

Supplementary Online Content

Han D, Lin A, Kuronuma K, et al. Association of plaque location and vessel geometry determined by coronary computed tomographic angiography with future acute coronary syndrome–causing culprit lesions. *JAMA Cardiol*. Published online January 26, 2022. doi:10.1001/jamacardio.2021.5705

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Additional Patient Characteristics Between ACS vs Control

	ACS (n=116)	Controls (n=116)	<i>P</i> value
Angina type			.03
Asymptomatic	19 (17.1)	36 (31.6)	
Noncardiac	10 (9.0)	15 (13.2)	
Atypical	51 (45.9)	42 (36.8)	
Typical	31 (27.9)	21 (18.4)	
Dyspnea, %	14 (14.6)	24 (25.8)	.05
Peripheral vascular disease	3 (3.6)	6 (7.3)	.29
Renal insufficiency	3 (3.1)	3 (3.4)	.89
Creatinine	1.1 ± 0.5	1.0±0.3	.68
Race/Ethnicity			.87
White	58 (64.4)	52 (61.2)	
East Asian	27 (30.0)	27 (31.8)	
Others	5 (5.6)	6 (7.1)	
Lipid profile			
Total Cholesterol	189.1±52.8	178.0±40.1	.25
Low-density Cholesterol	109.9±39.9	109.6±37.3	.97
High-density Cholesterol	47.0±13.2	47.1±12.9	.98
Medications			
Statin	49 (42.2)	46 (39.7)	.69
Aspirin	49 (42.2)	42 (36.2)	.31
ACEi/ARB	29 (25.0)	27 (23.3)	.79
Beta blocker	33 (28.4)	34 (29.3)	.82
Nitrates	2 (1.7)	2 (1.7)	.97
Interval coronary revascularization	70 (60.3)	32 (27.6)	<.001
Values are shown as mean ± standard deviation, median (interquartile range) or number (percentage). CAD, coronary artery disease; ACS, acute coronary syndrome; ACEi, Angiotensin-converting enzyme (ACE) inhibitors; ARB, Angiotensin II Receptor Blockers			

eTable 2. CCTA Lesion Characteristics According to the Number of AGCs in Patients With ACS

	AGC 0 (n=151)	AGC 1 (n=262)	AGC ≥2 (n=135)	P Value
Stenosis grade, n (%)				
Diameter stenosis				.07
1-24%	60 (39.7)	92 (35.1)	30 (22.2)	
25-49%	56 (37.1)	101 (38.6)	59 (43.7)	
50-69%	23 (15.2)	44 (16.8)	28 (20.7)	
>70%	12 (7.9)	25 (9.5)	18 (13.3)	
Adverse plaque characteristics, n(%)				
Positive remodeling	117 (77.5)	215 (82.1)	109 (81.3)	.51
Low attenuation plaque	13 (8.6)	46 (17.5)	29 (21.6)	.008
Spotty calcification	16 (10.6)	43 (16.4)	20 (14.9)	.27
Napkin-ring sign	0 (0.0)	9 (3.4)	11 (8.2)	.001
Quantitative plaque volume and burden				
Total plaque volume, mm ³	15.5 (6.9-30.8)	31.4 (12.3-91.6)	88.3 (26.2-154.9)	<.001
Calcified	3.8 (0.7-8.7)	7.2 (1.3-26.3)	21.7 (6.2-61.6)	<.001
Fibrous	7.3 (3.1-16.4)	14.4 (5.3-42.4)	31.0 (11.1-70.6)	<.001
Fibro-fatty	0.9 (0.1-4.6)	2.4 (0.2-13.8)	7.0 (0.7-20.6)	.001
Necrotic core	0 (0-0.1)	0 (0-0.5)	0.1 (0-0.8)	.02
Noncalcified	9.6 (4.1-22.4)	19.7 (6.4-60.1)	40.0 (14.6-89.1)	<.001
Total plaque burden, %	18.5 (10.8-27.4)	20.9 (12.1-32.3)	30.6 (19.3-39.3)	<.001
Calcified	4.1 (0.8-8.6)	5.5 (1.6-11.7)	10.9 (3.8-17.9)	<.001
Fibrous	8.6 (5.4-13.5)	9.7 (5.7-15.1)	12.2 (6.9-18.8)	<.001
Fibro-fatty	0.8 (0.1-3.9)	1.6 (0.2-5.1)	2.5 (0.4-6.3)	.011
Necrotic core	0 (0-0.1)	0 (0-0.2)	0.01 (0-0.3)	.006
Noncalcified plaque	10.7 (5.9-18.0)	12.3 (7.0-22.8)	17.0 (9.1-25.9)	.003
Values are shown as median (interquartile range) or number (percentage). CCTA, coronary computed tomography angiography; AGC, adverse geometric characteristics; ACS, acute coronary syndrome				

eTable 3. Univariable and Multivariable Cox Proportional Hazards Regression Analysis of AGCs for Risk of Culprit Lesions

	Univariable			Multivariable*		
	HR	95% CI	<i>P</i> Value	HR	95% CI	<i>P</i> Value
Bifurcation	3.61	2.33-5.59	<.001	2.14	1.39-3.29	<.001
Tortuosity	4.70	1.50-14.77	.008	2.31	1.01-5.27	.04
Short distance from ostium	2.06	1.37-3.08	<.001	2.71	1.73-4.24	<.001
Number of AGCs						
0	1 (Reference)			1 (Reference)		
1	3.05	1.50-6.14	.002	2.90	1.38-6.08	.005
≥2	7.82	3.89-15.75	<.001	6.84	3.33-14.04	<.001
* adjusted for diameter stenosis grade, number of adverse plaque characteristics, plaque area at the maximal stenosis section, minimum lumen area, total plaque, noncalcified plaque, and necrotic core volume AGCs, adverse geometrical characteristics; HR, hazard ratio; CI, confidence interval						

eTable 4. Multivariable Cox Proportional Hazards Regression Analysis of AGCs for Risk of Culprit Lesions (Patients With ACS vs Controls)

	Univariable			Multivariable*		
	HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value
Bifurcation	3.61	2.55-5.09	<.001	2.63	1.77-3.92	<.001
Tortuosity	1.73	0.73-4.10	.21	1.66	0.73-3.78	.22
Short ostium to lesion distance	2.17	1.47-3.19	<.001	1.55	1.02-2.33	.03
Number of AGCs						
0	1 (Reference)			1 (Reference)		
1	4.96	2.33-10.58	<.001	2.53	1.24-5.15	.01
≥2	9.70	4.69-20.08	<.001	4.43	2.17-9.05	<.001
* adjusted for diameter stenosis grade, number of adverse plaque characteristics, plaque area at the maximal stenosis section, minimum lumen area, total plaque, noncalcified plaque, and necrotic core volume AGCs, adverse geometrical characteristics; HR, hazard ratio; CI, confidence interval						

eTable 5. Clinical and CCTA Characteristics in Analyzed (n = 116) and Excluded (n=118) Patients With ACS From the ICONIC Study

	Analyzed (n=116)	Excluded (n=118)	<i>P</i> Value
Age	62.7 ± 11.5	61.7 ± 11.6	.49
Male	80 (68.9)	69 (58.5)	.10
Body mass index	27.3 ± 4.5	27.8 ± 5.6	.45
Hypertension	72 (62.1)	76 (65.5)	.59
Diabetes	26 (22.4)	20 (16.9)	.29
Dyslipidemia	67 (58.3)	62 (52.9)	.42
Family history of premature CAD	49 (43.4)	45 (39.1)	.52
Current smoker	29 (25.2)	43 (36.4)	.06
Type of ACS event			
STEMI	21 (18.1)	19 (16.1)	.68
NSTEMI	50 (43.1)	64 (54.2)	.09
MI, unspecified	3 (2.6)	3 (2.5)	.98
Unstable angina	42 (36.2)	32 (27.1)	.14
Angina type			.39
Asymptomatic	19 (17.1)	18 (16.2)	
Noncardiac	10 (9.0)	18 (16.2)	
Atypical	51 (45.9)	43 (38.7)	
Typical	31 (27.9)	32 (28.8)	
Dyspnea, %	14 (14.6)	26 (29.9)	.01
Race/Ethnicity			.80
White	58 (64.4)	54 (62.1)	
East Asian	27 (30.0)	26 (29.9)	
Others	5 (5.6)	7 (8.1)	
Lipid profile			
Total Cholesterol	189.1±52.8	198.3±41.7	.30
Low-density Cholesterol	109.9±39.9	128.2±42.2	.03
High-density Cholesterol	47.0±13.2	49.1±14.2	.44
Medications			

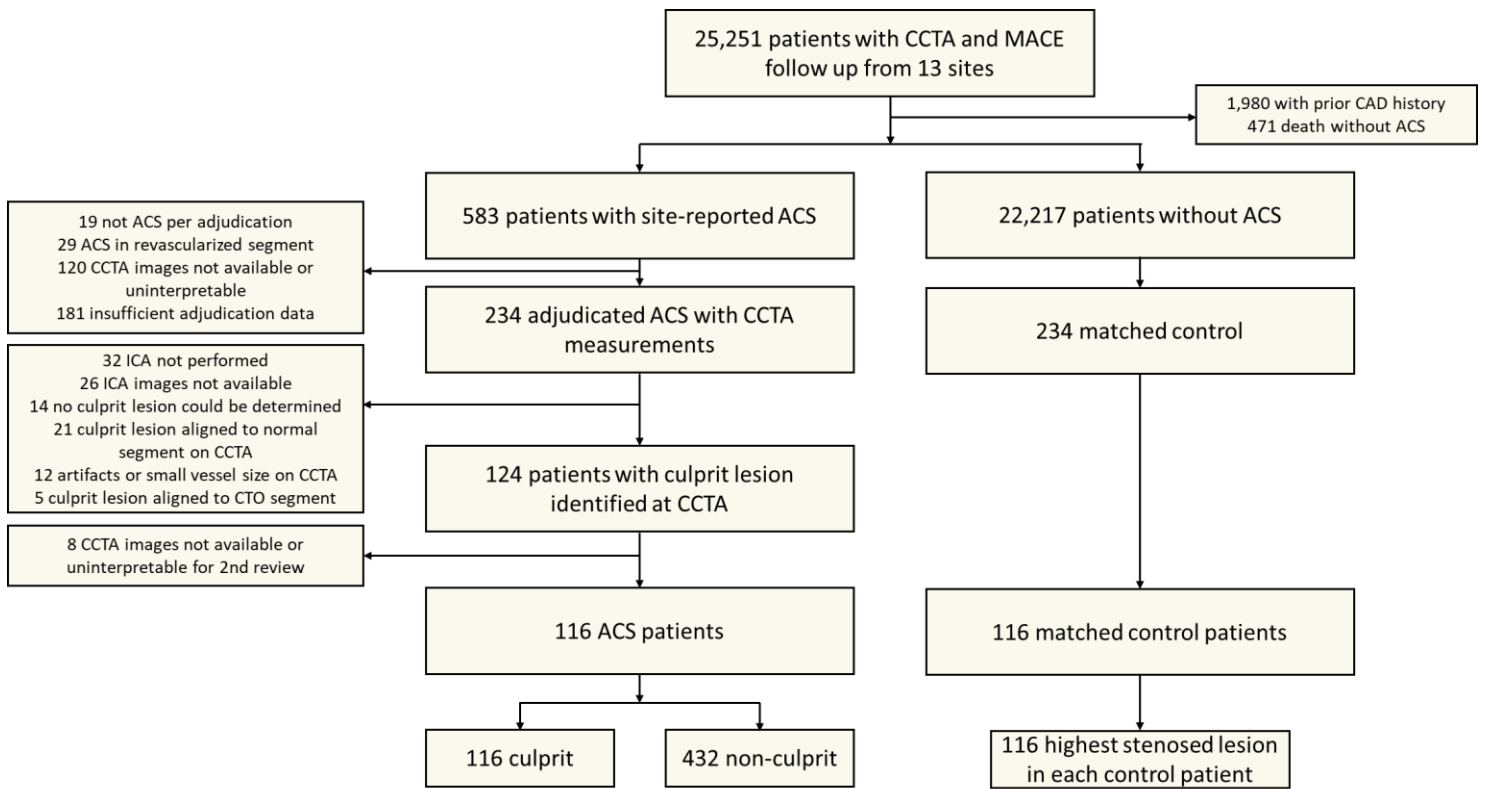
Statin	49 (42.2)	47 (39.8)	.29
Aspirin	49 (42.2)	43 (36.4)	.10
ACE/ARB	29 (25.0)	37 (31.4)	.28
Beta blocker	33 (28.4)	30 (25.4)	.35
Nitrates	2 (1.7)	9 (7.6)	.07
Interval coronary revascularization	70 (60.3)	48 (40.7)	.003
CCTA characteristics			
CAD severity			<.001
Normal	0 (0)	15 (12.7)	
Nonobstructive	49 (42.2)	55 (46.6)	
1-vessel obstructive	40 (34.5)	29 (24.6)	
2-vessel obstructive	12 (10.3)	13 (11.0)	
3-vessel/left main	15 (12.9)	6 (5.1)	
Diameter stenosis, %	45.4±15.9	31.1±18.9	<.001
Area stenosis, %	67.6±18.0	48.9±26.6	<.001
Total plaque volume, mm ³	296.1 (118.3-480.7)	109.9 (32.4-331.3)	<.001
Calcified	73.5 (21.4-181.0)	18.8 (0.1-84.5)	<.001
Fibrous	131.8 (57.2-200.6)	56.2 (13.6-137.1)	<.001
Fibro-fatty	32.7 (12.2-82.7)	15.8 (1.3-67.4)	.003
Necrotic core	2.0 (0.1-7.3)	0.8 (0-3.7)	.02
Noncalcified	1880.4 (73.3-306.9)	80.0 (22.7-214.6)	<.001
Total plaque burden, %	11.1 (5.7-19.6)	5.8 (1.6-15.5)	<.002
Calcified burden	3.7 (0.8-6.9)	0.8 (0.1-4.0)	<.001
Fibrous burden	5.2 (2.5-9.1)	2.7 (0.8-6.9)	<.001
Fibro-fatty burden	1.5 (0.5-3.4)	0.8 (0.1-3.0)	.01
Necrotic core burden	0.1 (0-0.3)	0.1 (0-0.2)	.04
Noncalcified plaque burden	7.4 (3.3-12.6)	4.0 (1.1-10.5)	<.001
Max cross-sectional plaque burden, %	70.8±16.6	55.6±26.9	<.001
Diffuseness, %	31.6±19.4	20.0±17.7	<.001
Number of total lesions	4.7 ± 2.4	2.9±2.2	<.001

Values are shown as mean \pm standard deviation, median (interquartile range) or number (percentage).

CAD, coronary artery disease; ACS, acute coronary syndrome; STEMI, ST elevation myocardial infarction; NSTEMI, Non-ST-elevation myocardial infarction

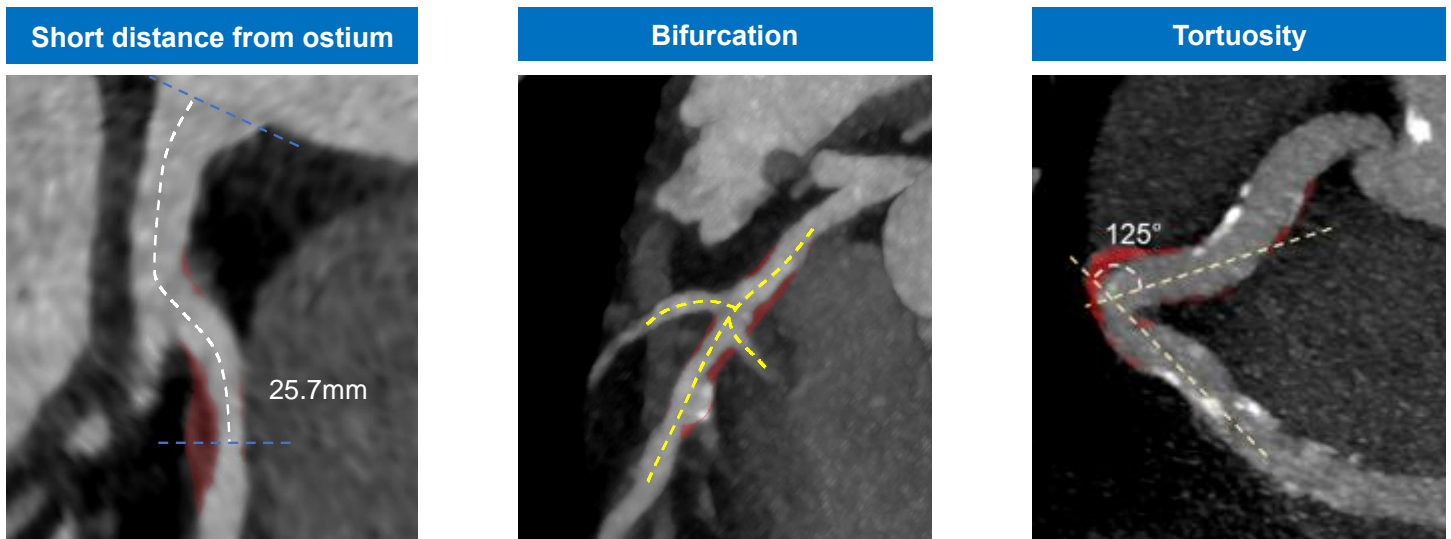
eFigure 1. Patient Selection and Study Design

Flow chart showing inclusion and exclusion criteria for the study population. ACS = acute coronary syndrome; CCTA = coronary computed tomography angiography; MACE = major adverse cardiovascular events.



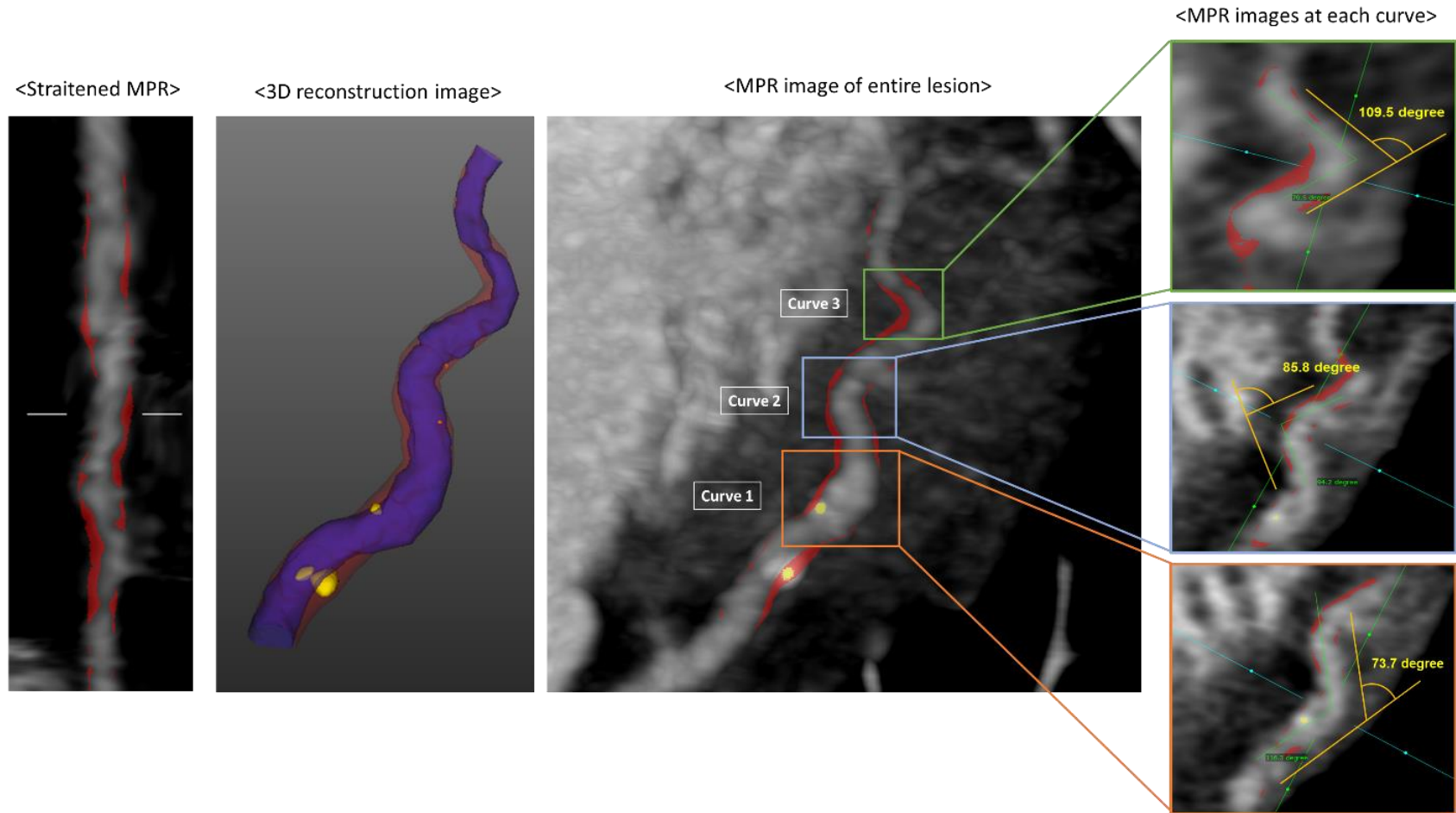
eFigure 2. Illustrations of Adverse Geometric Characteristics

Distance from ostium to lesion, lesion location at bifurcation or trifurcation, and vessel tortuosity were assessed as adverse geometric characteristics (AGCs) for individual plaques in patients with subsequent acute coronary syndrome. Red overlay depicts noncalcified plaque.



eFigure 3. Lesion Curve Assessment Using Semiautomated Software

Straitened MRP showed a coronary atherosclerotic plaque in the distal LAD. 3D reconstruction image represents the plaque was located at tortuous coronary segment. Vessel curvatures on the lesion were assessed at MPR image at each curve. Red and yellow overlay depict noncalcified and calcified plaque, respectively.



eFigure 4. Propensity Score Distribution of the 116 Case and 116 Control Pairs

