Age-related pancoronary vulnerability in patients with ST-elevation Myocardial Infarction

Supplemental Methods

The definitions in the clinical characteristics

Patients smoking actively within 1 month and no smoking for over 1 month were respectively defined as current smokers and former smokers. Diabetes mellitus was diagnosed once a patient met 1 of the following criteria: documented history or self-reported clinician diabetes mellitus, taking hypoglycemic medicine, fasting glucose ≥ 126mg/dL, 2h plasma glucose level ≥ 200mg/dL, classic symptom with casual plasma glucose level ≥ 200mg/dL or hemoglobin A1c (HbA1c) ≥ 6.5%. Hypertension was diagnosed as systolic blood pressure ≥ 140mmHg or diastolic blood pressure ≥ 90mmHg or current use of antihypertensive agents. Dyslipidemia was defined as total cholesterol (TC) level ≥ 220mg/dL, triglycerides ≥ 150 mg/dL, low-density lipoprotein cholesterol (LDL-C) ≥ 140mg/dL, high-density lipoprotein cholesterol (HDL-C) ≤ 40mg/dL, or current use of agents for dyslipidemia[1]. Estimated glomerular filtration (eGFR) was calculated according to the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Chronic kidney disease (CKD) was diagnosed as eGFR < 60mL/min per 1.73 m^2 [2].

The criteria in OCT analysis

A plaque was defined via OCT as a segment with a loss of the normal three-layered structure of the vessel wall[3, 4]. Proximal and distal references were identified as the sites with the largest lumen area proximal and distal to the stenosis but within the same segment. The mean reference lumen area was calculated. Percent area stenosis was calculated as ([Mean Reference Lumen Area - MLA] / Mean Reference Lumen Area) ×100. On cross-sectional OCT images, quantitative analysis was conducted at 1-mm intervals. A distance of at least 5 mm was regarded as two separated lesions on the longitudinal view[4]. Lipid-rich plaques (LRPs) had a maximal lipid arc > 90°. The lipid index was calculated using the mean lipid arc × lipid length formula. Microchannels were the presence of small (50-300μm), signal-poor structures with vesicular or tubular shape without connection to the lumen, recognized on ≥ 3 consecutive cross-sectional images. Cholesterol crystals were thin and linear regions of high signal intensity with high backscattering within a plaque. Calcification was a signal-poor or heterogeneous area delimited by sharp borders. Calcification arcs were measured in each

cross-sectional image and lengths obtained on the longitudinal view. Calcified lesions subtending an arc ≤ 90° and extending in length for 1-4mm were classified as spotty calcium. The calcium index was derived as the mean calcium arc × calcium length product. Thrombus was defined as an irregular mass (diameter > 250μm) on the face of the vessel wall or floating within the lumen[5, 6].

Supplementary Tables

Supplemental Table S1 Patient-level OCT findings among age groups

Variables	Age ≤48 years (n =158)	48 < Age ≤56 years (n =140)	56 < Age ≤63 years (n =149)	Age >63 years (n =141)	*P*-value
Non-culprit plaques	**n=383**	**n=412**	**n=424**	**n=434**	
High-risk OCT features					
MLA <3.5 (mm^2)	93 (58.9)	94 (67.1)	111 (74.5)	117 (83.0)	**<0.001**
FCT <75 (μm)	56 (35.4)	70 (50.0)	76 (51.0)	66 (46.8)	**0.041**
Max lipid arc >180 (º)	55 (34.8)	68 (48.6)	77 (51.7)	75 (53.2)	**0.001**
Macrophages	101 (63.9)	99 (70.7)	113 (75.8)	112 (79.4)	**0.001**
Other features					
LRP	91 (57.6)	99 (70.7)	102 (68.5)	98 (69.5)	**0.043**
Cholesterol crystals	35 (22.2)	45 (32.1)	60 (40.3)	57 (40.4)	**<0.001**
Microchannel	75 (47.5)	59 (42.1)	73 (49.0)	83 (58.9)	**0.032**
Calcification	61 (38.6)	60 (42.9)	97 (65.1)	102 (72.3)	**<0.001**
Spotty calcification	55 (34.8)	53 (37.9)	83 (55.7)	87 (61.7)	**<0.001**
Large calcification	25 (15.8)	34 (24.3)	71 (47.7)	77 (54.6)	**<0.001**
Thrombus	8 (5.1)	11 (7.9)	23 (15.4)	20 (14.2)	**0.002**
Pancoronary vulnerability					
High-risk plaques	22 (13.9)	25 (17.9)	33 (22.1)	34 (24.1)	**0.016**
Non-culprit plaque rupture	13 (8.2)	25 (17.9)	24 (16.1)	20 (14.2)	0.167
Non-culprit TCFA	47 (29.7)	58 (41.4)	61 (40.9)	55 (39.0)	0.103

Values are presented as n (%), mean ± SD or median (25th-75th percentile). FCT=fibrous-cap thickness; LRP=lipid rich plaque; MLA=minimal lumen area; OCT=optical coherence tomography; SD=standard deviation; TCFA=thin-cap fibroatheroma.

Supplemental Table S2 Univariable and multivariate analysis of high-risk plaques in STEMI patients≤56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	3.562	1.767-7.182	**<0.001**	3.179	1.501-6.733	**0.003**
Male	1.242	0.413-3.740	0.700			
Diabetes mellitus	1.725	0.786-3.788	0.174			
Hypertension	1.706	0.901-3.228	0.101			
Cigarette smoking	0.691	0.500-0.956	**0.026**			
CKD	0.474	0.060-3.764	0.480			
Dyslipidemia	1.624	0.797-3.308	0.181			
TC	1.077	1.000-1.160	**0.050**			
Triglyceride	1.015	0.989-1.041	0.267			
LDL-C	0.876	0.659-1.164	0.360			
HDL-C	1.045	0.957-1.140	0.331			
TC/HDL-C ratio	1.043	0.852-1.277	0.683			
Hs-CRP	0.966	0.897-1.041	0.366			
HbA1c	1.193	0.987-1.442	**0.068**			

OR for TC, Triglyceride and HDL-C were calculated for each 10.0mg/dL increase; OR for hs-CRP was calculated for each 1.0mg/L increase; OR for HbA1c was calculated for each 1% increase. CI = confidence interval; CKD = chronic kidney disease; HDL-C = high-density lipoprotein cholesterol; hs-CRP = high-sensitive C-reaction protein; LDL-C=low density lipoprotein cholesterol; OR = odds ratio; PR = plaque rupture; STEMI = ST-segment Elevation Myocardial Infarction; TC = total cholesterol.

Supplemental Table S3 Univariable and multivariate analysis of high-risk plaques in STEMI patients>56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	1.656	0.927-2.958	**0.089**			
Male	0.900	0.513-1.578	0.712			
Diabetes mellitus	0.606	0.256-1.432	0.254			
Hypertension	1.245	0.720-2.150	0.433			
Cigarette smoking	0.758	0.565-1.016	**0.064**			
CKD	0.701	0.256-1.922	0.490			
Dyslipidemia	1.852	1.024-3.349	**0.042**			
TC	1.036	0.963-1.114	0.343			
Triglyceride	1.020	0.982-1.059	0.313			
LDL-C	1.002	0.801-1.253	0.986			
HDL-C	0.976	0.892-1.067	0.592			
TC/HDL-C ratio	0.989	0.801-1.221	0.919			
Hs-CRP	1.036	0.992-1.083	0.111			
HbA1c	0.879	0.666-1.162	0.367			

ORs calculation and abbreviations are the same as Supplemental Table S2.

Supplemental Table S4 Univariable and multivariate analysis of non-culprit PR in STEMI patients≤56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	4.513	1.993-10.218	**<0.001**	3.802	1.604-9.014	**0.002**
Male	2.172	0.496-9.514	0.303			
Diabetes mellitus	0.859	0.316-2.335	0.765			
Hypertension	1.855	0.929-3.705	**0.080**			
Cigarette smoking	0.798	0.560-1.138	0.213			
CKD	2.390	0.617-9.255	0.207			
Dyslipidemia	1.433	0.658-3.119	0.365			
TC	1.120	1.032-1.216	**0.007**	1.094	1.002-1.195	**0.045**
Triglyceride	1.030	1.003-1.058	**0.029**			
LDL-C	0.773	0.558-1.071	0.122			
HDL-C	1.015	0.920-1.120	0.761			
TC/HDL-C ratio	1.202	0.986-1.465	**0.068**			
Hs-CRP	1.023	0.946-1.105	0.572			
HbA1c	1.107	0.892-1.373	0.357			

ORs calculation and abbreviations are the same as Supplemental Table S2.

Supplemental Table S5 Univariable and multivariate analysis of non-culprit PR in STEMI patients>56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	1.088	0.563-2.101	0.802			
Male	3.031	1.352-6.795	0.007	3.031	1.352-6.795	**0.007**
Diabetes mellitus	1.340	0.575-3.120	0.498			
Hypertension	1.177	0.619-2.237	0.619			
Cigarette smoking	1.078	0.769-1.510	0.665			
CKD	0.647	0.187-2.242	0.492			
Dyslipidemia	1.577	0.795-3.130	0.193			
TC	0.979	0.898-1.067	0.622			
Triglyceride	1.016	0.972-1.061	0.491			
LDL-C	1.049	0.810-1.358	0.715			
HDL-C	1.027	0.928-1.137	0.604			
TC/HDL-C ratio	1.019	0.804-1.292	0.876			
Hs-CRP	1.001	0.953-1.051	0.984			
HbA1c	0.985	0.730-1.328	0.920			

ORs calculation and abbreviations are the same as Supplemental Table S2.

Supplemental Table S6 Univariable and multivariate analysis of non-culprit TCFA in STEMI patients≤56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	3.839	2.305-6.392	**<0.001**	3.536	2.051-6.094	**<0.001**
Male	1.302	0.574-2.956	0.528			
Diabetes mellitus	0.836	0.422-1.657	0.608			
Hypertension	2.230	1.349-3.685	**0.002**	1.920	1.099-3.355	**0.022**
Cigarette smoking	0.837	0.650-1.078	0.168			
CKD	1.329	0.411-4.294	0.635			
Dyslipidemia	1.863	1.089-3.186	**0.023**			
TC	1.094	1.030-1.162	**0.003**			
Triglyceride	1.016	0.994-1.039	0.165			
LDL-C	0.776	0.621-0.971	**0.027**			
HDL-C	1.076	1.004-1.154	**0.037**			
TC/HDL-C ratio	1.169	0.991-1.378	**0.063**			
Hs-CRP	1.002	0.949-1.059	0.930			
HbA1c	1.061	0.895-1.258	0.495			

ORs calculation and abbreviations are the same as Supplemental Table S2.

Supplemental Table S7 Univariable and multivariate analysis of non-culprit TCFA in patients>56 years

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
Culprit PR	1.419	0.874-2.303	0.157			
Male	0.929	0.571-1.510	0.766			
Diabetes mellitus	2.381	1.232-4.601	**0.010**			
Hypertension	1.589	0.990-2.549	**0.055**			
Cigarette smoking	0.812	0.633-1.042	0.102			
CKD	0.468	0.192-1.139	**0.094**			
Dyslipidemia	1.554	0.951-2.537	**0.078**			
TC	1.027	0.965-1.093	0.402			
Triglyceride	1.016	0.982-1.051	0.367			
LDL-C	0.924	0.762-1.119	0.418			
HDL-C	1.039	0.963-1.120	0.322			
TC/HDL-C ratio	1.098	0.920-1.312	0.301			
Hs-CRP	0.982	0.942-1.024	0.401			
HbA1c	1.232	0.993-1.530	**0.058**			

ORs calculation and abbreviations are the same as Supplemental Table S2.

Reference

1. Dai J, Xing L, Jia H, et al. In vivo predictors of plaque erosion in patients with st-segment elevation myocardial infarction: A clinical, angiographical, and intravascular optical coherence tomography study. Eur Heart J 2018;39:2077-85.
2. Inker LA, Astor BC, Fox CH, et al. Kdoqi us commentary on the 2012 kdigo clinical practice guideline for the evaluation and management of ckd. Am J Kidney Dis 2014;63:713-35.
3. Sugiyama T, Yamamoto E, Bryniarski K, et al. Nonculprit plaque characteristics in patients with acute coronary syndrome caused by plaque erosion vs plaque rupture: A 3-vessel optical coherence tomography study. JAMA Cardiol 2018;3:207-14.
4. Vergallo R, Uemura S, Soeda T, et al. Prevalence and predictors of multiple coronary plaque ruptures: In vivo 3-vessel optical coherence tomography imaging study. Arterioscler Thromb Vasc Biol 2016;36:2229-38.
5. Tearney GJ, Regar E, Akasaka T, et al. Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: A report from the international working group for intravascular optical coherence tomography standardization and validation. J Am Coll Cardiol 2012;59:1058-72.
6. Cao M, Zhao L, Ren X, et al. Pancoronary plaque characteristics in stemi caused by culprit plaque erosion versus rupture: 3-vessel oct study. JACC Cardiovasc Imaging 2021;14:1235-45.