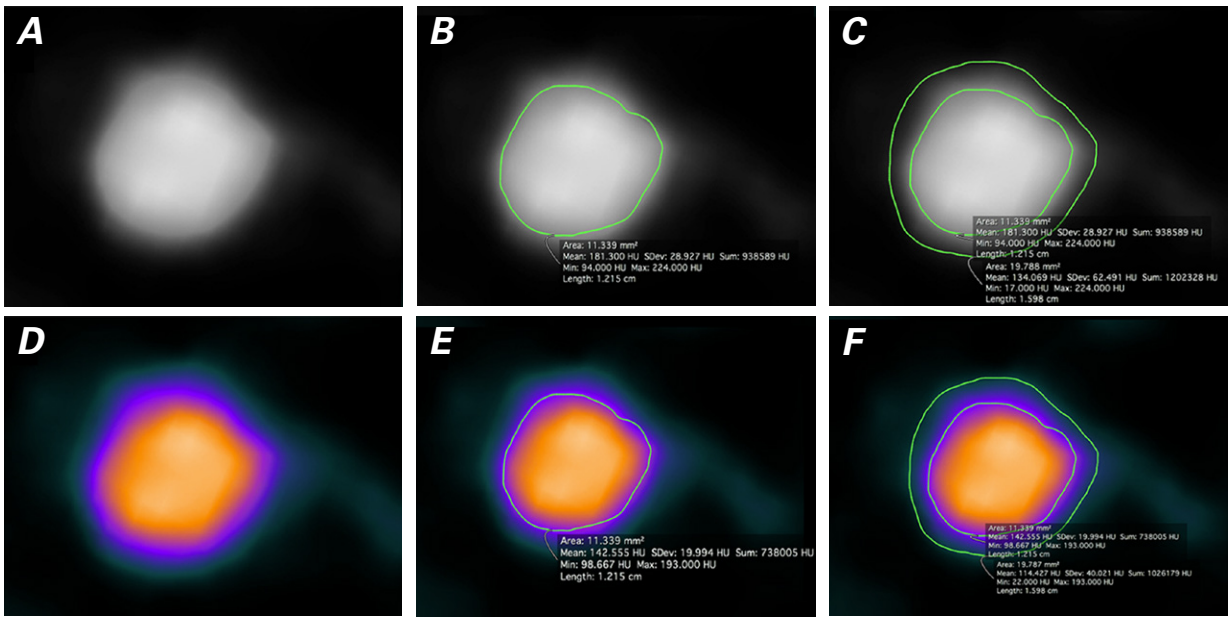

Fig. 1 *Computed tomographic angiograms (cross-sectional reconstruction images) show quantitative measurements of* ***A, B, C****) luminal areas (no-color look-up table mode) and* ***D, E, F****) the corresponding vessel areas (GE color mode) perpendicular to the centerline of the coronary artery.*

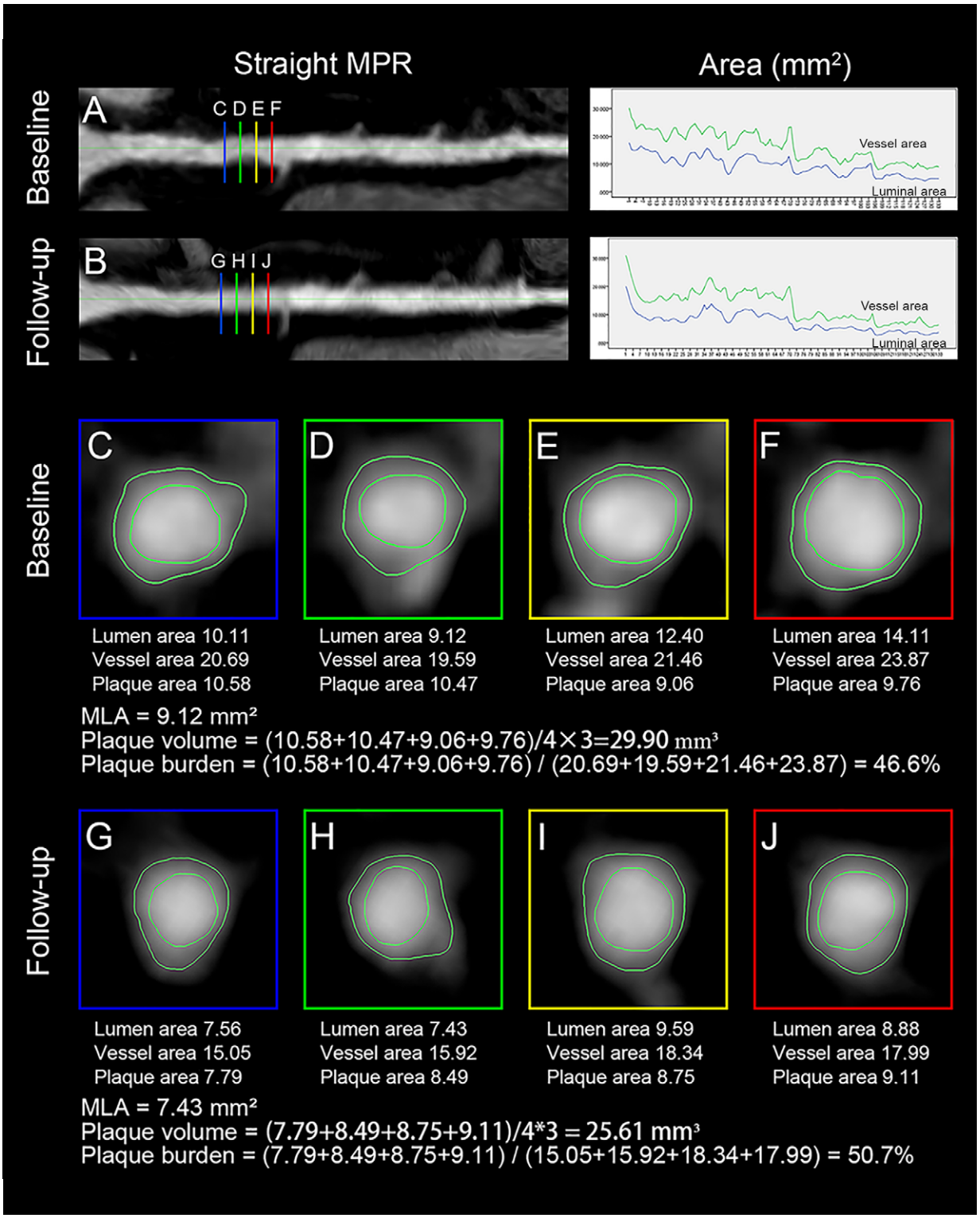

Fig. 2 *Example of the vessel analysis protocol. Straightened multiplanar reformatted (MPR) images from the right coronary artery* ***A****) at baseline and* ***B****) at 12-month follow-up show a 3-mm segment, divided into 4 sequential cross-sections. Starting from the ostium, the vessel area and luminal area of all contiguous, 1-mm-thick cross-sectional reconstructions of the RCA tree were measured (area graphs). Cross-sections of the 3-mm segments are shown* ***C, D, E, F****) at baseline and* ***G, H, I, J****) at follow-up. The luminal area and vessel area of each cross-section were measured directly. The plaque area was calculated by subtracting the luminal area from the vessel area, and the plaque burden was calculated as the sum of all 4 contiguous plaque areas, divided by the total vessel area. In the segment shown, the plaque burden increased from baseline to follow-up.*

MLA = minimum luminal area

tree were rendered in 1-mm-thick slices. Finally, the luminal area and vessel area of all cross-sectional reconstructions were measured manually (Fig. 1). To ensure accuracy in the detection of plaque and the outer vessel boundary, we set the window width (WW) to 155% and the window level (WL) to 65% of the average intensity within the lumen, as previous studies have described.[11,19]

Vessel Segmentation and Blinding

To efficiently evaluate the progression of coronary plaque at baseline and at 12-month follow-up, we divided the RCA into consecutive 3-mm-long segments, starting at the ostium. We chose 3 mm because the length was methodologically reliable, and the homogeneity of the morphologic properties of the local vascular plaque across this distance was good. Accordingly, we would be able to measure changes in the local vascular plaque as accurately as possible.[20,21]

To ensure that the arterial segments to be measured were identical at baseline and follow-up, and to maintain blinding of the segmentation methods, a specialist who did not participate in the subsequent data analysis segmented the coronary artery tree by using fixed anatomic landmarks—primarily multiple arterial branches—as fiducial points.

During segmentation, we excluded side branches and 1-mm segments adjacent to bifurcation of the main branches. Scans of segments with motion artifacts were also excluded.

Quantitative Measurement of Coronary Plaque

Minimum luminal area (*MLA*), plaque burden (*PB*), and plaque volume (*PV*) for each 3-mm segment were measured, as follows[22]:

$$MLA = \text{Narrowest area per segment,}$$

$$PB = \frac{\text{Sum of vessel area} - \text{sum of luminal area}}{\text{Sum of vessel area}} \times 100,$$

and

$$PV = \frac{\text{Sum of vessel area} - \text{sum of luminal area}}{n} \times 3,$$

where n is the number of cross-sections per segment (n = 4 in the current study).[23] Figure 2 shows an example of these calculations at baseline and follow-up.

Coronary Remodeling. As recommended for longitudinal studies,[22,24] remodeling was analyzed on the basis of changes in vessel area from baseline to follow-up. Positive remodeling was defined as an increase in vessel area; absence of remodeling, no substantial change in vessel area; and negative remodeling, a decrease in vessel area (Fig. 3). Positive remodeling was further classified as expansive (Δ vessel area / Δ plaque area >1) or incomplete (Δ vessel area / Δ plaque area = 0 to 1).

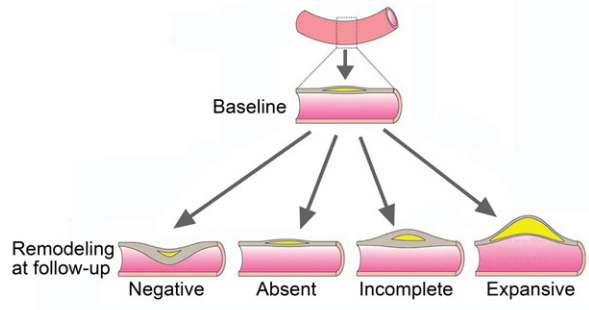

Fig. 3 *Illustration shows coronary remodeling patterns. Incomplete or expansive changes were considered to be positive remodeling.*

Statistical Analysis

Categorical variables are presented as number or percentage. Continuous variables are presented as mean ± SD or as median and interquartile range (IQR) (Table II). Continuous variables were analyzed by using the Kolmogorov-Smirnov test. Baseline and follow-up measurements for MLA, PB, and PV were compared by using the paired *t* test or the Wilcoxon signed-rank test, as appropriate. To evaluate interobserver and intraobserver variability, a subset of 8 coronary arteries was randomly selected and analyzed twice by the same observer, with a delay of one month, and once by a second observer. Intraobserver and interobserver variability were evaluated by intraclass correlation coefficients (ICC) and the Bland-Altman test. Statistical analyses were performed with use of SPSS 21.0 (IBM Corporation; Endicott, NY) and STATA® 13 (StataCorp LP; College Station, Texas). A *P* value <0.05 was considered statistically significant.

Results

We analyzed 625 RCA segments, each 3 mm long, from 21 patients with ACS. The median time between the baseline and follow-up scans was 12 months (IQR, 9–20 mo). Of the 21 patients studied, 8 had undergone at least one stent implantation in the left coronary artery (LCA) before baseline measurement, and 13 underwent stent implantation in the LCA a few days after baseline CTA imaging. No patient underwent stent implantation in the RCA after baseline CTA imaging. After discharge from the hospital, all patients were treated with secondary prevention methods, such as antiplatelet, lipid-lowering, and antihypertension medications.

Interobserver and Intraobserver Variability

We calculated interobserver variability for 215 randomly selected segments (Fig. 4). For MLA, the ICC was 0.96, and the Bland-Altman bias was –10% (95% limits of agreement [LOA], –42.8% to 22.8%). For PB, the ICC was 0.71, and the Bland-Altman bias was

TABLE II. Comparison of Quantitative Coronary CTA Results at Baseline and Follow-Up (*N*=625 Segments)

Variable	Baseline	Follow-Up	Change*	*P* Value**
Minimum luminal area (mm^2)				
Mean ± SD	6.2 ± 2.84	5.96 ± 3.14	–0.24 ± 1.79	—
Median (IQR)	5.18 (4.16–7.82)	5.38 (3.99–7.68)	–0.05 (–1.33 to 0.87)	0.012
Plaque burden (%)				
Mean ± SD	49.74 ± 8	52.17 ± 11.03	2.43 ± 11.07	—
Median (IQR)	48.23 (43.89–54.08)	49.86 (44.53–57.35)	0.34 (–4.32 to 6.35)	0.02
Plaque volume (mm^3)				
Mean ± SD	26.21 ± 9.19	26.73 ± 10	0.52 ± 6.44	—
Median (IQR)	24.35 (19.05–32.19)	24.94 (19.03–31.64)	0.33 (–3.05 to 3.54)	0.213

CTA = computed tomography angiography; IQR = interquartile range

P <0.05 was considered statistically significant.

*Changes in minimum luminal area, plaque burden, and plaque volume were calculated as follow-up value – baseline value.
**Wilcoxon signed-rank test

TABLE III. Results of Coronary Remodeling in 625 Segments

Patterns	No. of Segments (%)
Positive remodeling	248 (40)
Expansive	167 (27)
Incomplete	81 (13)
Absent	109 (17)
Negative	268 (43)

5.6% (95% LOA, –13.4% to 24.7%). For PV, the ICC was 0.85, and the Bland-Altman bias was 3.2% (95% LOA, –38.8% to 45.1%).

Intraobserver variability indicated excellent correlation with good limits of agreement. For MLA, the ICC was 0.99, and the Bland-Altman bias was 0 (95% LOA, –6% to 6%). For PB, the ICC was 0.96, and the Bland-Altman bias was –2.5% (95% LOA, –7.5% to 2.5%). For PV, the ICC was 0.98, and the Bland-Altman bias was –4.6% (95% LOA, –12.2% to 3.1%).

Quantitative Analysis of Coronary CTA Images

Between baseline and follow-up, the median MLA decreased 0.05 mm^2 (IQR, –1.33 to 0.87 mm^2; *P*=0.012); the median PB increased 0.34% (IQR, –4.32% to 6.35%; *P*=0.02); and there was no change in PV (0.33 mm^3 (–3.05 to 3.54 mm^3); *P*=0.213) (Table II). Table III shows the coronary remodeling patterns at follow-up. Among the 625 segments, 40% showed positive remodeling, 43% showed negative remodeling, and 17% showed no substantial change.

Discussion

This study shows the feasibility of using CTA to quantitatively evaluate the progression of nonculprit coronary plaque along the RCA in patients with ACS. The main finding was that, in patients who underwent PCI to the LCA and continued to be treated with conventional therapy after discharge from the hospital, the MLA of the RCA was reduced, whereas there was a slight increase in PB during the 12-month follow-up period. Our results also show that CTA yields good intra- and interobserver variability for MLA, PB, and PV.

When CTA is used for quantitative analysis, WW and WL settings can affect the measured values of vessel and luminal areas. Investigators have shown that setting WW and WL based on the mean luminal density is better than using a fixed threshold,[25] and that CT provides optimal matching with IVUS in the quantitative measurement of plaques when appropriate WW and WL settings are used.[11,19] On the basis of these findings and the results of our preliminary tests, we set the WW to 155% and the WL to 65% of the average luminal density. In addition, we found that the ICC was better for intraobserver variability than for interobserver variability; this was caused by differences between the 2 observers in the estimation of the mean luminal density.

The segmentation method is very important in evaluating plaque progression within the RCA tree. Until recently, most studies focused on only a small segment of the coronary tree or a specific subset of lesions.[9-13] In 2012, Papadopoulou and colleagues[9] evaluated plaque progression in the entire coronary tree, which they divided into 17 segments on the basis of the coronary CTA analysis guidelines provided by the Society of Cardiovascular Computed Tomography Guidelines Committee.[18] However, when long segments are used, characterizing the morphology of the coronary arteries and the parameters we examined in our study—MLA, PB, and PV—is difficult. Dividing the arteries into shorter, 3-mm segments enables us to obtain a better morphologic representation.

The use of CTA to evaluate coronary plaque progression is likely to increase, particularly with further improvements in hardware and software. Whereas IVUS

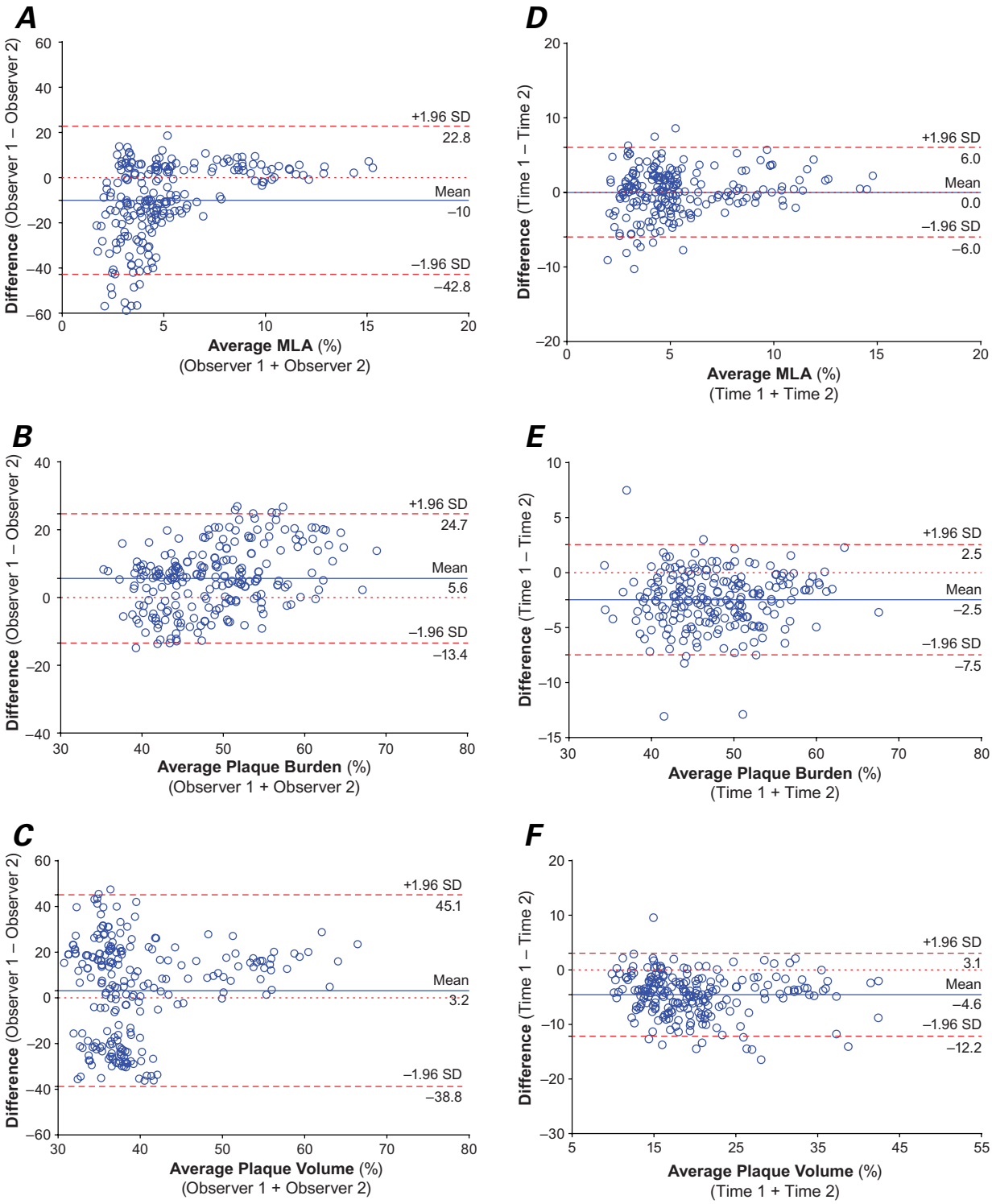

Fig. 4 *Bland-Altman plots show* ***A, B, C****) interobserver and* ***D, E, F****) intraobserver variability for the* ***A, D****) minimum luminal area (MLA),* ***B, E****) plaque burden, and* ***C, F****) plaque volume.*

is considered the gold standard for evaluating plaque progression, it is invasive, and it cannot measure severe stenosis (>90%) in segments and distal small vessels with a diameter >2 mm). Previous studies comparing IVUS and CTA support the feasibility of using the latter to evaluate atherosclerotic plaque size, PB, remodeling, eccentricity, and plaque progression.[14,21,26,27] To ensure the accuracy of the evaluation, we have found that adhering to a standard CTA protocol at baseline and at follow-up is necessary; preferably, the studies

should be performed on the same scanner. Moreover, standards for evaluating plaque are essential to reduce the difference between intraobserver and interobserver variability.

Our study has some limitations. First, it was a single-center trial with a small sample size of only 21 patients. Therefore, multivariate analysis to evaluate the impact of baseline variables on plaque progression at follow-up was not possible. Second, because this was a retrospective pilot study, identifying patients who had undergone CTA at 2 different time points was difficult. Of 1,028 patients with initial CTA images, only 21 were eligible; thus, this study did not include a comparison group with stable angina pectoris. Third, although the evaluation of coronary plaque composition is beneficial in predicting acute coronary events, we did not take it into consideration because the accuracy of CTA for this purpose remains questionable. Finally, we used a manual method for the quantitative measurement of CTA images. Because this process takes a long time and requires experienced clinicians, using it in large-scale studies or the clinic is not practical.

Despite these limitations, we think that CTA is a feasible method of quantitatively evaluating coronary plaque progression, provided that appropriate WW and WL settings are used.

References

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3(11):e442.
2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics--2014 update: a report from the American Heart Association. Circulation 2014;129(3):e28-e292.
3. Timmins LH, Molony DS, Eshtehardi P, McDaniel MC, Oshinski JN, Samady H, Giddens DP. Focal association between wall shear stress and clinical coronary artery disease progression. Ann Biomed Eng 2015;43(1):94-106.
4. Corban MT, Eshtehardi P, Suo J, McDaniel MC, Timmins LH, Rassoul-Arzrumly E, et al. Combination of plaque burden, wall shear stress, and plaque phenotype has incremental value for prediction of coronary atherosclerotic plaque progression and vulnerability. Atherosclerosis 2014;232(2):271-6.
5. Stone PH, Saito S, Takahashi S, Makita Y, Nakamura S, Kawasaki T, et al. Prediction of progression of coronary artery disease and clinical outcomes using vascular profiling of endothelial shear stress and arterial plaque characteristics: the PREDICTION Study. Circulation 2012;126(2):172-81.
6. Samady H, Eshtehardi P, McDaniel MC, Suo J, Dhawan SS, Maynard C, et al. Coronary artery wall shear stress is associated with progression and transformation of atherosclerotic plaque and arterial remodeling in patients with coronary artery disease. Circulation 2011;124(7):779-88.
7. Brown BG, Zhao XQ. Is intravascular ultrasound the gold standard surrogate for clinically relevant atherosclerosis progression? J Am Coll Cardiol 2007;49(9):933-8.
8. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011;364(3):226-35.
9. Papadopoulou SL, Neefjes LA, Garcia-Garcia HM, Flu WJ, Rossi A, Dharampal AS, et al. Natural history of coronary atherosclerosis by multislice computed tomography. JACC Cardiovasc Imaging 2012;5(3 Suppl):S28-37.
10. Priester TC, Litwin SE. Measuring progression of coronary atherosclerosis with computed tomography: searching for clarity among shades of gray. J Cardiovasc Comput Tomogr 2009;3 Suppl 2:S81-90.
11. Leber AW, Becker A, Knez A, von Ziegler F, Sirol M, Nikolaou K, et al. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. J Am Coll Cardiol 2006;47(3):672-7.
12. Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. J Am Coll Cardiol 2009;54(1):49-57.
13. Versteylen MO, Kietselaer BL, Dagnelie PC, Joosen IA, Dedic A, Raaijmakers RH, et al. Additive value of semiautomated quantification of coronary artery disease using cardiac computed tomographic angiography to predict future acute coronary syndrome. J Am Coll Cardiol 2013;61(22):2296-305.
14. Lehman SJ, Schlett CL, Bamberg F, Lee H, Donnelly P, Shturman L, et al. Assessment of coronary plaque progression in coronary computed tomography angiography using a semiquantitative score. JACC Cardiovasc Imaging 2009;2(11):1262-70.
15. Inoue K, Motoyama S, Sarai M, Sato T, Harigaya H, Hara T, et al. Serial coronary CT angiography-verified changes in plaque characteristics as an end point: evaluation of effect of statin intervention. JACC Cardiovasc Imaging 2010;3(7):691-8.
16. Hoffmann H, Frieler K, Schlattmann P, Hamm B, Dewey M. Influence of statin treatment on coronary atherosclerosis visualised using multidetector computed tomography [published erratum appears in Eur Radiol 2011;21(7):1576]. Eur Radiol 2010;20(12):2824-33.
17. Tardif JC, L'allier PL, Ibrahim R, Gregoire JC, Nozza A, Cossette M, et al. Treatment with 5-lipoxygenase inhibitor VIA-2291 (Atreleuton) in patients with recent acute coronary syndrome. Circ Cardiovasc Imaging 2010;3(3):298-307.
18. Abbara S, Arbab-Zadeh A, Callister TQ, Desai MY, Mamuya W, Thomson L, Weigold WG. SCCT guidelines for performance of coronary computed tomographic angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee. J Cardiovasc Comput Tomogr 2009;3(3):190-204.
19. Nakazato R, Shalev A, Doh J-H, Koo BK, Gransar H, Gomez MJ, et al. Aggregate plaque volume by coronary computed tomography angiography is superior and incremental to luminal narrowing for diagnosis of ischemic lesions of intermediate stenosis severity. J Am Coll Cardiol 2013;62(5):460-7.
20. Koskinas KC, Chatzizisis YS, Papafaklis MI, Coskun AU, Baker AB, Jarolim P, et al. Synergistic effect of local endothelial shear stress and systemic hypercholesterolemia on coronary atherosclerotic plaque progression and composition in pigs. Int J Cardiol 2013;169(6):394-401.
21. Koskinas KC, Feldman CL, Chatzizisis YS, Coskun AU, Jonas M, Maynard C, et al. Natural history of experimental coronary atherosclerosis and vascular remodeling in relation to endothelial shear stress: a serial, in vivo intravascular ultrasound study. Circulation 2010;121(19):2092-101.
22. Mintz GS, Garcia-Garcia HM, Nicholls SJ, Weissman NJ, Bruining N, Crowe T, et al. Clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound regression/progression studies. EuroIntervention 2011;6(9):1123-30.

23. Badak O, Schoenhagen P, Tsunoda T, Magyar WA, Coughlin J, Kapadia S, et al. Characteristics of atherosclerotic plaque distribution in coronary artery bifurcations: an intravascular ultrasound analysis. Coron Artery Dis 2003;14(4):309-16.
24. Sipahi I, Tuzcu EM, Schoenhagen P, Nicholls SJ, Crowe T, Kapadia S, Nissen SE. Static and serial assessments of coronary arterial remodeling are discordant: an intravascular ultrasound analysis from the Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) trial. Am Heart J 2006;152(3):544-50.
25. Funabashi N, Kobayashi Y, Kudo M, Asano M, Teramoto K, Komuro I, Rubin GD. New method of measuring coronary diameter by electron-beam computed tomographic angiography using adjusted thresholds determined by calibration with aortic opacity. Circ J 2004;68(8):769-77.
26. Papadopoulou SL, Neefjes LA, Schaap M, Li HH, Capuano E, van der Giessen AG, et al. Detection and quantification of coronary atherosclerotic plaque by 64-slice multidetector CT: a systematic head-to-head comparison with intravascular ultrasound. Atherosclerosis 2011;219(1):163-70.
27. Voros S, Rinehart S, Qian Z, Vazquez G, Anderson H, Murrieta L, et al. Prospective validation of standardized, 3-dimensional, quantitative coronary computed tomographic plaque measurements using radiofrequency backscatter intravascular ultrasound as reference standard in intermediate coronary arterial lesions: results from the ATLANTA (assessment of tissue characteristics, lesion morphology, and hemodynamics by angiography with fractional flow reserve, intravascular ultrasound and virtual histology, and noninvasive computed tomography in atherosclerotic plaques) I study. JACC Cardiovasc Interv 2011;4(2):198-208.