ORIGINAL ARTICLE

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Impact of the angiographic burden on the incidence of out-of-hospital ventricular fibrillation in patients with acute myocardial infarction

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Abstract

Ventricular fibrillation (VF) is a catastrophic complication of spontaneous (type 1) acute myocardial infarction (AMI). This study sought to clarify the angiographic coronary characteristics related to out-of-hospital VF in AMI patients. We retrospectively reviewed 464 consecutive cases of suspicious AMI, including type 1 AMI, with or without out-of-hospital VF. In addition to patient demographics, proximal left coronary artery (LCA) disease, multivessel disease (MVD), and chronic total occlusion (CTO) were assessed via coronary angiography and compared between patients with and without out-of-hospital VF. Coronary angiography was evaluated for 74 patients with out-of-hospital VF and for 237 without. Male sex (93.2 vs. 83.1%; $P = 0.036$), Killip class ≥ 2 (89.2 vs. 16.5%; $P < 0.001$), and ST elevation myocardial infarction (83.8 vs. 66.7%; $P = 0.003$) were more frequent in the out-of-hospital VF group. The culprit lesions located in the proximal left coronary artery (62.2 vs. 29.5%; $P < 0.001$), MVD (75.7 vs. 41.8%, $P < 0.001$), and CTO (43.2 vs. 10.5%, $P < 0.001$) were more frequently observed in patients with out-of-hospital VF. Multivariate logistic regression analysis identified the culprit lesion located in the proximal LCA [odds ratio (OR) 2.86; 95% confidence interval (CI) 1.34–6.08], the presence of CTO (OR 8.52; 95% CI 3.35–21.65), and MVD (OR 3.69; 95% CI 1.57–8.65) as predictors of out-of-hospital VF. For type 1 AMI patients, advanced disease burden including the culprit lesion located in the proximal LCA and coexistence of CTO or MVD might be associated with out-of-hospital VF.

Keywords Acute myocardial infarction · Chronic total occlusion · Multivessel disease · Out-of-hospital ventricular fibrillation

Abbreviations

AMI	Acute myocardial infarction
CAG	Coronary angiography
CIs	Confidence intervals
CTO	Chronic total occlusion
ECPR	Extracorporeal cardiopulmonary resuscitation
LCA	Left coronary artery
LMT	Left main trunk
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
MVD	Multivessel disease
OHCA	Out-of-hospital cardiac arrest
OR	Odds ratio
PCI	Percutaneous coronary intervention
ROSC	Return of spontaneous circulation
STEMI	ST elevation myocardial infarction
VF	Ventricular fibrillation

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Introduction

Out-of-hospital ventricular fibrillation (VF) is a critical complication of acute myocardial infarction (AMI). Short-term mortality after hospital admission (30-day mortality or in-hospital) has improved for patients with AMI [1–3] with the advancements in coronary care units, the use of contemporary reperfusion strategies [3–5], and preventative therapies

such as aspirin [4, 5]. However, out-of-hospital cardiac arrest (OHCA) including out-of-hospital VF has been assumed to occur in 3–20% of patients with AMI [6–8], and the mortality rate is still considered high. Preventive strategies that reduce the risk of out-of-hospital VF at the onset of AMI as well as prevention of AMI have been unsolved issues.

Coronary angiography (CAG) for anatomical evaluations followed by percutaneous coronary intervention (PCI) has become a standardized strategy for AMI patients. These procedures have been widely used to evaluate and investigate the coronary anatomy of the patients with out-of-hospital VF. Previous studies have shown that the culprit lesion located in the left coronary artery (LCA) was a risk factor for OHCA in AMI patients with return of spontaneous circulation (ROSC) [9]. However, it has been difficult to evaluate the angiographic anatomy of the coronary artery in patients with sustained VF; therefore, those subjects were excluded from the previous studies. As a result, in patients with more critical conditions, angiographic factors associated with out-of-hospital VF have not been fully elucidated. At our institutions, extracorporeal cardiopulmonary resuscitation (ECPR) has been routinely used for patients with out-of-hospital VF, which has made it possible to perform CAG for not only patients with ROSC, but also patients with sustained VF immediately after establishment of ECPR. Therefore, we were able to evaluate and investigate the angiographic coronary anatomy of consecutive OHCA patients after AMI.

The current study sought to compare AMI patients presenting with and without out-of-hospital VF to identify the angiographic factors related to the occurrence of out-of-hospital VF.

Materials and methods

Design and patients

We retrospectively compared type 1 AMI [10] patients with and without out-of-hospital VF. We enrolled consecutive patients aged ≥ 18 years with suspected type 1 AMI diagnosed within 6 h from onset who were admitted to Kobe University Hospital, Kobe Red Cross Hospital, or Hyogo Emergency Medical Center from September 1, 2010 to December 31, 2015. Type 1 AMI was defined according to the third universal definition of myocardial infarction [10]. We excluded patients who did not undergo CAG, patients who were not diagnosed with type 1 AMI or out-of-hospital VF including ventricular tachycardia, and patients with pulseless electrical activity, asystole, and complete atrioventricular block from the analysis. We performed ECPR for patients with continuous or recurrent VF on arrival. The decision to perform urgent PCI was made by an interventional cardiologist. After PCI, patients were transferred to

the intensive care unit, where standard procedures were continued. Hypothermia was offered to all comatose patients except those for whom it was not indicated due to complications. All patients were managed according to updated international guidelines.

Data collection

Demographic details, medical history, clinical and laboratory findings, conventional risk factors for coronary artery disease, CAG findings, and medical management of all included patients were recorded on admission. Medical records were retrieved from the electronic medical records systems of each participating hospital. The study protocol and utilization of the data for the current analysis were approved by the local institutional review boards of all participating hospitals. All study participants provided informed consent. All authors take complete responsibility for the integrity of the data and accuracy of the data analysis. The study was entered in **UMIN ID**: UMIN000030253.

(https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000034551).

Coronary angiography

All patients received at least 5000 U of intravenous heparin, at least 162 mg of aspirin, and 300 mg of clopidogrel before undergoing CAG, which was performed immediately after establishing percutaneous cardiopulmonary support for patients with sustained VF on arrival. Coronary angiograms were performed in various projections to identify the infarct-related coronary artery, lesions in the non-infarct-related coronary artery, and collateral circulation. Left ventriculography was not performed in the acute phase.

Definition of out-of-hospital VF and anatomical assessments

Out-of-hospital VF was defined as irregular erratic electrical impulses detected on 12-lead electrocardiogram or automatic external defibrillator that varied in amplitude and contour, were without distinct QRS complexes or T waves, and were accompanied by hemodynamic compromise before arrival. We investigated patients with and without out-of-hospital VF. Onset-to-arrival time was defined as the time from symptom onset to hospital arrival. Door-to-balloon time was defined as the time from hospital arrival to reperfusion. Total ischemic time was defined as the time from symptom onset to reperfusion.

Angiograms were visually assessed at the treating hospital. The coronary arteries were divided into segments according to conventional terminology. The culprit lesion was considered a fresh occlusion on angiography or the

presence of thrombus on angiography or intravascular ultrasound. Coronary stenosis ≥ 50% at the left main trunk (LMT) or ≥ 70% at the non-LMT on angiographic assessment was considered significant. Multivessel disease (MVD) was defined as the presence of two or more affected vessels or LMT disease. CTOs were characterized by vessel narrowing that resulted in either complete or nearly complete blockade of antegrade blood flow estimated by CAG (Thrombolysis in Myocardial Infarction grade 0–1 flow). Collateral source arteries were defined as the arteries in the perfused CTO territory on angiography.

Clinical outcome measures

In-hospital mortality was defined as all-cause death, including cardiac or neurological causes. Patients discharged with Cerebral Performance Category scores [11] of 1 or 2 were defined as survivors with favorable neurological outcomes. Patients with out-of-hospital VF were separately analyzed for patients with continued or recurrent VF on arrival and those with ROSC on arrival.

Statistical analysis

Univariate analysis of categorical variables was performed using the Chi square test. Continuous variables were presented as mean ± standard deviation. Univariate analysis of continuous variables was performed using the Student's t test or analysis of variance. For multiple comparisons, the α significance level was calculated using Bonferroni correction to adjust for multiplicity. The multivariate analysis for the prediction of out-of-hospital VF was performed using logistic regression. Potential confounders were entered if they were clinically significant for groups with $P < 0.05$. Statistical significance was defined as $P < 0.05$ or confidence intervals (CIs) that did not include 1.0. All probability values are two-tailed. All analyses were performed using SPSS software version 24.0.

Results

Patient characteristics

We retrospectively analyzed 464 consecutive patients who were suspected to have AMI and who were admitted to our institutions from September 1, 2010 to December 31, 2015. We excluded 13 patients who did not undergo CAG, 76 patients who were not diagnosed with AMI, 20 who were not diagnosed with type 1 AMI, and 44 who were not diagnosed with out-of-hospital VF (including 10 patients with ventricular tachycardia, 14 patients with pulseless electrical activity, 19 patients with asystole, and 1 patients with

complete atrioventricular block) from the analysis. Finally, our study population consisted of 311 patients; there were 74 type 1 AMI patients with out-of-hospital VF and 237 type 1 AMI patients without out-of-hospital VF as a control group (Fig. 1).

Patients' baseline characteristics on admission are summarized in Table 1. Male sex (93.2 vs. 83.1%; $P = 0.036$), Killip class ≥ 2 (89.2 vs. 16.5%; $P < 0.001$), and ST elevation myocardial infarction (STEMI) (83.8 vs. 66.7%; $P = 0.003$) were more frequent in the out-of-hospital VF group. Patients with out-of-hospital VF had lower serum potassium levels (3.7 ± 0.6 vs. 4.1 ± 0.5; $P < 0.001$). The left ventricular ejection fraction (LVEF) was lower in patients with out-of-hospital VF (29.0 ± 17.6 vs. 47.1 ± 12.2; $P < 0.001$).

The onset-to-arrival time was shorter in patients with out-of-hospital VF than in those without (37.5 ± 15.6 vs. 101.5 ± 65.1; $P < 0.001$). The door-to-balloon time was also shorter in patients with out-of-hospital VF than in those without (54.1 ± 16.0 vs. 68.6 ± 16.8; $P < 0.001$). Therefore, total ischemic time was shorter in patients with out-of-hospital VF than in those without (91.5 ± 22.4 vs. 170.0 ± 67.3; $P < 0.001$). Table 2 shows the characteristics and pre-hospital treatment for out-of-hospital VF. Among 46 patients for whom information before collapse was available, the development of VF occurred within 6 h from symptom onset. However, 28 patients had no information regarding symptoms before hemodynamic collapse. ECPR was performed for 59 patients (79.7%), and 15 patients (20.3%) achieved ROSC.

Angiographic characteristics

CAG and PCI were performed for all 311 AMI patients with or without out-of-hospital VF. Angiographic data are summarized in Table 3. The angiographic culprit lesion was associated with the risk of out-of-hospital VF (Table 4). The culprit lesion distribution was significantly different between patients with and without out-of-hospital VF. The culprit locations in patients with out-of-hospital VF were the LMT, left anterior descending artery, left circumflex artery, or right coronary artery for 10.8, 48.7, 10.8, or 29.7%, respectively (Table 3). Culprit lesions located in the LMT or proximal left anterior descending artery resulted in a high risk of out-of-hospital VF (OR 6.93 and 2.39, respectively; 95% CI 1.83–26.26 and 1.03–5.56, respectively) (Table 4).

The rate of MVD was higher in patients with out-of-hospital VF than in those without out-of-hospital VF (75.7 vs. 41.8%; $P < 0.001$). Moreover, triple-vessel disease was found more often in patients with out-of-hospital VF than in those without out-of-hospital VF (41.9 vs. 16.0%; $P < 0.001$) (Table 3). CTO occurred more frequently in patients with out-of-hospital VF (43.2 vs. 10.5%; $P < 0.001$) (Table 3).
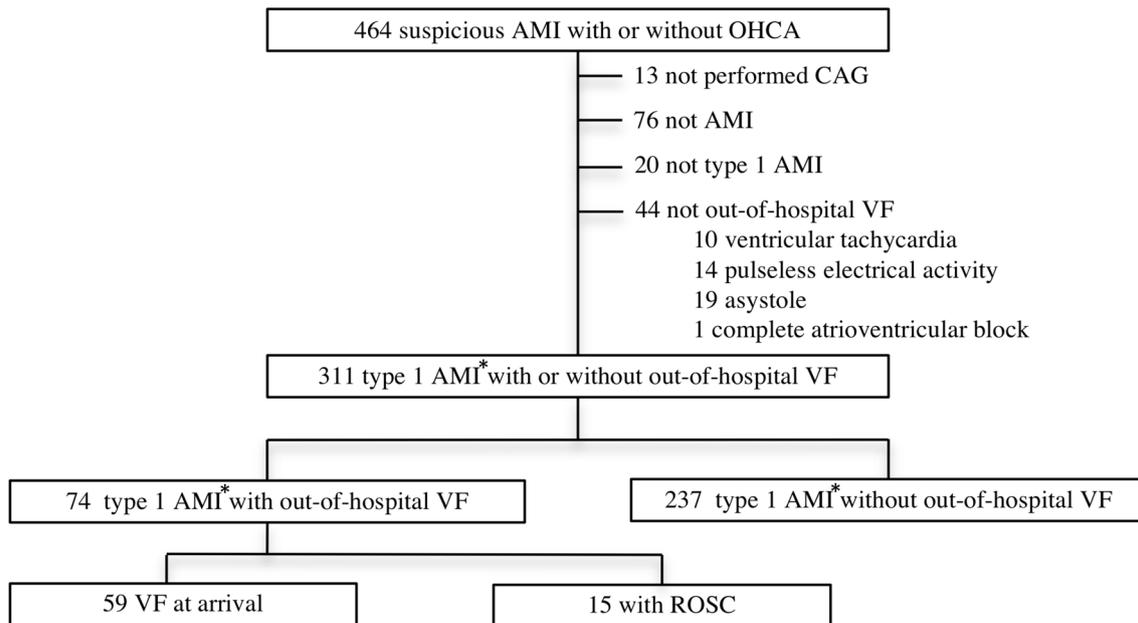
Fig. 1 Study population and clinical status on arrival. Flow of study participants based on inclusion and exclusion criteria and the clinical status on arrival of type 1 AMI patients with out-of-hospital VF. *AMI* acute myocardial infarction, *OHCA* out-of-hospital cardiac arrest, *CAG* coronary angiography, *VF* ventricular fibrillation, *ROSC* return of spontaneous circulation, *ECPR* extracorporeal cardiopulmonary resuscitation, *IABP* intra-aortic balloon pumping. *type 1 AMI was defined according to the third universal definition of myocardial infarction

Multivariate analysis

Independent predictors of out-of-hospital VF identified via logistic regression analysis are shown in Table 5. Prior myocardial infarction or revascularization, STEMI, hypokalemia, and LVEF < 40% were associated with an increased risk of out-of-hospital VF. CTO was strongly associated with an increased risk of out-of-hospital VF (OR 8.52; 95% CI 3.35–21.65). Proximal LCA disease (OR 2.86; 95% CI 1.34–6.08) and MVD (OR 3.69; 95% CI 1.57–8.65) were also associated with an increased risk of out-of-hospital VF.

Angiographic characteristics of patients with CTO

Table 6 shows the angiographic characteristics of patients with CTO. A representative case is shown in Fig. 2. CTO was present in 32 patients with out-of-hospital VF and in 25 patients without. In this CTO subgroup, there was no significant difference in the location of CTO between patients with and without out-of-hospital VF. However, the rate of collateral source artery events was higher for patients with out-of-hospital VF than for patients without out-of-hospital VF (46.9 vs. 20.0%; $P = 0.032$).

Clinical outcomes

The status on arrival and clinical outcomes of AMI patients with out-of-hospital VF are summarized in Table 7. Among patients with out-of-hospital VF, 59 patients had VF on arrival and underwent ECPR. Fifteen patients had ROSC naturally or defibrillation with an automated external defibrillator. The in-hospital mortality rates were 47.5, 13.3, and 3.8% for patients with VF on arrival, with ROSC on arrival, and without VF. Favorable neurological outcomes occurred for 23.7, 60.0, and 96.2%, respectively.

Discussion

In the current study, we analyzed the angiographic predictors of out-of-hospital VF for type 1 AMI patients beyond the conventional risk factors previously reported and identified by the presence of MVD and CTO as independent risk factors for out-of-hospital VF in the multivariate analysis. Interestingly, the CTO subgroup analysis showed that the incidence of collateral source artery events was higher for patients with out-of-hospital VF.

Table 1 Baseline patient characteristics

	With VF ($n = 74$)	Without VF ($n = 237$)	P value
Age (years ± standard deviation)	64.1 ± 9.4	66.2 ± 12.8	0.111
Male	69 (93.2%)	197 (83.1%)	0.036
Past history			
History of CAD[a]	15 (20.3%)	39 (16.5%)	0.261
History of MI	10 (13.7%)	27 (11.5%)	0.612
Prior PCI	3 (4.1%)	33 (14.0%)	0.021
Prior CABG	7 (9.6%)	3 (1.3%)	0.002
Coronary risk factors			
Hypertension	50 (71.4%)	149 (63.4%)	0.216
Dyslipidemia	27 (38.6%)	102 (43.4%)	0.472
Diabetes mellitus	22 (31.4%)	68 (28.9%)	0.688
History of smoking	38 (69.1%)	144 (67.0%)	0.765
Familial history	1 (1.4%)	12 (6.2%)	0.098
Killip class ≥ 2	66 (89.2%)	39 (16.5%)	< 0.001
ECG on arrival			
ST elevation	62 (83.8%)	158 (66.7%)	0.003
Medication on admission			
Beta-blocker	9 (13.0%)	26 (11.6%)	0.738
ACEi/ARB	19 (27.5%)	57 (25.3%)	0.715
MRA	4 (5.8%)	3 (1.3%)	0.055
Statin	16 (23.2%)	55 (24.4%)	0.831
Antiplatelet	16 (23.2%)	50 (22.2%)	0.866
Laboratory findings			
Potassium (mEq/L)	3.7 ± 0.6	4.1 ± 0.5	< 0.001
Cardiac enzymes			
Troponin I on arrival (ng/mL)	2.4 ± 6.4	7.3 ± 26.6	0.023
CK on arrival (IU/L)	211 ± 231	481 ± 839	0.012
CK-MB on arrival (ng/mL)	42 ± 36	46 ± 91	< 0.001
Peak CK (IU/L)	5045 ± 5911	2262 ± 2902	< 0.001
LVEF (%)	29.0 ± 17.6	47.1 ± 12.2	< 0.001
Onset-to-arrival time (min.)	37.5 ± 15.6	101.5 ± 65.1	< 0.001
Door-to-balloon time (min.)	54.1 ± 16.0	68.6 ± 16.8	< 0.001
Total ischemic time (min.)	91.5 ± 22.4	170.0 ± 67.3	< 0.001

Values are presented as number (%) or mean ± standard deviation

ACEi angiotensin-converting-enzyme inhibitor, *ARB* angiotensin II receptor blocker, *CABG* coronary artery bypass graft, *CAD* coronary artery disease, *CK* creatine kinase, *LVEF* left ventricular ejection fraction, *MI* myocardial infarction, *MRA* mineralocorticoid receptor antagonist, *PCI* percutaneous coronary intervention, *VF* ventricular fibrillation

[a]CAD was defined as prior MI, PCI, or CABG

Association between baseline characteristics and out-of-hospital VF

The historically poor prognoses of AMI patients with out-of-hospital VF led to the need to investigate the risks and improve prognoses. Previous studies have identified male sex, STEMI, hypokalemia, and larger enzymatic infarct size as predictors for out-of-hospital VF in AMI patients [12]. Previous studies have described that the frequency of left ventricular dysfunction and Killip score ≥ 2 for patients with out-of-hospital VF were higher compared to patients without

[13, 14]. Consistent with those reports, these conventional factors were more frequently observed for patients with out-of-hospital VF than for those without in the current study (Table 1).

Although these factors acknowledged a coincidence with the previous research, the proportion of out-of-hospital VF was higher than that of previous studies. Of 311 consecutive patients with AMI, there were 74 (23.8%) with out-of-hospital VF. VF has been reported to occur in approximately 3–20% of AMI cases [6–8]. The higher prevalence in the current population could be explained by the urgent

Table 2 Characteristics and pre-hospital treatment of patients with out-of-hospital ventricular fibrillation

	Patients without-of-hospital VF ($n = 74$)
Collapse within six hours of symptom	46/46 (100%)
Bystander CPR	66/74 (89.2%)
Collapse before arrival at EMS	69/74 (93.2%)
Defibrillation	72/74 (97.3%)
Average number of shock	2.3 ± 1.1
ROSC on arrival	15/74 (20.3%)
ECPR	59/74 (79.7%)

Values are presented as number (%) or mean ± standard deviation

CPR cardiopulmonary resuscitation, *ECPR* extracorporeal cardiopulmonary resuscitation, *EMS* emergency medical services, *ROSC* return of spontaneous circulation, *VF* ventricular fibrillation

transportation of patients with out-of-hospital VF who were to undergo ECPR at our tertiary care centers for out-of-hospitals cardiac arrest and ischemic heart diseases. In addition, of the 311 consecutive patients with AMI, 220 (70.7%) had STEMI. The proportion of STEMI among those with acute coronary syndrome has been reported to be approximately 20% in the USA [15]. However, the proportion of STEMI was 60–69% in Japan [16, 17], which was higher than that in the USA. The reason for the higher proportion of STEMI in the current study was that more patients with STEMI were transferred to our tertiary care center to receive primary PCI as early as possible. Moreover, although STEMI is the major cause of OHCA [12], it is difficult to accurately diagnose STEMI for patients with OHCA because of their critical status. Therefore, a significant proportion of patients with

out-of-hospital VF may have died without being diagnosed with STEMI. However, in the current study, ECPR could increase the chance of an accurate diagnosis of STEMI for patients with an unknown cause of VF and OHCA. Consequently, the rate of STEMI in the current study might be higher than that in previous studies [15].

In patients with out-of-hospital VF, the onset-to-arrival times were an index of pre-hospital delay and were shorter than in patients without out-of-hospital VF (Tables 1). The results possibly reflected out-of-hospital VF leading to immediate transportation after the arrival of emergency medical services for out-of-hospital VF patients. Close collaboration with regional emergency medical services could help to shorten the pre-hospital time. In the current study, because we analyzed patients with AMI within 6 h of onset, it should be noted that for patients whose symptom onset to collapse time is unknown, the onset was defined as the time of collapse. In addition, in patients with out-of-hospital VF, the door-to-balloon times were shorter than in patients without out-of-hospital VF. The results possibly reflected direct ambulance transportation to the cardiac catheterization laboratory and CAG followed by primary PCI performed simultaneously with resuscitation.

Association between angiographic characteristics and out-of-hospital VF

In addition to the aforementioned conventional risks, the widespread use of CAG and primary PCI clarified the angiographic characteristics of the coronary anatomy of patients with out-of-hospital VF. In the current AMI population, the culprit lesion located in the proximal LCA was identified as an independent risk factor for out-of-hospital VF according

Table 3 Coronary angiographic characteristics

	Patients with out-of-hospital VF ($n = 74$)	Patients without out-of-hospital VF ($n = 237$)	P value
Culprit lesion			0.010
LMT	8 (10.8%)	5 (2.1%)	
LAD	37 (48.7%)	116 (48.9%)	
LCx	8 (10.8%)	35 (14.8%)	
RCA	21 (29.7%)	81 (34.2%)	
Proximal LCA	46 (62.2%)	71 (29.5%)	< 0.001
LMT disease	15 (20.3%)	14 (5.9%)	0.001
Diseased vessel			0.001
Single vessel disease	18 (24.3%)	138 (58.2%)	
Double vessel disease	25 (33.8%)	61 (25.7%)	
Triple vessel disease	31 (41.9%)	38 (16.0%)	
At least 2 vessel (multivessel) disease	56 (75.7%)	99 (41.8%)	< 0.001
Coexistence of CTO	32 (43.2%)	25 (10.5%)	< 0.001

Values are presented as number (%)

CTO chronic total occlusion, *LAD* left anterior descending artery, *LCA* left coronary artery, *LCx* left circumflex artery, *LMT* left main trunk, *RCA* right coronary artery

Table 4 Association of angiographic culprit lesion with out-of-hospital ventricular fibrillation

	No. of out-of-hospital VF	OR	95% CI
RCA			
Proximal	9 (12.2)	Reference	–
Non-proximal	12 (16.2)	1.24	0.47–3.26
LMT	8 (10.8)	6.93	1.83–26.26
LAD			
Proximal	32 (43.2)	2.39	1.03–5.56
Non-proximal	5 (6.8)	0.38	0.12–1.22
LCx			
Proximal	6 (8.1)	2.41	0.65–8.94
Non-proximal	2 (2.7)	0.48	0.12–1.94

Values are presented as number (%)

LAD left anterior descending artery, *LCx* left circumflex artery, *LMT* left main trunk, *OR* odds ratio, *RCA* right coronary artery, *VF* ventricular fibrillation

to the multivariate analysis (Table 5). Moreover, the existence of MVD was also associated with an increased risk of out-of-hospital VF (Table 5). A previous case–control study [13] and registry study [9] similarly revealed that the culprit lesion located in the proximal LCA was associated with a high risk for OHCA in STEMI patients.

On the other hand, these previous studies [9, 13] described that the extent of coronary artery disease was not associated with higher odds of out-of-hospital VF. Patients with only ROSC or only good neurological prognosis were analyzed, and patients without successful resuscitation were excluded. However, in the current study, we investigated patients with out-of-hospital VF; 79.7% of those patients did not have ROSC on arrival and 68.9% had poor neurological outcomes. Hence, our study population had more critical conditions compared with those of the previous studies. A possible explanation for the discrepancy might be the difference in patient characteristics and disease severity.

Table 6 Characteristics of patients with chronic total occlusion

	Patients with out-of-hospital VF (n = 32)	Patients without out-of-hospital VF (n = 25)	P value
Culprit lesion of AMI			
LMT	2 (6.3%)	1 (4.0%)	0.706[a]
LAD	15 (46.9%)	12 (48.0%)	0.933[a]
LCx	5 (15.6%)	4 (16.0%)	0.969[a]
RCA	10 (31.3%)	8 (32.0%)	0.952[a]
Collateral source artery event	15 (46.9%)	5 (20.0%)	0.032
CTO lesion			
LMT	0 (0%)	0 (0%)	NA
LAD	12 (37.5%)	10 (40.0%)	0.847[b]
LCx	7 (21.9%)	7 (28.0%)	0.594[b]
RCA	13 (40.6%)	8 (32.0%)	0.503[b]

Values are presented as number (%)

AMI acute myocardial infarction, *CTO* chronic total occlusion, *LAD* left anterior descending artery, *LCx* left circumflex artery, *LMT* left main trunk, *RCA* right coronary artery, *VF* ventricular fibrillation

[a] α significance level was 0.008
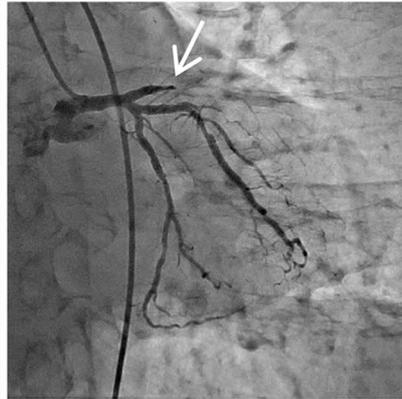
[b] α significance level was 0.013

Impact of CTO on out-of-hospital VF

Previous reports, including patients not presenting with acute ischemia such as AMI were analyzed, described the coexistence of CTO itself [18] or infarct-related artery CTO [19] as a predictor of ventricular arrhythmia for ischemic cardiomyopathy patients with stable coronary artery disease. However, for patients with AMI, the association between the coexistence of CTO and out-of-hospital VF was not fully clarified. The current study revealed that coexistence of CTO was independent risk factors for out-of-hospital VF (Table 5). Interestingly, in the subgroup analysis of patients with CTO, although the distributions of the culprit lesion
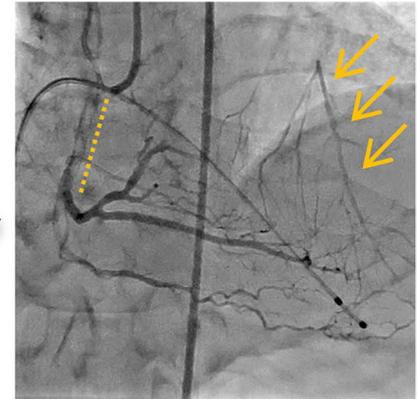
Table 5 Independent predictors of out-of-hospital ventricular fibrillation in multivariate logistic regression analysis

	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
Male	2.43	0.68–8.64		
Prior MI or revascularization	2.50	0.947–6.58		
Hypokalemia (< 4.0 mEq/l)	5.39	2.28–12.75	5.24	2.24–12.29
STEMI	5.45	1.96–15.14	5.48	1.98–15.15
LVEF < 40%	4.88	2.22–10.75	4.92	2.24–10.83
Culprit located proximal LCA	2.91	1.36–6.25	2.86	1.34–6.08
Coexistence of CTO	8.20	3.20–21.00	8.52	3.35–21.65
Multivessel disease	3.60	1.53–8.48	3.69	1.57–8.65

CI confidence interval, *CTO* chronic total occlusion, *LCA* left coronary artery, *LMT* left main trunk, *MI* myocardial infarction, *OR* odds ratio, *STEMI* ST elevation myocardial infarction, *VF* ventricular fibrillation

Pre-revascularization

Post-revascularization

A: RCA (culprit lesion)

B: LCA (CTO lesion in LAD)

C: RCA and LAD via collateral flow

Fig. 2 Representative images of coronary artery anatomy in an out-of-hospital ventricular fibrillation patient with chronic total occlusion. Coronary angiography (CAG) images of an out-of-hospital ventricular fibrillation (VF) patient with chronic total occlusion (CTO). **a**, **b** CAG before revascularization. The red arrow indicates the culprit lesion in acute occlusion in the right coronary artery (RCA) (**a**). The white arrow indicates the CTO lesion in the left anterior descending artery (LAD) (**b**). **c** CAG after revascularization. The yellow arrows indicate LAD flow via collateral flow. The yellow line indicates the stented segment

Table 7 Clinical outcome

	VF on arrival (n = 59)	ROSC (n = 15)	Without VF (n = 237)
In-hospital mortality	28 (47.5%)	2 (13.3%)	9 (3.8%)
Favorable neurological outcome[a]	14 (23.7%)	9 (60.0%)	228 (96.2%)

Values are presented as number (%)

ROSC return of spontaneous circulation, *VF* ventricular fibrillation

[a]Patients discharged with the Cerebral Performance Category scores of 1 and 2 were defined as survivors with favorable neurological outcome

location and CTO lesions were similar between those with and without out-of-hospital VF, the proportion of collateral source artery events was higher for patients with out-of-hospital VF (Table 6). A possible explanation for this finding could be that a collateral source event caused ischemia in two vessel territories: the culprit vessel territory and the territory of collateral perfusion. Collateral flow is considered to perfuse large areas in a CTO territory [20, 21]. A previous study demonstrated that a large area of acute ischemia was associated with the risk for out-of-hospital VF in AMI patients [12]. Therefore, occlusion of a collateral source artery causing the large ischemic area of the culprit vessel territory and the territory of collateral perfusion could trigger VF.

Limitations

Although this study is the first to our knowledge to compare angiographic studies of AMI patients with out-of-hospital VF, including patients presenting with VF on hospital arrival without ROSC, this study had several limitations.

First, as with any observational, nonrandomized study, our study may have been limited by selection bias. Although our study population had more critical conditions compared with populations of previous studies, we did not include the patients who died before hospital arrival. Second, the lack of information regarding pre-existing LVEF was a limitation. The information regarding pre-existing LVEF is only available with a prospective study design. In addition, it was difficult to obtain information regarding LVEF immediately after onset for patients with VF on arrival due to their critical conditions. Although we try to perform transthoracic echocardiography after ECPR, we were able to obtain information regarding LVEF for only 81% of patients with out-of-hospital VF. Third, we could not investigate the exact time from symptom onset to collapse or the time from the true initial arrhythmia occurrence to wearing an automated external defibrillator for patients with out-of-hospital VF; therefore, we could not determine whether the patient had VF or another critical ventricular arrhythmia.

Conclusion

For type 1 AMI patients, an advanced disease burden including the culprit lesion located in the proximal LCA and the coexistence of CTO or MVD may be associated with the occurrence of out-of-hospital VF. The findings of this study may help to prevent out-of-hospital VF, to identify high-risk patients, and to perform earlier initiation of preventive therapies. Further study is warranted to assess the effectiveness of pre-emptive treatment for patients suspected of having coronary artery disease to reduce the occurrence of this catastrophic event.

Compliance with ethical standards

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