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ORIGINAL RESEARCH

Prevalence, Features, and Prognosis of Artery-to-Artery Embolic ST-Segment–Elevation Myocardial Infarction: An Optical Coherence Tomography Study

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BACKGROUND: The major underlying mechanisms contributing to acute coronary syndrome are plaque rupture, plaque erosion, and calcified nodule. Artery-to-artery embolic myocardial infarction (AAEMI) was defined as ST-segment–elevation myocardial infarction caused by migrating thrombus formed at the proximal ruptured plaque. The aim of this study was to investigate the prevalence and clinical features of AAEMI by using optical coherence tomography.

METHODS AND RESULTS: This study retrospectively enrolled 297 patients with ST-segment–elevation myocardial infarction who underwent optical coherence tomography before percutaneous coronary intervention. Patients were divided into 4 groups consisting of plaque rupture, plaque erosion, calcified nodule, and AAEMI according to optical coherence tomography findings. The prevalence of AAEMI was 3.4%. The culprit vessel in 60% of patients with AAEMI was right coronary artery. Minimum lumen area at the culprit site was larger in AAEMI compared with plaque rupture, plaque erosion, and calcified nodule (4.0 mm^2 [interquartile range (IQR), 2.2–4.9] versus 1.0 mm^2 [IQR, 0.8–1.3] versus 1.0 mm^2 [IQR, 0.8–1.2] versus 1.1 mm^2 [IQR, 0.7–1.6], $P<0.001$). Lumen area at the rupture site was larger in patients with AAEMI compared with patients with plaque rupture (4.4 mm^2 [IQR, 2.5–6.7] versus 1.5 mm^2 [IQR, 1.0–2.4], $P<0.001$). In patients with AAEMI, the median minimum lumen area at the occlusion site was 1.2 mm^2 (IQR, 1.0–2.1), 40% of them had nonstent strategy, and the 3-year major adverse cardiac event rate was 0%.

CONCLUSIONS: AAEMI is a rare cause for ST-segment–elevation myocardial infarction and has unique morphological features of plaque including larger lumen area at rupture site and smaller lumen area at the occlusion site.

Key Words: artery-to-artery embolic myocardial infarction ■ optical coherence tomography ■ plaque rupture ■ ST-segment–elevation myocardial infarction

Coronary thrombus formation plays key roles in the onset of acute coronary syndrome (ACS) including ST-segment–elevation myocardial infarction (STEMI). Previous pathological and optical coherence tomography (OCT) studies reported that the 3 most common underlying mechanisms that contribute to ACS are plaque rupture (PR), plaque erosion (PE), and calcified nodule (CN).[1–3] In these reports, they demonstrated that ≈60% to 70% of ACS cases were caused by PR, 30% to 40% by PE, 3% to 8% by CN, and 1% to 17% by others including coronary embolism.[1–3] Previous large database and autopsy studies of acute myocardial infarction (MI) reported that the incidence of coronary embolism was 2.9% to 13.0%.[4–6]

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CLINICAL PERSPECTIVE

What Is New?

- In patients with ST-segment–elevation myocardial infarction, the prevalence of artery-to-artery embolic myocardial infarction (AAEMI), which was defined as ST-segment–elevation myocardial infarction caused from migrating thrombus formed at the proximal ruptured plaque, was 3.4%.
- AAEMI had unique morphological features of plaque including larger lumen area at the proximal rupture site and smaller lumen area at the distal occlusion site.
- In patients with AAEMI, 60% of patients had a culprit lesion in the right coronary artery, 40% of patients had nonstent strategy, and the 3-year major adverse cardiac event rate was 0%.

What Are the Clinical Implications?

- AAEMI is a rare cause for ST-segment–elevation myocardial infarction, and optical coherence tomography is the most promising technique for identifying not only plaque rupture, plaque erosion, and calcified nodule but also AAEMI in ST-segment–elevation myocardial infarction.
- Optical coherence tomography–guided primary percutaneous coronary intervention could avoid metallic stent implantation in nearly half of patients with AAEMI without increasing recurrence of myocardial infarctions.

Nonstandard Abbreviations and Acronyms

AAE	artery-to-artery embolism
AAEMI	artery-to-artery embolic myocardial infarction
CN	calcified nodule
MACE	major adverse cardiac events
MLA	minimum lumen area
PE	plaque erosion
PR	plaque rupture
TIMI	thrombolysis in myocardial infarction

Coronary embolism is divided into 3 types: (1) direct, (2) paradoxical, and (3) iatrogenic. Direct coronary emboli most commonly originate from the left atrial appendage (58%), followed by the left ventricle (25%), the aortic or mitral valves (15%), and rarely from the proximal coronary artery.[4] In the cerebral circulation, it was reported that embolism caused by the migration of thrombus formed at the proximal stenosed vessel, known as artery-to-artery embolism (AAE) infarction, is one of the important causes of cerebral infarction,[7–9] and the prevalence of AAE cerebral infarction is ≈7% to 18% of patients with cerebral infarction.[7–10] Meanwhile, the prevalence of coronary embolism caused by the migration of thrombus formed at the proximal coronary artery with PR, known as artery-to-artery embolic MI (AAEMI), might be underestimated in patients with acute MI because of the lack of diagnostic modalities that properly identify the condition.

OCT is a high-resolution (≈10–20 μm) imaging modality. OCT allows us to identify the microstructure of luminal surface not only at the occlusion site but also within the whole length of the occluded coronary vessel including the proximal site. OCT is currently the most promising technique for identifying PR, PE, CN, and others in ACS.[2,3,11] In the present study, we sought to investigate the prevalence and clinical features of AAEMI using OCT.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

This is a retrospective study in patients with STEMI who underwent primary percutaneous coronary intervention (PCI) for a de novo lesion with OCT guidance between May 2014 and April 2018 at Wakayama Medical University in Wakayama, Japan. STEMI was defined as continuous chest pain lasting >30 minutes, arrival at our hospital within 12 hours from the onset of the symptom, ST-segment elevation >0.1 mV in ≥2 contiguous leads on 12-lead ECG, and elevation of cardiac troponin I greater than the upper reference limit.[12] Exclusion criteria for use of OCT in our hospital were cardiogenic shock, chronic kidney failure (serum creatinine >2.0 mg/dL) without hemodialysis, small or extremely tortuous vessels, vessels with coronary bypass grafting, and aorto-ostial coronary lesions. We excluded patients with STEMI caused by vasospasm, coronary embolization from cardiac chamber or valve, and spontaneous coronary artery dissection. Furthermore, we excluded patients with no preintervention OCT image and poor OCT image quality including massive thrombus. We retrospectively enrolled 297 patients with STEMI who underwent preintervention OCT (Figure 1). This retrospective study was approved by Wakayama Medical University's ethics committee, and written informed consent was obtained from all patients.

OCT Imaging and Primary PCI

Oral aspirin (200 mg) and prasugrel (20 mg) were administered before coronary catheterization. During coronary catheterization, patients received intravenous heparin (a bolus of 100 IU/kg and additional doses aimed at achieving an activated clotting time of 250–300 seconds). Thrombolysis was not performed for any patient. Coronary

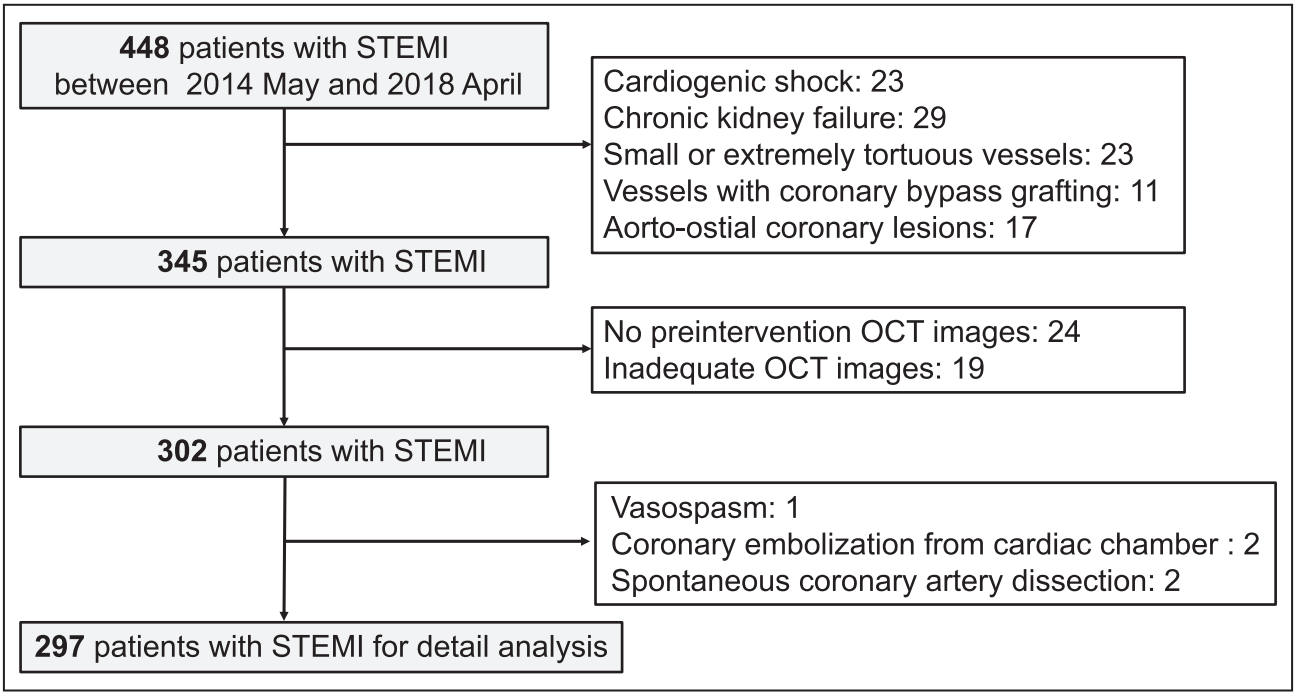

Figure 1. Flow chart of patient inclusion.
Of the 448 patients with ST-segment–elevation myocardial infarction (STEMI), 297 patients were enrolled for analysis. OCT indicates optical coherence tomography.

angiography was performed in the standard manner. The culprit lesion was identified on the basis of the findings of a coronary angiogram as well as an ECG and transthoracic echocardiogram. In patients with a thrombolysis in myocardial infarction (TIMI) flow grade ≤2, aspiration thrombectomy with a 5.1-F aspiration catheter (Thrombuster III GR [Kaneka] or Export Advance [Medtronic Japan]) or balloon angioplasty with a small balloon of ≤2.0 mm in diameter was allowed before OCT imaging. Intracoronary isosorbide dinitrate (2–3 mg) was administered before the OCT procedure. A frequency domain OCT (FD-OCT) imaging system (ILUMIEN OPTIS [Abbott Vascular] or LUNAWAVE [Terumo]) were used in the present study. The OCT catheter was advanced distally to the culprit lesion over a 0.014-inch conventional angioplasty guidewire. The OCT images were acquired during intracoronary contrast injection and automatic catheter pullback. After OCT imaging, PCI was performed using a coronary stent with a conventional technique. Decision-making related to the PCI strategy was left to the discretion of the individual PCI operator. All patients received antiplatelet therapy with prasugrel (3.75 mg/d) and aspirin (100 mg/d) for at least 12 months after primary PCI.

Definition of AAEMI

The definition of AAEMI used in this study consisted of the following 5 criteria: (1) angiographic evidence of STEMI with TIMI flow grade ≤2, (2) no morphological feature of ACS such as PR, PE, or CN assessed by OCT at the angiographic occlusion site, (3) PR with fresh thrombus assessed by OCT at the proximal culprit site, (4) distance from occlusion site to proximal culprit site measured by OCT ≥30 mm, and (5) no evidence of atrial fibrillation and/or thrombus of cardiac chamber (Figure 2). Previous OCT and intravascular ultrasound studies have reported that the PR or maximum necrotic core site was located proximal to the minimum lumen area (MLA) site in most patients with acute MI, and the distance between the PR site and the MLA site, and the maximum necrotic core site and the MLA site were 4.2±5.8 mm and 10.9±20.8 mm, respectively.[13–15] To distinguish between PR that was located proximal to the MLA site within 1 lesion and AAEMI, we employed the distance from occlusion site to the proximal culprit site ≥30 mm as one of the criteria for AAEMI. The representative case of AAEMI is shown in Figure 3.

OCT Image Analysis

All OCT images were analyzed by 2 independent investigators (Y.I. and K.S.) who were blinded to the clinical and angiographic data. When there was any discordance between the observers, a consensus reading was obtained. OCT images before PCI were analyzed using previously validated criteria for plaque characterization.[11] Lipid was semiquantified by measuring the lipid arc. When the lipid arc stretched for

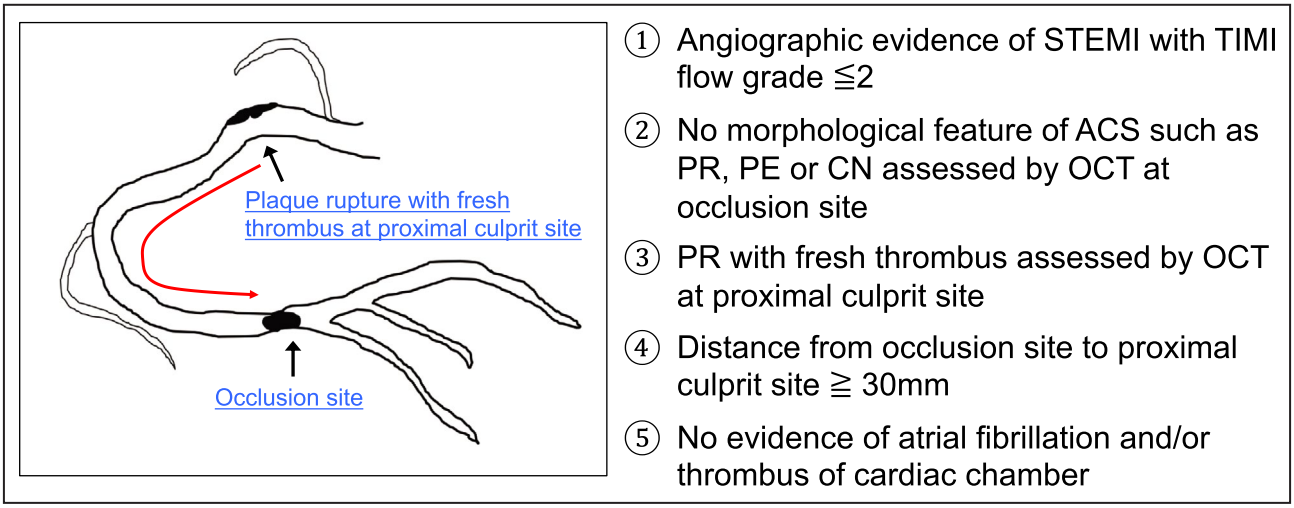

Figure 2. Definition of artery-to-artery embolic myocardial infarction (AAEMI).
The definition of AAEMI used in this study consisted of 5 criteria. ACS indicates acute coronary syndrome; CN, calcified nodule; OCT, optical coherence tomography; PE, plaque erosion; PR, plaque rupture; STEMI, ST-segment–elevation myocardial infarction; and TIMI, thrombolysis in myocardial infarction.

>90°, the plaque was deemed to be lipid-rich. For lipid plaque, the maximal lipid arc was measured. Thin-cap fibroatheroma was defined as a plaque with lipid arc >90° with the thinnest fibrous cap thickness <65 μm. PR was defined as the presence of fibrous cap discontinuity and a cavity formation in the plaque.[2,3,11,13,16] PE was identified by the presence of attached thrombus overlying an intact and visualized

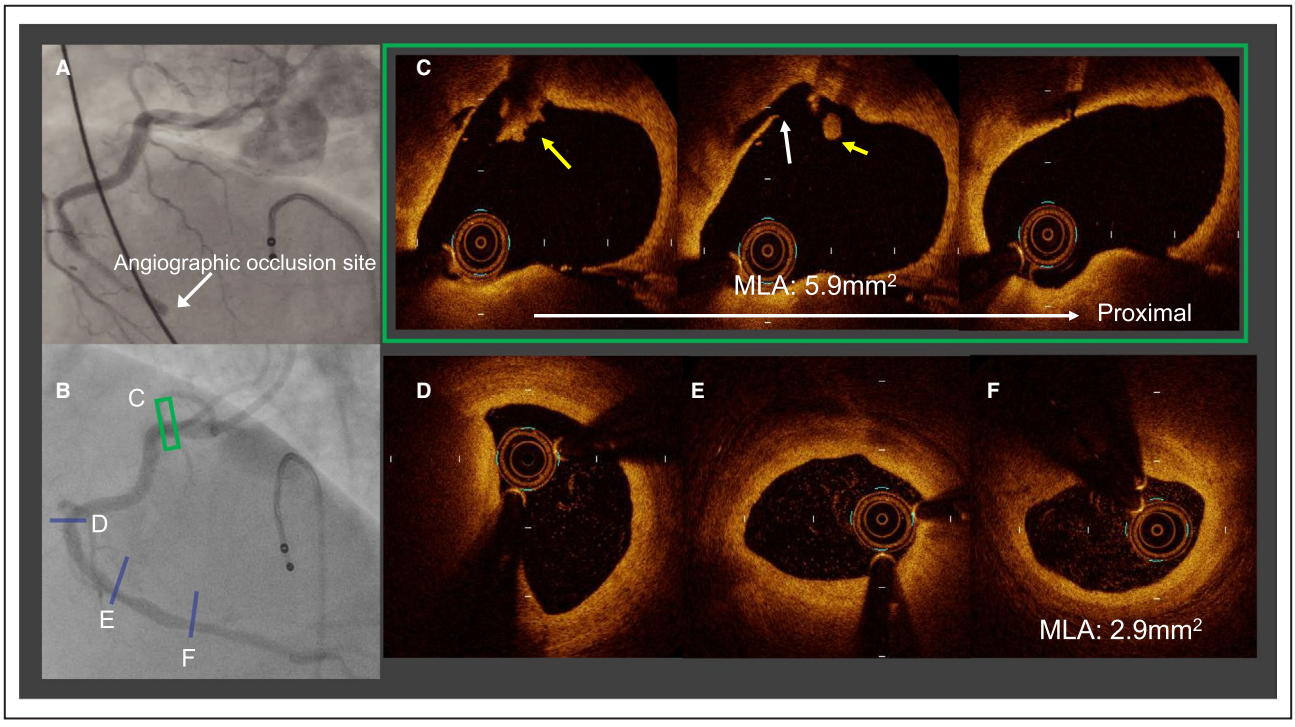

Figure 3. Representative case of artery-to-artery embolic myocardial infarction (AAEMI).
A, Angiography showing total occlusion at the mid right coronary artery. **B**, Angiography after aspiration thrombectomy showing thrombolysis in myocardial infarction 3 coronary flow. **C**, Optical coherence tomography (OCT) after thrombectomy showing some thrombus (yellow arrow) and plaque rupture (white arrow) at the proximal site of the culprit vessel. The minimum lumen area (MLA) was 5.9 mm^2. **D** through **F**, There was no plaque rupture, plaque erosion, or calcified nodule at the angiographic occlusion site. The MLA at the occlusion site was 2.9 mm^2. The distance from the occlusion site to the proximal culprit site was 60 mm.

plaque and the absence of fibrous cap disruption, luminal surface irregularity at the culprit lesion in the absence of thrombus, or attenuation of underlying plaque by thrombus without superficial lipid or calcification immediately proximal or distal to the site of thrombus.[2,3,16] CN was defined by fibrous cap disruption detected over a calcified plaque characterized by protruding calcification, superficial calcium, or the presence of substantive calcium proximal and/or distal to the lesion.[2,3,16] The culprit lesions that did not meet the aforementioned criteria were classified as "others."[2,3,11] Intracoronary thrombus was defined as a mass attached to the luminal surface or floating within the lumen.[2,3,11,13,16] The quantitative measurements of cross-sectional OCT images, including lumen area and ruptured cavity area, were performed by manual trace at 1-mm intervals throughout the culprit and thrombotic occlusion sites. The maximal ruptured cavity and MLA sites were decided based on these tracings. The lumen area (LA) at the rupture site was measured at the maximal ruptured cavity site. In patients with AAEMI, MLA at the angiographic occlusion site was decided based on a landmark such as branches, and the distance from the MLA at angiographic occlusion site to the proximal ruptured plaque site was measured.

Coronary Angiography Analysis

Quantitative coronary angiography analysis was performed using a validated automated edge detection algorithm (CAAS-5, Pie Medical Imaging B.V.) by experienced investigators (Y.S. and T.W.) who were blinded to the clinical information and OCT findings. The reference vessel diameter, minimal luminal diameter, and percent diameter stenosis were measured in the culprit lesion.

Cardiac Enzyme Measurements

Blood samples were obtained on admission and serially every 3 hours for the first 24 hours after primary PCI, and the peak values of creatine kinase myocardial band were determined.

Major Adverse Cardiac Events

Major adverse cardiac events (MACE) were defined as the combination of cardiac death, recurrent MI, or clinically driven target vessel revascularization. Cardiac death was defined as any death not clearly attributable to a noncardiac cause.[17] MI was defined as a clinical episode of typical chest pain with development of new Q waves in ≥2 contiguous leads on ECG or elevation of the creatine kinase myocardial band fraction greater than the upper reference limit, which were attributed to the target coronary artery.[12] Target vessel revascularization was defined as subsequent revascularization of the target vessel by either PCI or coronary artery bypass grafting. In-hospital and long-term outcomes were investigated through telephone interview or medical record review.

Statistical Analysis

All statistical analysis was performed with the statistical software package JMP 14.0 software (SAS Institute Inc). Categorical variables are presented as number (percentage), and the comparisons were performed with chi-square or Fisher exact test (for an expected cell value <5). Continuous variables were presented as medians and interquartile ranges (IQRs) and were compared among AAEMI, PR, PE, and CN by Kruskal–Wallis analysis using Steel-Dwass test for multiple comparisons. All *P* values were 2-sided, and $P<0.05$ was considered statistically significant.

RESULTS

Baseline Clinical Characteristics

We analyzed 297 patients with STEMI that was caused by PR, PE, CN, or AAEMI (Figure 1). The frequency of PR, PE, CN, and AAEMI was 193 (64.1%), 67 (22.1%), 27 (9.0%), and 10 (3.4%), respectively.

The baseline clinical characteristics are summarized in Table 1. Peak creatine kinase myocardial band level in AAEMI was not significantly but numerically lower than those in PR (116 [IQR, 69–201] versus 234 [IQR, 88–385], $P=0.180$).

OCT Findings

OCT findings are shown in Table 2. The frequency of lipid-rich plaque at the culprit site was higher in AAEMI compared with PE and CN (100% versus 49% [$P=0.007$] and versus 63% [$P=0.012$], respectively). Lipid arc was greater in AAEMI compared with PE and CN (262° [IQR, 213–286] versus 70° [IQR, 46–95] ($P<0.001$) and versus 87° [IQR, 65–115] ($P<0.001$), respectively). The LA at the rupture site was significantly larger in AAEMI compared with PR (4.4 mm^2 [IQR, 2.5–6.7] versus 1.5 mm^2 [IQR, 1.0–2.4], $P<0.001$). MLA at the culprit site was significantly larger in AAEMI compared with PR, PE, and CN (4.0 mm^2 [IQR, 2.2–4.9] versus 1.0 mm^2 [IQR, 0.8–1.3] versus 1.0 mm^2 [IQR, 0.8–1.2] versus 1.1 mm^2 [IQR, 0.7–1.6], $P<0.001$). In AAEMI, the median MLA at the occlusion site was 1.2 mm^2 [IQR, 1.0–2.1], and the median distance between the proximal culprit site and the occlusion site was 39 mm [IQR, 35–66].

Table 1. Baseline Patient Clinical Characteristics

	AAEMI (n=10)	PR (n=193)	PE (n=67)	CN (n=27)	*P* Value
Age, y	73 (68–78)	71 (62–78)	67 (59–83)	73 (64–83)	0.258
Men	7 (70)	145 (75)	47 (70)	18 (67)	0.725
Coronary risk factor					
Hypertension	8 (80)	134 (69)	48 (72)	18 (67)	0.865
Dyslipidemia	7 (70)	110 (57)	34 (51)	14 (52)	0.618
Diabetes mellitus	5 (50)	70 (36)	24 (36)	11 (41)	0.808
Cigarette smoking	2 (20)	81 (42)	33 (49)	12 (44)	0.343
Obesity	0 (0)	51 (26)	15 (22)	2 (7)	0.228
Previous PCI	0 (0)	13 (7)	5 (7)	0 (0)	0.428
Previous MI	0 (0)	14 (7)	2 (3)	0 (0)	0.242
Medications					
Aspirin	2 (20)	24 (12)	8 (12)	5 (19)	0.615
ACEI/ARB	5 (50)	56 (29)	18 (27)	8 (30)	0.518
β-Blocker	2 (20)	15 (8)	4 (6)	3 (11)	0.349
Statin	3 (30)	36 (19)	12 (18)	3 (11)	0.591
Insulin	0 (0)	9 (5)	6 (9)	2 (7)	0.456
Peak creatine kinase myocardial band, IU/L	116 (69–201)	234 (88–385)	131 (52–295)	85 (42–333)	<0.004*

Values are given as number (percentage) or median (interquartile range). ACEI/ARB indicates angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; CN, calcified nodule; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

**P* value: 0.180 in artery-to-artery embolic myocardial infarction (AAEMI) vs plaque rupture (PR) and 0.015 in PR vs plaque erosion (PE).

Angiographic Findings, Procedural Characteristics, and Clinical Features of Patients With AAEMI

Angiographic findings and procedural characteristics are shown in Table 3 and clinical features of patients with AAEMI are shown in Table 4. The frequency of right coronary artery (RCA) as the culprit vessel tended to be higher in AAEMI compared with PR, PE, and CN (60% versus 48% versus 33% versus 30%, *P*=0.052). TIMI flow grade 0 or 1 on initial angiogram and after passage of a guidewire were seen in 243 (82%) and 55 (19%) of 297 patients, respectively; the frequencies of which were not different among

Table 2. OCT Findings

	AAEMI (n=10)	PR (n=193)	PE (n=67)	CN (n=27)	*P* Value
Lipid-rich plaque	10 (100)	193 (100)	33 (49)	17 (63)	<0.001*
Lipid arc, °	262 (213–286)	301 (276–325)	70 (46–95)	87 (65–115)	<0.001†
TCFA	4 (40)	138 (72)	22 (33)	0 (0)	<0.001‡
Ruptured cap thickness, μm	70 (60–90)	60 (50–70)	…	…	0.053
Maximal ruptured cavity area, mm^2	0.7 (0.4–1.5)	1.2 (0.7–1.8)	…	…	0.639
LA at rupture site, mm^2	4.4 (2.5–6.7)	1.5 (1.0–2.4)	…	…	<0.001
MLA at culprit site, mm^2	4.0 (2.2–4.9)	1.0 (0.8–1.3)	1.0 (0.8–1.2)	1.1 (0.7–1.6)	<0.001§
MLA at occlusion site, mm^2	1.2 (1.0–2.1)	…	…	…	…
Distance between proximal culprit site and occlusion site, mm	39 (35–66)	…	…	…	…

Values are given as number (percentage) or median (interquartile range). LA indicates lumen area; MLA, minimum lumen area; OCT, optical coherence tomography; and TCFA indicates thin-cap fibroatheroma.

**P* value: 0.007 in artery-to-artery embolic myocardial infarction (AAEMI) vs plaque erosion (PE), 0.012 in AAEMI vs calcified nodule (CN), <0.001 in plaque rupture (PR) vs PE, and <0.001 in PR vs CN.

†*P* value: 0.013 in AAEMI vs PR, <0.001 in AAEMI vs PE, <0.001 in AAEMI vs CN, <0.001 in PR vs PE, and <0.001 in PR vs CN.

‡*P* value: 0.069 in AAEMI vs PR, 0.003 in AAEMI vs CN, <0.001 in PR vs PE, <0.001 in PR vs CN, and <0.001 in PE vs CN.

§*P* value: <0.001 in AAEMI vs PR, <0.001 in AAEMI vs PE, and <0.001 in AAEMI vs CN.

Table 3. Angiographic Findings and Procedural Characteristics

	AAEMI (n=10)	PR (n=193)	PE (n=67)	CN (n=27)	*P* Value
Pre-PCI angiographic findings					
Culprit vessel					
LAD	3 (30)	86 (44)	36 (54)	14 (52)	0.378
LCX	1 (10)	15 (8)	9 (13)	5 (18)	0.253
RCA	6 (60)	92 (48)	22 (33)	8 (30)	0.052
Reference vessel diameter, mm	2.6 (2.4–2.8)	2.6 (2.3–2.9)	2.6 (2.3–2.9)	2.5 (2.3–2.7)	0.413
Minimum lumen diameter, mm	0.4 (0–1.1)	0 (0–0.5)	0.1 (0–0.5)	0 (0–0.3)	0.128
Percent diameter stenosis, %	86 (64–100)	100 (80–100)	96 (80–100)	100 (87–100)	0.228
Initial TIMI flow grade 0/1/2/3	5/4/1/0	130/27/23/13	37/16/13/1	18/6/3/0	0.099
TIMI flow grade after passage of a guidewire 0/1/2/3	0/1/4/5	6/27/44/116	2/15/20/30	1/3/4/19	0.413
Collateral flow grade ≤2	9 (90)	181 (94)	60 (90)	26 (96)	0.509
Procedural characteristics					
Thrombectomy before OCT imaging	6 (60)	131 (68)	36 (54)	18 (67)	0.214
Small balloon angioplasty before OCT imaging	1 (10)	26 (13)	11 (16)	4 (15)	0.928
Stent use	6 (60)	192 (99)	66 (99)	27 (100)	<0.001*
No. of stents per lesion	1 (0–1)	1 (1–1)	1 (1–1)	1 (1–1)	0.141
Stent diameter, mm	2.75 (0–3.4)	3 (2.8–3.5)	3 (2.5–3.5)	3 (2.8–3.3)	0.053
Total stent length, mm	20 (0–33)	23 (18–24)	23 (18–24)	24 (18–28)	0.332
Post-PCI angiographic findings					
TIMI flow grade ≤2	1 (10)	40 (21)	9 (13)	5 (19)	0.772
No reflow phenomenon	1 (10)	36 (19)	9 (13)	5 n	0.881
Myocardial brush grade 0/1/2/3	0/0/1/9	1/9/31/152	1/2/15/49	0/1/6/20	0.872

Values are given as number (percentage) or median (interquartile range). LAD indicates left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCA, right coronary artery; and TIMI, thrombolysis in myocardial infarction.

*P value: <0.001 in artery-to-artery embolic myocardial infarction (AAEMI) vs plaque rupture (PR), <0.001 in AAEMI vs plaque erosion (PE), and 0.032 in AAEMI vs calcified nodule (CN).

AAEMI, PR, PE, and CN (90% versus 81% versus 79% versus 89% [*P*=0.726]: initial angiogram and 10% versus 17% versus 25% versus 15% [*P*=0.381]: after passage of a guidewire). Thrombectomy and small balloon angioplasty before OCT imaging were performed in 191 (64%) and 42 (14%) of 297 patients, respectively; the frequencies of which were not different among the 4 groups (*P*=0.214 and *P*=0.928). The frequency of stent use was significantly lower in AAEMI compared with PR, PE, and CN (60% versus 99% versus 99% versus 100%, *P*<0.001). Of 6 patients with AAEMI and stent use, 2 patients had stent implantation for the occlusion site only. In 4 patients without stent implantation, 2 patients had thrombectomy only and the other 2 patients had balloon angioplasty after thrombectomy. No patients with AAEMI took anticoagulation therapy after primary PCI. The median follow-up period in AAEMI was 43 months (IQR, 30–56 months). Patients with AAEMI had no MACE.

DISCUSSION

The major findings of this study are as follows: (1) the prevalence of AAEMI in patients with STEMI was 3.4%, (2) 60% of patients with AAEMI had a culprit lesion in the RCA, (3) LA at the rupture site and MLA at the culprit site were larger in AAEMI compared with others, (4) 40% of patients with AAEMI had nonstent strategy, and (5) the 3-year MACE rate in AAEMI was 0%. To the best of our knowledge, this is the first study to discuss the prevalence, clinical features, and prognosis of patients with AAEMI.

Prevalence of AAEMI

AAE infarction is the concept in the cerebral circulation, which is caused by embolism attributable to the migration of thrombus formed at the proximal stenosed vessel. AAE infarction is one of the important causes of cerebral infarction.[7–9] Previous studies have reported that the prevalence of AAE cerebral infarction was ≈7%

Table 4. All AAEMI Cases

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Age, y	75	72	83	69	65	76	65	92	70	73
Sex	Woman	Woman	Man	Man	Man	Man	Man	Woman	Man	Man
Target vessel	RCA	LAD	LCX	RCA	LAD	RCA	RCA	RCA	LAD	RCA
Maximal ruptured cavity area, mm^2	0.4	0.5	0.4	2.9	2.5	1.1	0.5	1.1	0.2	0.8
LA at rupture site, mm^2	12.0	4.4	4.3	1.6	2.6	6.1	7.1	3.6	2.1	4.2
MLA at culprit site, mm^2	10.0	3.9	4.3	1.6	2.3	4.6	5.9	3.0	1.9	6.5
LMA at occlusion site, mm^2	5.6	0.9	1.9	0.6	1.0	1.0	2.9	1.3	1.2	1.3
Distance between culprit site and occlusion site, mm	76	34	39	64	30	38	60	72	36	40
Thrombectomy	+	–	–	+	–	–	+	+	+	+
Total number of stents	0	1	2	2	1	1	0	1	0	0
Stent implantation for culprit site	–	+	+	+	–	–	–	+	–	–
Stent implantation for occlusion site	–	–	+	+	+	+	–	–	–	–
Antiplatelet therapy after PCI	Aspirin	Aspirin, prasugrel	Aspirin, prasugrel	Aspirin, prasugrel	Aspirin, prasugrel	Aspirin, prasugrel	Aspirin	Aspirin, prasugrel	Aspirin, prasugrel	Aspirin, prasugrel
Anticoagulation therapy after PCI	–	–	–	–	–	–	–	–	–	–

AAEMI indicates artery-to-artery embolic myocardial infarction; LA, lumen area; LAD, left anterior descending artery; LCX, left circumflex artery; MLA, minimum lumen area; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

to 18% and the main embolic source was the proximal plaque site of the internal carotid artery.[7–10] The present study showed that the prevalence of AAEMI according to our diagnostic criteria for AAEMI was 3.4%. In comparison with the prevalence of AAE cerebral infarction, that of AAEMI in this study was low. One possible explanation for this difference between AAEMI and AAE cerebral infarction may be attributable to the differences in vessel and lumen size. The vessel diameter of the cerebral artery, especially in the extracranial arteries such as the internal carotid artery and vertebral artery, is 4 to 6 mm, whereas that of the coronary artery is 2 mm to 4 mm, which is nearly half of the extracranial artery. In the coronary artery compared with the extracranial artery, thrombosis leading to complete occlusion at the proximal plaque site may tend to occur as a result of the smaller vessel size. Another possible explanation is that patients with STEMI have the dynamic nature of thrombosis with waxing and waning thrombosis and flow. The findings of coronary angiography and OCT in the present study is a snapshot of one moment during the natural history of STEMI. Therefore, AAEMI may occur significantly more frequently but transiently. Furthermore, it cannot be denied that some cases of AAEMI may be the nidus for commonly seen long thrombotic occlusions during STEMI, where thrombus develops from a distal emboli propagating proximally to the rupture site. Hence, the prevalence of AAEMI according to the definition in the present study may be underestimated, and the true prevalence of AAEMI may remain unknown. In order to clarify this, larger prospective clinical trials are required.

Characteristics of AAEMI

Noncomplete occlusive thrombus formation at the culprit plaque site caused by PR often migrates to the distal vessel, which causes AAEMI with embolic complete occlusion at the distal coronary artery. This entity, AAEMI, is considered as a minor subset of PR, not as a separate entity such as PE or CN. The recognition of this entity does not eliminate the current stratification of STEMI causes. Meanwhile, AAEMI has some unique features. First, the culprit vessel in 6 of 10 patients with AAEMI (60%) was the RCA. One possible explanation may be the difference in flow velocity between the right and left coronary arteries. Previous studies reported that the coronary flow velocity was lower in the RCA compared with the left coronary artery.[18,19] The lower velocity in the RCA may promote embolic complete occlusion at the distal coronary artery.

Previously, our OCT studies reported that the LA at the rupture site was smallest in STEMI, followed by non–ST-segment elevation ACS and asymptomatic coronary artery disease.[13,20] These results support the theory that a smaller lumen with a ruptured plaque might be an important determinant leading to ACS. The present OCT findings showed that the LA at the rupture site was larger in AAEMI compared with PR. Compared with the results of our previous OCT study, LA at the rupture site was larger in AAEMI compared with non–ST-segment elevation ACS (4.4 mm^2 versus 2.7 mm^2), whereas MLA at the occlusion site in AAEMI was smaller compared with MLA at the culprit site in non–ST-segment elevation ACS (1.2 mm^2 versus 1.7 mm^2). Patients with AAEMI may have freedom from complete occlusive thrombus formation at the proximal culprit site caused by PR because of a larger LA at the rupture site. Unfortunately, these patients experience embolic complete occlusion at the distal coronary artery because of a smaller LA. The onset of AAEMI may be related in part to these differences in MLA between AAEMI and other types of ACS.

Treatment and Long-Term Prognosis of Patients With AAEMI

A previous OCT study demonstrated the feasibility and safety of antithrombotic therapy without stenting in patients with PE, who have residual vessel stenosis <70% and TIMI grade 3 flow after thrombectomy.[21] In the present study, all patients with AAEMI underwent PCI, of which 4 patients (40%) who had residual vessel stenosis <70% at the occlusion site and TIMI grade 3 flow, underwent thrombectomy only or additive balloon angioplasty without stent use. Patients with AAEMI including the no-stent strategy had no in-hospital MACE, which is similar to the previous study. Furthermore, it is notable that none of the patients with AAEMI developed MACE during 3 years of follow-up. Previous studies demonstrated that patients who have ACS with PR have a worse prognosis compared with patients who have other types of ACS.[21–23] In the present study, the lipid arc at the culprit site and infarct size was smaller in patients with AAEMI compared with patients with PR. These features of AAEMI may contribute to better long-term prognosis.

Clinical Implications

AAEMI is a rare cause for STEMI, and OCT is the most promising technique for identifying not only PR, PE, and CN but also AAEMI in STEMI. Furthermore, OCT-guided primary PCI could help avoid metallic stent implantation in nearly half of patients with AAEMI without increasing recurrence of MI.

Limitations

First, aspiration thrombectomy and balloon angioplasty with a <2.0 mm diameter balloon were

performed before OCT imaging in patients with TIMI flow grade ≤2. These modalities might have modified the culprit lesion morphologies. Second, residual thrombus might affect analysis of the plaque behind it. Especially, they might make it difficult to distinguish PR from non-PR. However, the number of excluded patients with poor OCT image quality including massive thrombus was small (n=19). Third, transthoracic echocardiography examination was performed in all patients in the present study before emergent coronary angiography according to the recommendation of the Japanese Circulation Society 2018 Guideline.[24] It cannot be denied that the use of transthoracic echocardiography during STEMI diagnosis may be a source of delay that could lead to a change in thrombus burden. However, transthoracic echocardiography examinations in these patients were finished within 3 minutes to minimize a change in thrombus burden and achieve a door-to-balloon time <90 minutes. Finally, this was a retrospective study using an OCT registry database at a single institution with a relatively small sample size, especially in patients with AAEMI (only 10 patients). Therefore, the existence of selection bias cannot be completely excluded, and the prevalence (3.4%) and characteristics of AAEMI may be uncertain. The present results should be viewed as preliminary and await confirmation by larger clinical trials.

CONCLUSIONS

AAEMI is a rare cause for STEMI and has unique morphological features of plaque including larger LA at the proximal rupture site and a smaller LA at the distal occlusion site.

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