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Culprit lesion morphology in young patients with ST-segment elevated myocardial infarction: A clinical, angiographic and optical coherence tomography study

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HIGHLIGHTS

- Largest prospective optical coherence tomography study of STEMI in young patients.
- Mechanisms of STEMI in young and older patients were different.
- Age was an independent predictor of culprit lesion morphology in STEMI patients.
- Culprit lesions in patients aged ≤50 years have less vulnerable characteristics.

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ABSTRACT

Background and aims: About 20% of patients with ST-segment elevated myocardial infarction (STEMI) are young adults. Morphological characteristics of culprit lesion in young STEMI patients have not been systematically evaluated *in vivo*. The present study aimed to investigate culprit lesion characteristics in young patients *versus* older patients using optical coherence tomography (OCT).

Methods: 1442 STEMI patients who underwent OCT examination of culprit lesion were included and divided into young group (age ≤50 years, n = 400) and older group (age > 50 years, n = 1042). Clinical characteristics, angiography and OCT findings were compared between the two groups.

Results: Culprit lesions in STEMI patients aged ≤50 years had more plaque erosion (32.0% *vs.* 21.1%, $p < 0.001$) and larger minimal lumen area (2.3 ± 1.7 mm^2 *vs.* 1.9 ± 1.1 mm^2, $p < 0.001$) than in those aged > 50 years. As compared with older patients, lipid rich plaque (80.5% *vs.* 87.2%, $p = 0.001$), thin cap fibroatheroma (TCFA, 59.5% *vs.* 69.5%, $p < 0.001$), calcification (31.3% *vs.* 48.7%, $p < 0.001$), spotty calcification (25.3% *vs.* 36.1%, $p < 0.001$) and cholesterol crystals (26.3% *vs.* 38.4%, $p < 0.001$) were less frequently observed in young patients. A gradient increase in typical plaque vulnerability was observed from age ≤50 years to 50–70 years to > 70 years. In multivariate regression analysis, age ≤50 years was independently associated with less frequency of plaque rupture, TCFA, spotty calcification, cholesterol crystals and smaller lumen area stenosis.

Conclusions: Morphological characteristics of culprit lesion in young STEMI patients were different from those in older patients. Patients aged ≤50 years had more plaque erosion and less vulnerable plaque features.

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1. Introduction

About 20% of patients with ST-segment elevated myocardial infarction (STEMI) are young adults [1,2]. Previous evidence showed that a great proportion of young STEMI patients are male and cigarette smoker, together with other traditional risk factors including dyslipidemia and genetic predisposition [3,4]. However, culprit lesion morphological characteristics have not been systemically assessed in young STEMI patients. The present study aimed to investigate the differences of culprit plaque characteristics in young patients *versus* older patients, and determine the independent predictors of culprit lesion features by using optical coherence tomography (OCT).

2. Patients and methods

2.1. Study design and patient population

This is a prospective observational cohort of STEMI patients admitted to the 2nd Affiliated Hospital of Harbin Medical University (Harbin, China) who underwent OCT examination of culprit lesion during emergency percutaneous coronary intervention (PCI) (ClinicalTrials.gov; NCT03084991). The main exclusion criteria were: cardiogenic shock, severe kidney and/or liver dysfunction, allergy to contrast media, contraindications for anti-thrombotic therapy, left main disease, chronic total occlusion, extremely tortuous and heavily calcified vessels in which OCT guidewire was unable to pass. Between August 2014 and December 2017, a total of 1660 eligible STEMI patients were included in the present study. Among them, 218 patients were excluded from analysis for the following reasons: (i) pre-dilation before OCT examination (n = 31), (ii) poor OCT image quality (n = 95), (iii) in-stent thrombosis or neoatherosclerosis (n = 58), (iv) massive thrombus (n = 34). Finally, the present study included 1442 STEMI patients who were divided into two groups according to their age at onset of STEMI: young group (age ≤50 years, n = 400) and older group (age > 50 years, n = 1042). Patients aged > 50 years were further divided into 50 < age≤70 years (n = 859) and > 70 years (n = 183). The study flow-chart is shown in Fig. 1. The study was approved by the Ethics Committee of our institution and written informed consent was obtained from all enrolled patients.

Identification of STEMI, culprit lesion and traditional coronary risk factors are detailed in the Supplemental Materials.

2.2. Quantitative coronary analysis

Patients were treated with loading dose of dual anti-platelet therapy before intervention procedures. Coronary angiography was performed via the radial or femoral approach using guiding catheters after intracoronary injection of 100–200 μg of nitroglycerin. Angiographic images were analyzed using quantitative coronary angiography analysis system (CAAS 5.10.1, Pie Medical Imaging BV, Maastricht, the Netherlands). Lesion location and length, minimal lumen diameter (MLD), reference lumen diameter (RLD), diameter stenosis (DS), initial thrombolysis in myocardial infarction (TIMI) flow and TIMI flow at the end of the procedure were measured by an independent investigator (S.Z.) who was blinded to patients' clinical information.

2.3. OCT image acquisition and analysis

OCT imaging of culprit lesions was acquired with the C7-XR/ILUMIEN OCT system (Abbott Vascular, Santa Clara, CA, USA). OCT images were digitally archived to database and analyzed in the imaging core lab by two experienced investigators (C.F. and J.D.) who were blinded to patients' information.

The culprit lesions were diagnosed using established criteria, and identification of culprit lesion type (plaque rupture, plaque erosion, calcified nodule and others) is presented in the **Supplemental Materials** [5]. Minimal lumen area (MLA) and reference lumen area (RLA) were analyzed and lumen area stenosis (LAS) was calculated as (1-MLA/RLA) × 100. For lipid plaque, lipid core length was recorded in the longitudinal view, and lipid arc was measured in each 1 mm in the cross-sectional view, and then maximal lipid arc and mean lipid arc were calculated. Lipid rich plaque (LRP) was identified as a lipid plaque with lipid arc > 90° in any cross-section. Minimal fibrous cap thickness (FCT) was measured three times in the thinnest place to obtain a mean value. Thin cap fibroatheroma (TCFA) was identified as LRP with minimal FCT < 65 μm. When detecting a low backscattering heterogeneous region with well-delineated border underlying the plaque, calcification was recorded and minimal depth and maximum calcium

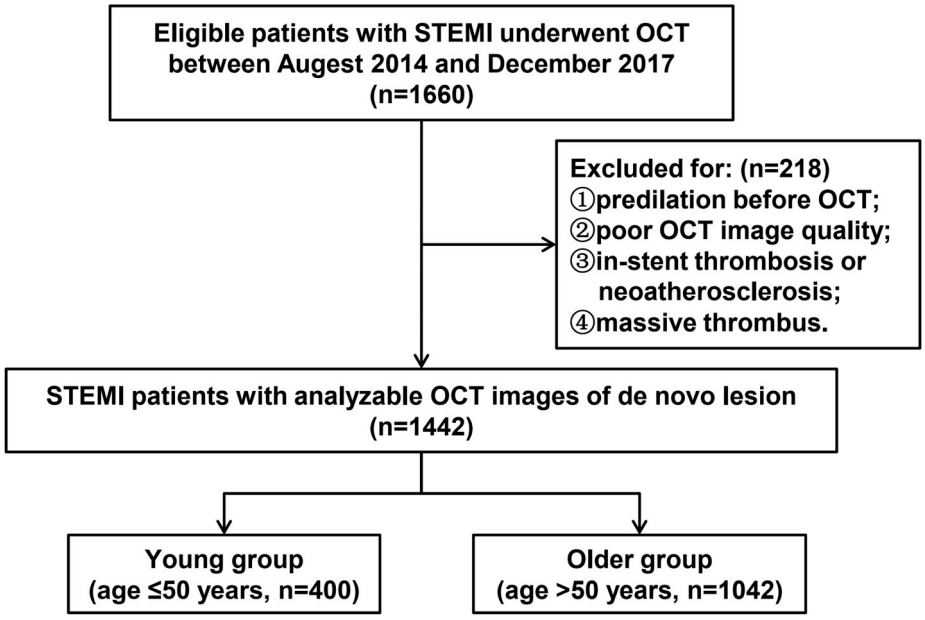

Fig. 1. Flow chart of patient selection.
OCT, optical coherence tomography; STEMI, ST-segment elevated myocardial infarction.

Table 1
Clinical and angiographic characteristics of young (≤50 years) and older (> 50 years) STEMI patients.

Variables	Overall (n = 1442)	Young group (n = 400)	Older group (n = 1042)	*p* value
Age, years	57.5 ± 11.2	43.9 ± 5.2	62.7 ± 8.0	< **0.001**
Male, n (%)	1052 (73.0)	367 (91.8)	685 (65.7)	< **0.001**
Coronary risk factors				
Smoking status, n (%)				< **0.001**
Current smoker	781 (54.2)	267 (66.8)	514 (49.3)	
Former smoker	128 (8.9)	24 (6.0)	104 (10.0)	
Non-smoker	533 (37.0)	109 (27.3)	424 (40.7)	
Diabetes mellitus, n (%)	311 (21.6)	72 (18.0)	239 (22.9)	**0.041**
Hypertension, n (%)	684 (47.4)	171 (42.8)	513 (49.2)	**0.027**
CKD, n (%)	145 (10.1)	21 (5.3)	124 (11.9)	< **0.001**
Dyslipidemia, n (%)	896 (62.1)	278 (69.5)	618 (59.3)	< **0.001**
Laboratory test				
TC, mg/dl	184.3 ± 41.6	190.0 ± 41.9	182.1 ± 41.3	**0.001**
TG, mg/dl	135.1 (93.0–172.8)	150.2 (101.9–207.5)	128.5 (89.9–163.0)	< **0.001**
HDL-C, mg/dl	49.5 ± 11.9	49.0 ± 13.4	49.7 ± 11.3	0.307
LDL-C, mg/dl	117.5 ± 36.6	121.4 ± 40.5	116.1 ± 34.8	**0.015**
hs-CRP, mg/L	5.1 (2.0–11.9)	4.4 (1.7–11.4)	5.3 (2.1–12.0)	**0.025**
Angiographic findings				
Culprit vessel, n (%)				**0.030**
LAD	745 (51.7)	228 (57.0)	517 (49.6)	
LCX	146 (10.1)	40 (10.0)	106 (10.2)	
RCA	551 (38.2)	132 (33.0)	419 (40.2)	
Initial TIMI flow ≤1, n (%)	1047 (72.6)	273 (68.3)	774 (74.3)	**0.022**
Pre-DS, %	91.0 ± 15.7	89.2 ± 17.2	91.6 ± 15.0	**0.010**
Thrombus aspiration, n (%)	1223 (84.8)	336 (84.0)	887 (85.1)	0.594
Post-DS, %	65.6 ± 14.0	63.7 ± 14.2	66.4 ± 13.8	**0.002**
MLD, mm	1.0 ± 0.5	1.1 ± 0.5	1.0 ± 0.4	< **0.001**
RLD, mm	3.0 ± 0.6	3.0 ± 0.6	2.9 ± 0.6	**0.001**
Lesion length, mm	18.3 ± 9.3	18.3 ± 8.8	18.3 ± 9.5	0.981
MVD, n (%)	699 (48.5)	149 (37.3)	550 (52.8)	< **0.001**

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles).
A *p*-value < 0.05 was considered statistically significant.
CKD, chronic kidney disease; DS, diameter stenosis; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitive C-reactive protein; LAD, left anterior descending artery; LCX, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; MLD, minimal lumen diameter; MVD, multi-vessel disease; RCA, right coronary artery; RLD, reference lumen diameter; TC, total cholesterol; TG, triglyceride; TIMI, thrombolysis in myocardial infarction.

arc were analyzed. Spotty calcification was defined as calcification with maximum arc < 90°. Micro-vessel, macrophages and cholesterol crystals were recorded according to the established criteria [6].

2.4. Statistical analysis

All data in the present study were analyzed by an independent statistician (L.L.) using SPSS 20.0. Data were recorded as n (%) for categorical variables, mean ± standard deviations for normally distributed continuous variables and median (interquartile range) for abnormal distributed continuous variables. Kolmogorov-Smirnov test was used to test the normality of variables. The significance of variables in patients aged ≤50 years and > 50 years was conducted using the Student's *t*-test for normally distributed continuous variables and Mann-Whitney *U* test, respectively, for abnormally distributed continuous variables. Comparisons of variables among 3 groups (≤50 years, 50–70 years and > 70 years) were performed using one-way analysis of variance (ANOVA), followed by Bonferroni's test as the *post-hoc* test to compare mean values among 3 groups. Categorical variables were compared using the Chi-square test. Logistic regression analysis was used to identify independent predictors of plaque rupture, TCFA, spotty calcification, cholesterol crystals and lumen area stenosis. Linear regression analysis was used to identify independent predictors of LAS. Baseline characteristics of patients [age ≤50 years, male, current smoker, diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease (CKD), pre-MI, pre-PCI, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)] were taken into the regression model. Variables with $p < 0.1$ in the univariate analysis were included in the multivariate model. Data were considered significantly different when a two-tailed p value was < 0.05.

3. Results

3.1. Clinical characteristics

Clinical characteristics of young and older STEMI patients are presented in Table 1. The average age of overall included patients was 57.5 years, with 43.9 years in the young group and 62.7 years in the older group. There were 91.8% male patients in the young group and 65.7% in the older group ($p < 0.001$). As compared with the older group, patients in the young group were more likely to be current smoker and had more dyslipidemia but less CKD, diabetes mellitus and hypertension. Laboratory data showed that young patients had higher TC, TG, and LDL-C. The level of high-sensitive C-reactive protein was lower in young patients.

3.2. Angiographic findings

The angiographic features of culprit lesions are listed in Table 1. Culprit lesions in the young group were more frequently located in the left anterior descending artery (LAD, $p = 0.030$) with fewer multi-vessel disease ($p < 0.001$). Culprit lesions in young patients were less severe (less initial TIMI flow ≤1, larger RLD and MLD, smaller DS) than in patients aged > 50 years.

Table 2
OCT findings of culprit lesions in young (≤50 years) and older (> 50 years) STEMI patients.

Variables	Overall (n = 1442)	Young group (n = 400)	Older group (n = 1042)	*p* value
Culprit lesion type, n (%)				**< 0.001**
Plaque rupture	972 (67.4)	241 (60.3)	731 (70.2)	
Plaque erosion	348 (24.1)	128 (32.0)	220 (21.1)	
Calcified nodule	23 (1.6)	4 (1.0)	19 (1.8)	
Others	99 (6.9)	27 (6.8)	72 (6.9)	
MLA, mm^2	2.0 ± 1.3	2.3 ± 1.7	1.9 ± 1.1	**< 0.001**
Mean RLA, mm^2	7.5 ± 2.9	7.9 ± 2.9	7.4 ± 2.9	**0.001**
LAS, %	71.9 ± 14.3	70.3 ± 15.4	72.5 ± 13.7	**0.008**
Plaque type, n (%)				**0.001**
Lipid plaque	1244 (86.3)	326 (81.5)	918 (88.1)	
Fibrous plaque	198 (13.7)	74 (18.5)	124 (11.9)	
LRP, n (%)	1231 (85.4)	322 (80.5)	909 (87.2)	**0.001**
TCFA, n (%)	962 (66.7)	238 (59.5)	724 (69.5)	**< 0.001**
Lipid length, mm	13.3 ± 6.8	13.4 ± 6.6	13.2 ± 6.9	0.704
Mean lipid arc, °	237.7 ± 48.5	228.7 ± 48.5	240.8 ± 48.1	**< 0.001**
Maximal lipid arc, °	327.6 ± 53.6	320.6 ± 59.3	330.1 ± 51.2	**0.006**
Minimal FCT, μm	55.2 ± 30.3	60.6 ± 37.8	53.3 ± 26.9	**< 0.001**
Calcification, n (%)	632 (43.8)	125 (31.3)	507 (48.7)	**< 0.001**
Max calcification arc, °	81.9 (50.2–123.3)	75.4 (49.6–109.1)	84.7 (50.2–125.8)	0.168
Calcification depth, um	66.7 (26.7–150.0)	83.3 (41.7–205.0)	60.0 (26.7–143.0)	**0.001**
Spotty calcification, n (%)	477 (33.1)	101 (25.3)	376 (36.1)	**< 0.001**
Micro-vessel, n (%)	634 (44.0)	187 (46.8)	447 (42.9)	0.187
Macrophage, n (%)	1166 (80.9)	314 (78.5)	852 (81.8)	0.158
Cholesterol crystal, n (%)	505 (35.0)	105 (26.3)	400 (38.4)	**< 0.001**

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles).
A *p*-value < 0.05 was considered statistically significant.
FCT, fibrous cap thickness; LAS, lumen area stenosis; LRP, lipid rich plaque; MLA, minimal lumen area; RLA, reference lumen area; TCFA, thin cap fibroatheroma.

3.3. Optical coherence tomography findings

The OCT findings of culprit lesions are summarized in Table 2. Although plaque rupture was the most frequent mechanism for STEMI, plaque erosion accounted for 32.0% of culprit lesion types in the young group and 21.1% in the older group ($p < 0.001$). The young group had larger MLA ($p < 0.001$) and smaller LAS ($p = 0.008$) than the older group. The majority of culprit lesion plaques (88.1%) in the older group were lipidic, and fibrous plaques were found to be more frequent in the young group ($p = 0.001$). In addition, LRP and TCFA were significantly fewer in the young group than in the older group ($p = 0.001$, $p < 0.001$; respectively). As compared with older patients, calcification and spotty calcification were less frequently observed and more deeply seated in young patients. The frequency of cholesterol crystals was significantly lower in the young group than in the older group ($p < 0.001$).

3.4. Culprit lesion features in STEMI patients aged 50–70 years and > 70 years

Clinical features, angiographic findings and OCT culprit lesion features in STEMI patients aged 50–70 years and > 70 years, as well as comparisons with patients aged < 50 years, are summarized in Supplemental Tables 1–3. Angiographic analysis showed there was no significant difference between patients aged 50–70 years and > 70 years in the distribution of culprit lesion, TIMI flow, MLD, RLD, DS. However, multi-vessel disease was more frequently to be observed in STEMI patients aged > 70 years than those aged 50–70 years. As for OCT findings, prevalence of plaque rupture (78.1% *vs.* 68.5%, $p < 0.001$) and calcified nodule (4.4% *vs.* 1.3%, $p < 0.001$) were significantly higher while the prevalence of plaque erosion (12.6% *vs.* 22.9%, $p < 0.001$) was significantly lower in STEMI patients aged > 70 years than those aged 50–70 years. The prevalence of LRP, TCFA, calcification, spotty calcification, macrophage were lower in patients aged 50–70 years than in those aged > 70 years. Fig. 2 summarizes the key findings of comparisons among three age groups.

3.5. Predictors of culprit lesion morphology

In multivariate analysis (Supplemental Table 4), age ≤50 years was an independent predictor of less plaque rupture, TCFA, spotty calcification, cholesterol crystals and smaller LAS.

4. Discussion

With a large prospective observational cohort of 1660 STEMI patients with OCT images, the main findings of the current study are as follows: 1) mechanisms of STEMI in young and older patients were different. The prevalence of plaque erosion in STEMI patients aged ≤50 years was higher than in those aged > 50 years. 2) As compared with older STEMI patients, characteristics of typical vulnerable plaque (including small lumen size, TCFA, superficial calcification, spotty calcification and cholesterol crystals) were less observed in young STEMI patients. Age was an independent predictor of culprit lesion morphology in STEMI patients. We summarized critical findings in Fig. 3.

4.1. Mechanisms of STEMI in young and older patients

In this study, we found that mechanisms of STEMI in young patients were different from older patients. The most common mechanism for STEMI patients was plaque rupture with prevalence of about 65%, regardless of age [7–9]. However, we found the prevalence of plaque erosion (32.1%) was higher in young STEMI patients and decreased with aging. In sudden cardiac death (SCD) caused by acute thrombus, Burke et al. [10] reported that acute rupture was less frequent in patients aged ≤50 years compared with those aged > 50 years. Similarly, a previous OCT study reported that STEMI patients with plaque erosion tended to be younger than those with plaque rupture [8]. Furthermore,

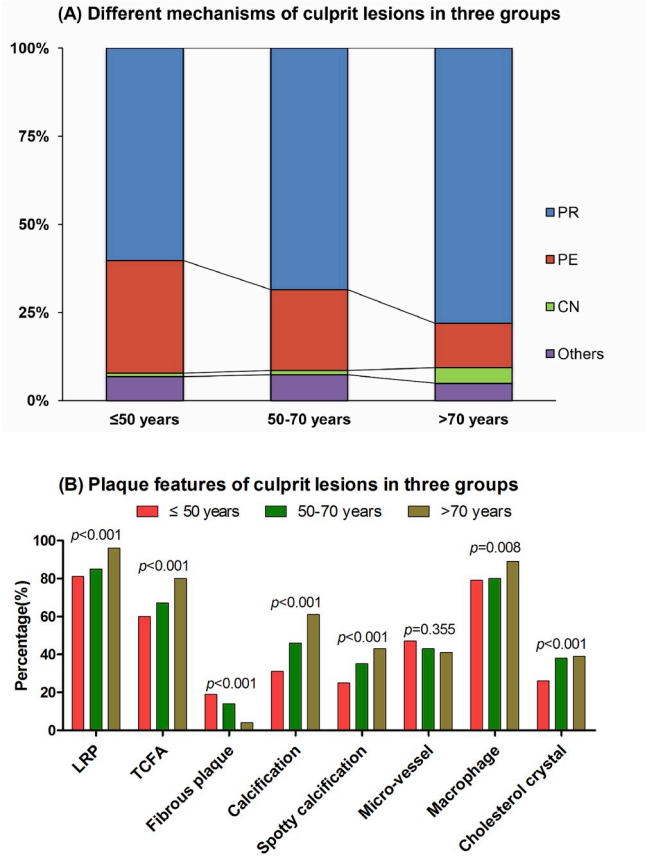

Fig. 2. Comparison of culprit lesion features among STEMI patients aged ≤50 years, 50–70 years and > 70 years.
(A) Different mechanisms of culprit lesion in three groups (STEMI patients aged ≤50 years, 50–70 years and > 70 years). The prevalence of plaque rupture (60.3% *vs.* 68.5% *vs.* 78.1%, $p < 0.001$), plaque erosion (32.0% *vs.* 22.9% *vs.* 12.6%, $p < 0.001$) and calcified nodule (1.0% *vs.* 1.3% *vs.* 4.4%, $p < 0.001$) was significantly different among the three age groups. (B) Plaque features of culprit lesions in three groups (STEMI patients aged ≤50 years, 50–70 years and > 70 years). Plaque features of culprit lesions were significantly different among the three age groups, including LRP, TCFA, fibrous plaque, calcification, spotty calcification, micro-vessel, macrophage and cholesterol crystal. CN, calcified nodule; LRP, lipid-rich plaque; PE, plaque erosion; PR, plaque rupture; TCFA, thin cap fibroatheroma.

Dai et al. [9] demonstrated that age < 50 years was strongly associated with plaque erosion.

We found that young STEMI patients were more likely to be current smokers. Smoking is an important risk factor and trigger for acute coronary thrombosis by altering endothelial function, platelet function and other hemostatic processes [11,12]. As many postmortem and *in vivo* studies suggest, current smoking was the predominant risk factor for eroded plaque [9,10,13]. Burke and colleagues discovered that smoking was an important predictor for plaque erosion, predisposing both males and females to acute thrombus, especially premenopausal females [10,12,14]. Plaque erosion was caused by dysfunction or desquamation of endothelial cells with subsequent thrombus formation, frequently detected in fibrous plaques rich in hyaluronan [15]. Pedicino et al. reported that enhanced expression of hyaluronidase 2 (HYAL2, an enzyme that degrades hyaluronan) in peripheral blood mononuclear cells under conditions of disturbed blood flow leads to degradation of high-molecular-weight hyaluronan to proinflammatory low-molecular-weight (LMW) hyaluronan, which, in turn, promotes endothelial activation and detachment via toll-like receptor-2 stimulation, as well as neutrophil recruitment. Finally, LMW hyaluronan induces increased platelet-monocyte binding, thus promoting thrombus formation [16,17]. Intriguingly, *HYAL2* gene expression was highest in smoker patients presenting with plaque erosion on OCT [17]. In our study, 66.8% of young STEMI patients were current smokers and the frequency of fibrous plaque was higher in young individuals than the older ones. These findings may partly explain the higher prevalence of plaque erosion in young STEMI patients.

4.2. Plaque vulnerability in young and older patients

Consistent with previous postmortem and *in vivo* studies [10,18], the present study observed that young STEMI patients had a larger lumen size and a smaller coronary stenosis than the older ones. With the stimulation of various risk factors during aging, lipid components gradually deposit in the coronary artery tree, resulting in lipid pool growth, fibrous cap thinning, together with increased plaque burden and coronary stenosis [19]. Postmortem and intravascular ultrasound (IVUS) studies have suggested that plaque burden gradually increases with aging [18]. In addition, the frequency of TCFA was higher in older patients.

Calcium deposition in the coronary artery wall is a common progression of atherosclerosis with aging [20]. Importantly, we found calcium deposits in older STEMI patients were superficial, with more spotty calcification than in younger patients, which may increase peak stress in local fibrous cap. Coronary superficial and spotty calcium deposits in culprit lesions might play an important role in the destabilization of coronary plaques and occasionally associate with plaque rupture [21]. Zhan et al. have found calcification depth < 63 μm was a crucial cutoff value for plaque rupture [22]. A recent OCT study suggested, in acute coronary syndrome patients with calcified culprit lesion, superficial calcific sheet was the most prevalent phenotype associated with severe coronary stenosis and myocardial damage [23]. In addition, spotty calcification was considered as a marker of accelerated coronary artery disease progression and patients with spotty calcification were older [24]. In the present study, there was more superficial and spotty calcification in culprit lesions with advancing age (Supplemental Table 3). Based on existing evidence, we considered older STEMI patients, with more superficial and spotty calcium deposits, have more vulnerable plaque characteristics than the young ones.

Cholesterol crystals are not only a hallmark of atherosclerosis, but also correlate with coronary inflammation and plaque vulnerability [25–27]. Culprit plaques with cholesterol crystals are more vulnerable and tend to rupture in STEMI patients [25]. A recent study showed clinical outcomes were also worse in patients with cholesterol crystals in the culprit lesion than in those without cholesterol crystals [26]. We found that the prevalence of cholesterol crystals was significantly higher in old STEMI patients (50–70 and > 70 years of age) than in the young ones (≤50 years of age), suggesting less vulnerable features of coronary plaque in young STEMI patients.

4.3. Study limitations

The present study has some limitations. First, this was an observational study consisting of uncontrollable factors, which may lead to some bias. Second, the present study was carried out in a single center, although the sample size was large. Third, STEMI patients with severe complications (cardiac shock, severe kidney dysfunction or other contraindications of OCT examination) were excluded from this study. Fourth, limitations of near infrared light partially reduced the ability to detect microstructures underlying the lipid plaque. Fifth, unlike IVUS, plaque burden and remodeling cannot be analyzed by OCT.

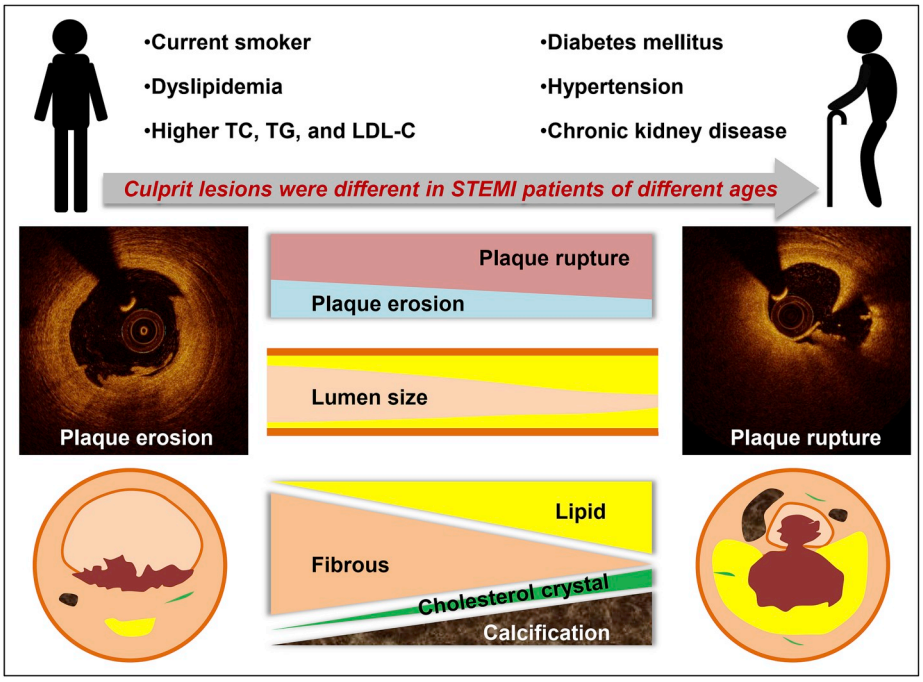

Fig. 3. Representative optical coherence tomography images and schematic drawings of culprit lesions in STEMI patients of different ages.
Culprit lesion features were different in STEMI patients of different ages. With aging, the prevalence of plaque rupture was increasing and that of plaque erosion was decreasing, plaque components were changing and lumen size was narrowing.

4.4. Conclusions

In conclusion, morphological characteristics of culprit lesion in young STEMI patients were different from those in older patients. Patients aged ≤50 years had more plaque erosion and less vulnerable plaque features.

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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Author contributions

Chao Fang: substantial contribution to the conception and design of research, data acquisition, manuscript drafting and critical manuscript revision. Jiannan Dai: substantial contribution to the conception and design of research, data acquisition and critical manuscript revision. Shaotao Zhang, Yidan Wang, Jifei Wang, Xiling Zhang, Na Feng, Yini Wang: substantial contribution to data acquisition. Lulu Li: substantial contribution to statistical analysis. Huai Yu, Guo Wei, Huimin Liu, Maoen Xu, Xuefeng Ren, Lijia Ma: substantial contribution to patients enrollment and cardiac intervention. Yingfeng Tu, Lei Xing: substantial contribution to data acquisition and critical manuscript revision. Jingbo Hou, Bo Yu: substantial contribution to the design of research and critical manuscript revision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2019.08.011.

References

[1] L. Choudhury, J.D. Marsh, Myocardial infarction in young patients, Am. J. Med. 107 (1999) 254–261.
[2] A. Avezum, M. Makdisse, F. Spencer, J.M. Gore, K.A. Fox, et al., Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE), Am. Heart J. 149 (2005) 67–73.
[3] S.T. Chhabra, T. Kaur, S. Masson, R.K. Soni, N. Bansal, et al., Early onset ACS: an age based clinico-epidemiologic and angiographic comparison, Atherosclerosis 279 (2018) 45–51.
[4] K.S. Rathod, D.A. Jones, S. Gallagher, V.S. Rathod, R. Weerackody, et al., Atypical risk factor profile and excellent long-term outcomes of young patients treated with primary percutaneous coronary intervention for ST-elevation myocardial infarction, Eur. Heart J. Acute. Cardiovasc. Care. 5 (2016) 23–32.
[5] H. Jia, F. Abtahian, A.D. Aguirre, S. Lee, S. Chia, et al., In vivo diagnosis of plaque erosion and calcified nodule in patients with acute coronary syndrome by intravascular optical coherence tomography, J. Am. Coll. Cardiol. 62 (2013) 1748–1758.
[6] F. Prati, E. Regar, G.S. Mintz, E. Arbustini, C. Di Mario, et al., Expert review document on methodology, terminology, and clinical applications of optical coherence tomography: physical principles, methodology of image acquisition, and clinical application for assessment of coronary arteries and atherosclerosis, Eur. Heart J. 31 (2010) 401–415.
[7] G. Niccoli, R.A. Montone, L. Di Vito, M. Gramegna, H. Refaat, et al., Plaque rupture and intact fibrous cap assessed by optical coherence tomography portend different outcomes in patients with acute coronary syndrome, Eur. Heart J. 36 (2015) 1377–1384.
[8] T. Higuma, T. Soeda, N. Abe, M. Yamada, H. Yokoyama, et al., A combined optical coherence tomography and intravascular ultrasound study on plaque rupture, plaque erosion, and calcified nodule in patients with ST-segment elevation myocardial infarction: incidence, morphologic characteristics, and outcomes after percutaneous coronary intervention, JACC Cardiovasc. Interv. 8 (2015) 1166–1176.
[9] J. Dai, L. Xing, H. Jia, Y. Zhu, S. Zhang, 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. 39

(2018) 2077–2085.
[10] A.P. Burke, A. Farb, J. Pestaner, G.T. Malcom, A. Zieske, et al., Traditional risk factors and the incidence of sudden coronary death with and without coronary thrombosis in blacks, Circulation 105 (2002) 419–424.
[11] R.S. Barua, J.A. Ambrose, Mechanisms of coronary thrombosis in cigarette smoke exposure, Arterioscler. Thromb. Vasc. Biol. 33 (2013) 1460–1467.
[12] A.P. Burke, A. Farb, G.T. Malcom, Y.H. Liang, J. Smialek, et al., Coronary risk factors and plaque morphology in men with coronary disease who died suddenly, N. Engl. J. Med. 336 (1997) 1276–1282.
[13] R. Virmani, F.D. Kolodgie, A.P. Burke, A. Farb, S.M. Schwartz, Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions, Arterioscler. Thromb. Vasc. Biol. 20 (2000) 1262–1275.
[14] A.P. Burke, A. Farb, G.T. Malcom, Y. Liang, J. Smialek, et al., Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women, Circulation 97 (1998) 2110–2116.
[15] F.D. Kolodgie, A.P. Burke, A. Farb, D.K. Weber, R. Kutys, et al., Differential accumulation of proteoglycans and hyaluronan in culprit lesions: insights into plaque erosion, Arterioscler. Thromb. Vasc. Biol. 22 (2002) 1642–1648.
[16] C.H. Lu, C.H. Lin, K.J. Li, C.Y. Shen, C.H. Wu, et al., Intermediate molecular mass hyaluronan and CD44 receptor interactions enhance neutrophil phagocytosis and IL-8 production via p38- and ERK1/2-MAPK signalling pathways, Inflammation 40 (2017) 1782–1793.
[17] D. Pedicino, R. Vinci, A.F. Giglio, E. Pisano, I. Porto, et al., Alterations of hyaluronan metabolism in acute coronary syndrome: implications for plaque erosion, J. Am. Coll. Cardiol. 72 (2018) 1490–1503.
[18] J. Ruiz-Garcia, A. Lerman, G. Weisz, A. Maehara, G.S. Mintz, et al., Age- and gender-related changes in plaque composition in patients with acute coronary syndrome: the PROSPECT study, EuroIntervention 8 (2012) 929–938.
[19] E.G. Lakatta, D. Levy, Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease, Circulation 107 (2003) 139–146.
[20] P. Greenland, M.J. Blaha, M.J. Budoff, R. Erbel, K.E. Watson, Coronary calcium score and cardiovascular risk, J. Am. Coll. Cardiol. 72 (2018) 434–447.
[21] M. Mizukoshi, T. Kubo, S. Takarada, H. Kitabata, Y. Ino, et al., Coronary superficial and spotty calcium deposits in culprit coronary lesions of acute coronary syndrome as determined by optical coherence tomography, Am. J. Cardiol. 112 (2013) 34–40.
[22] Y. Zhan, Y. Zhang, J. Hou, G. Lin, B. Yu, Relation between superficial calcifications and plaque rupture: an optical coherence tomography study, Can. J. Cardiol. 33 (2017) 991–997.
[23] T. Sugiyama, E. Yamamoto, F. Fracassi, H. Lee, T. Yonetsu, et al., Calcified plaques in patients with acute coronary syndromes, JACC Cardiovasc. Interv. 12 (2019) 531–540.
[24] Y. Kataoka, K. Wolski, K. Uno, R. Puri, E.M. Tuzcu, et al., Spotty calcification as a marker of accelerated progression of coronary atherosclerosis: insights from serial intravascular ultrasound, J. Am. Coll. Cardiol. 59 (2012) 1592–1597.
[25] J. Dai, J. Tian, J. Hou, L. Xing, S. Liu, et al., Association between cholesterol crystals and culprit lesion vulnerability in patients with acute coronary syndrome: an optical coherence tomography study, Atherosclerosis 247 (2016) 111–117.
[26] K. Fujiyoshi, Y. Minami, K. Ishida, A. Kato, A. Katsura, et al., Incidence, factors, and clinical significance of cholesterol crystals in coronary plaque: an optical coherence tomography study, Atherosclerosis 283 (2019) 79–84.
[27] A. Janoudi, F.E. Shamoun, J.K. Kalavakunta, G.S. Abela, Cholesterol crystal induced arterial inflammation and destabilization of atherosclerotic plaque, Eur. Heart J. 37 (2016) 1959–1967.