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Clinical Impact of Ventricular Tachycardia and/or Fibrillation During the Acute Phase of Acute Myocardial Infarction on In-Hospital and 5-Year Mortality Rates in the Percutaneous Coronary Intervention Era

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Background: The aim of this study was to investigate the prognostic impact of acute-phase ventricular tachycardia and fibrillation (VT/VF) on ST-segment elevation myocardial infarction (STEMI) patients in the percutaneous coronary intervention (PCI) era.

Methods and Results: Using the database of the Osaka Acute Coronary Insufficiency Study (OACIS), we studied 4,283 consecutive patients with STEMI who were hospitalized within 12h of STEMI onset and underwent emergency PCI. Acute-phase VT/VF, defined as ≥3 consecutive ventricular premature complexes and/or VF within the 1st week of hospitalization, occurred in 997 (23.3%) patients. In-hospital mortality risk was significantly higher in patients with acute-phase VT/VF than inthose without (14.6% vs. 4.3%, adjusted hazard ratio (HR) 1.83, P=0.0013). Among patients discharged alive, 5-year mortality rates were comparable between patients with and without acute-phase VT/VF. Subgroup analysis showed that acute-phase VT/VF was associated with increased 5-year mortality after discharge in high-risk patients (GRACE Risk Score ≥115; adjusted HR 1.60, P=0.043), but not in intermediate- or low-risk patients.

Conclusions: Even in the PCI era, acute-phase VT/VF was associated with higher in-hospital deaths of STEMI patients. However, the 5-year prognostic impact of acute-phase VT/VF was limited to high-risk patients. (*Circ J* 2016; **80:** 1539–1547)

Key Words: Acute myocardial infarction; Percutaneous coronary intervention; Prognosis; Ventricular tachycardia; Ventricular fibrillation

Ventricular tachycardia and fibrillation (VT/VF) are fatal arrhythmias that cause cardiac collapse and are major complications of acute myocardial infarction (AMI). Studies conducted in the pre-primary percutaneous coronary intervention (PCI) era of the 1980s and 1990s have demonstrated that the acute phase of VT/VF following AMI is strongly

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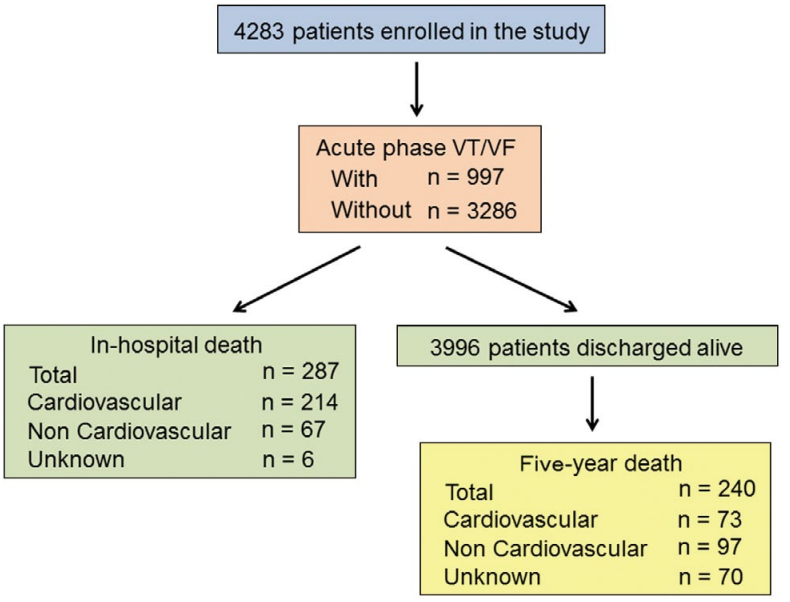

Figure 1. Schematic of the stratification of the patients based on in-hospital and 5-year mortality rates. VT/VF, ventricular tachycardia and fibrillation.

associated with increased in-hospital death; however, the effect of VT/VF on long-term mortality rates remains unclear.[1–7]

Recently, PCI has become a widely used therapeutic approach for the treatment of AMI patients.[8–10] As compared with fibrinolytic therapy, PCI has better clinical outcomes in terms of higher success rates of infarct vessel reperfusion and greater reduction of infarct area.[8] Clinically, these benefits likely result in a lower incidence of recurrent ischemia, re-infarction, and heart failure, and, consequently, an improved survival rate.[9,11,12] For these reasons, acute-phase VT/VF may have an altered prognostic significance after the implementation of PCI as a primary strategy for AMI. The purpose of the present study was to investigate the incidence, predictors, and prognostic effects of acute-phase VT/VF in ST-segment elevation myocardial infarction (STEMI) patients in the PCI era.

Methods

The OACIS Registry

The Osaka Acute Coronary Insufficiency Study (OACIS) is a prospective, multicenter, observational study in which 25 collaborating hospitals (1 university hospital, 24 regional core centers) in the Osaka region of Japan record demographic, procedural, and outcome data, and collect blood samples from patients with AMI (UMIN-CTR ID: UMIN000004575). The objectives of this registry are to collect uniform prospective data on AMI patients that can be used to assess clinical variables, therapeutic procedures, and clinical events, as well as to collect samples of genomic DNA that can be used to investigate whether common genetic traits are involved in the pathogenesis and prognosis of AMI. This study complied with the Declaration of Helsinki, and the study protocol was approved by the ethics committee of each participating hospital. A detailed description of the OACIS has been published.[13,14] Briefly, patients hospitalized within 1 week of AMI onset were prospectively registered and followed for 5 years. AMI was diagnosed if ≥2 of the following 3 criteria were met: (1) clinical history of central chest pressure, pain, or tightness lasting ≥30 min; (2) ST-segment elevation >0.1 mV in at least 1 standard or 2 precordial leads; and (3) a rise in serum creatine phosphokinase concentration to more than twice the normal laboratory value.

Study Patients

Among 10,074 consecutive patients registered in the OACIS between April 1998 and March 2011, patients with STEMI who were hospitalized within 12 h of symptom onset and underwent primary PCI were included in the present study. Patients who had cardiopulmonary arrest on arrival were excluded from the study. Acute-phase VT/VF was defined as ≥3 consecutive ventricular premature complexes and/or VF documented by ECG or cardiac monitoring during the first week of hospitalization. Underlying baseline risk of death was estimated using the risk score derived from the data of the Global Registry of Acute Coronary Events (GRACE).[15] All patients provided written informed consent to participate in this study.

Data Collection

Research cardiologists and specialized research nurses recorded patients' data during hospital stays. In-hospital data were transmitted to the data collection center for processing and analysis. Collaborating hospitals were encouraged to enroll consecutive AMI patients irrespective of their treatment or outcome. Additional data for patients were obtained 3 and 12 months after discharge for AMI and annually thereafter for up to 5 years. Information on subsequent clinical events was gathered when visiting outpatient clinics or by verbal or written contact with patients or family members. Causes of out-of-hospital deaths were classified by blinded review of the circumstances surrounding each death by the principal investigator at each site. Recurrent MI infarction was defined as recurrence of AMI regardless of the lesion derived from culprit site that was used in the previous study.[16] Stroke included ischemic cerebral infarction derived from each patient's chart or by questionnaire. Atrial tachyarrhythmia was defined as atrial fibrillation and/or atrial tachycardia recorded by ECG. Major bleeding was defined as intracranial hemorrhage, bleeding requiring

Table 1. Clinical Characteristics of Patients With STEMI on Admission

	VT/VF		P value	Tertiles of GRACE risk score			P value
	(–) n=3,286	(+) n=997		Low n=1,476	Intermediate n=1,403	High n=1,404	
Age, years	65±12	65±12	0.73	54±8	66±7	76±8	
Male, %	77.4	77.2	0.92	89.0	77.6	64.1	<0.0001
BMI, kg/m²	23.8±3.4	23.8±3.6	0.81	24.7±3.6	23.7±3.2	22.8±3.4	<0.0001
Clinical history							
Hypertension, %	57.4	58.8	0.45	51.9	57.6	64.7	<0.0001
Diabetes mellitus, %	35.0	28.7	0.0003	33.6	34.8	33.4	0.45
Dyslipidemia, %	46.8	42.8	0.034	55.3	44.2	36.9	<0.0001
Smoking, %	65.5	67.6	0.22	79.8	66.9	49.1	<0.0001
Myocardial infarction, %	11.4	11.7	0.79	4.4	9.7	20.7	<0.0001
Prior PCI, %	8.4	7.9	0.65	4.5	7.3	13.0	<0.0001
Prior CABG, %	1.2	1.6	0.40	0.2	0.8	2.7	<0.0001
Presenting characteristics							
Onset to admission <6 h, %	85.5	90.0	0.0002	88.3	85.7	85.3	0.031
Heart rate, beats/min	77±21	79±25	0.022	75±18	75±20	81±27	
Systolic BP, mmHg	138±32	127±32	<0.0001	145±30	136±30	124±33	
Killip class							
I, %	85.2	71.0	<0.0001	98.1	91.2	54.0	
II, %	8.4	10.5		1.0	5.1	21.8	
III, %	2.4	3.5		0.2	0.9	7.4	
IV, %	4.0	14.8		0.7	2.8	16.9	
Peak creatine kinase, IU/L	3,152±2,930	5,012±4,723	<0.0001	3,281±2,942	3,481±3,283	4,016±4,213	<0.0001
GFR, ml/min	66±25	64±38	0.12	76±23	65±22	59±22	
Blood glucose, mg/dl	182±81	192±91	0.0014	174±74	183±81	196±93	<0.0001
GRACE risk score	102±28	108±31	<0.0001	73±14	103±7	136±16	

BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; GRACE, Global Registry of Acute Coronary Events; GFR, glomerular filtration rate; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; VT/VF, ventricular tachycardia and fibrillation.

surgery, transfusion or ≥4 g/dl decrease in hemoglobin level.

Statistical Analysis

Continuous values are expressed as the mean±SD unless otherwise indicated. Categorical data are presented as absolute values and/or frequencies. Baseline characteristics of the groups were compared using a t-test or repeated measures analysis of variance to compare continuous variables, and chi-square or Fisher's exact tests were used for categorical variables. Multivariable logistic regression analysis with a stepwise method was performed to identify factors associated with acute-phase VT/VF, and Cox proportional hazard models were built to investigate the effect of acute-phase VT/VF and other cofactors on in-hospital and long-term mortality rates. The variables examined in these analyses were sex, age, body mass index ≥25 kg/m², diabetes mellitus, hypertension, dyslipidemia, previous MI, smoking, Killip class ≥II, time from AMI onset to presentation <6 h, peak creatine kinase level, infarct-related artery, postprocedural TIMI flow grade, stent usage, thrombectomy, collateral vessels, and multivessel disease, in addition to the following complications during hospitalization: re-MI, cerebral infarction, atrial tachyarrhythmia, and major bleeding.

Among patients who were discharged alive, the following variables were also incorporated into the models: antiplatelet, β-blocker, angiotensin-converting-enzyme inhibitor or angiotensin II-receptor blocker, statin, and class I or III antiarrhythmic drugs. Clinical correlates included in the multivariable analyses were selected using a stepwise method with entry and exit criteria set at P values of 0.05 and 0.10, respectively. All analyses were conducted using SPSS software for Windows (version 15.0; SPSS, Inc, Chicago, IL, USA).

Results

Clinical Characteristics

Among the 10,074 patients registered in the OACIS registry, 5,791 patients were excluded for 1 or more of the following reasons: hospital admission later than 12 h after the onset of AMI (n=3,974), non-STEMI (n=1,515), absence of emergency PCI (n=1,314), and cardiopulmonary arrest on arrival (n=189). Of the remaining 4,283 patients, 997 (23.3%) developed acute-phase VT/VF (Figure 1).

Baseline characteristics of patients stratified by the presence or absence of acute-phase VT/VF are presented in Table 1. Patients with acute-phase VT/VF had a shorter time from symptom onset to hospital arrival, less stable hemodynamics, and higher GRACE risk scores on admission. In addition, these patients had more severe myocardial ischemia on coronary angiography and a higher prevalence of culprit lesions of the left main artery, and were also more likely to be treated with coronary stent implantation, or intracoronary thrombectomy (Table 2). Clinical events and characteristics during hospitalization are listed in Table 3. Patients with acute-phase VT/VF had lower cardiac function and higher prescription rates of diuretics, β-blockers, and class III antiarrhythmic drugs.

Study patients were divided into 3 groups according to the tertiles of GRACE risk score: lowest tertile, ≤90 (low-risk

Table 2. Angiographic Findings of Patients With STEMI on Admission

	VT/VF		P value	Tertiles of GRACE risk score			P value
	(–) n=3,286	(+) n=997		Low n=1,476	Intermediate n=1,403	High n=1,404	
Infarct-related artery							
Left main, %	1.2	6.4	<0.0001	0.8	1.6	4.9	<0.0001
Left anterior descending, %	47.8	45.7	0.23	50.2	46.4	45.0	0.014
Left circumflex, %	10.5	7.0	0.0007	9.9	9.6	9.5	0.92
Right coronary, %	37.2	39.4	0.22	36.1	39.6	37.6	0.14
Multivessel disease, %	34.0	41.6	<0.0001	26.6	34.5	47.3	<0.0001
Preprocedural TIMI flow							
Grade 0, %	60.3	66.5	0.007	61.0	61.3	62.9	0.56
Grade I, %	10.2	9.5		10.0	11.0	9.3	
Grade II, %	17.5	14.5		16.8	16.1	17.5	
Grade III, %	12.0	9.6		12.2	11.6	10.4	
Postprocedural TIMI flow							
Grade 0, %	2.7	3.1	0.46	2.6	3.0	2.8	0.0007
Grade I, %	1.4	1.3		1.1	1.1	1.8	
Grade II, %	8.1	9.7		6.4	8.2	11.2	
Grade III, %	87.8	85.9		89.9	87.7	84.1	
Stent implantation, %	73.7	81.4	<0.0001	74.9	75.6	76.0	0.76
Intracoronary thrombectomy, %	39.0	52.1	<0.0001	41.9	41.8	42.3	0.95

Abbreviations as in Table 1.

Table 3. Clinical Events and Characteristics During Hospitalization of Patients With STEMI on Admission

	All patients		Low-risk group			Intermediate-risk group			High-risk group			P value*
	VT/VF			VT/VF			VT/VF			VT/VF		
	(–) n=3,286	(+) n=997	Total	(–) n=1,171	(+) n=305	Total	(–) n=1,124	(+) n=279	Total	(–) n=991	(+) n=413	
Event												
Acute-phase VT/VF, %			20.7			19.9			29.4			<0.0001
Hospital stay, days	26±23	28±30†	22±15	22±15	22±13	26±21	25±20	26±21	31±35	30±32	34±41	<0.0001
Discharge within 7days, %	1.9	1.1	1.9	2.0	1.3	1.6	1.7	1.4	1.5	1.8	0.7	0.70
All-cause death, %	4.3	14.6‡	1.4	0.6	4.3‡	3.8	2.5	9.3‡	15.2	10.7	25.9‡	<0.0001
Cardiovascular death, %	3.4	10.2‡	1.2	0.6	3.3‡	2.7	1.8	6.5‡	11.3	8.6	17.9‡	<0.0001
Non-cardiovascular death, %	0.9	3.8‡	0.2	0.0	1.0‡	1.1	0.7	2.4‡	3.5	2.2	6.9‡	<0.0001
Medical therapy atdischarge												
Diuretics, %	23.7	34.4‡	16.2	12.8	25.2‡	22.7	22.2	23.3	42.4	34.8	37.0	<0.0001
Antiplatelets, %	97.4	97.2	98.4	97.8	94.4‡	97.8	95.3	88.9‡	95.4	85.5	71.2‡	<0.0001
β-blockers, %	44.1	61.6‡	45.1	40.6	59.0‡	48.7	45.0	55.9‡	50.4	41.0	45.5	<0.0001
ACEI/ARB, %	76.0	74.4	78.8	77.6	78.4	76.1	75.3	68.8†	70.8	64.3	49.4‡	<0.0001
Statins, %	40.4	44.8†	47.7	46.0	52.1	40.9	39.2	42.3	33.6	29.4	25.4	<0.0001
Antiarrhythmic drugs												
Class I, %	4.8	5.9	3.5	3.0	4.6	5.4	5.1	4.7	6.6	6.0	5.6	0.0011
Class III, %	0.5	2.7‡	0.2	0.1	0.7	0.7	0.4	1.4	2.3	0.9	4.1‡	<0.0001

*Difference between the 3 risk groups. †P<0.05 and ‡P<0.005 for the difference between patients with and without VT/VF. ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II-receptor blocker; VT/VF, acute-phase ventricular tachycardia and fibrillation.

group); intermediate tertile, 91–114 (intermediate-risk group); and highest tertile, ≥115 (high-risk group). Patients with higher baseline risk of death were more likely to be female, and have a lower body mass index (Table 1). In addition, patients in the high-risk group were more likely to have previous history of MI and coronary procedures, and present with unstable hemodynamics, severe myocardial damage and impaired glucose tolerance. High-risk patients also had more severe myocardial ischemia on angiography, and poorer coronary procedural outcomes (Tables 2,S1). Further, more patients with higher baseline risk had acute-phase VT/VF and prescription of diuretics, β-blockers, and class I or III antiarrhythmic drugs (Table 3).

Factors Associated With Acute-Phase VT/VF

To identify potential determinants of acute-phase VT/VF, multivariate logistic analyses were performed (Table S2). Among all patients, factors associated with an increased risk of acute-

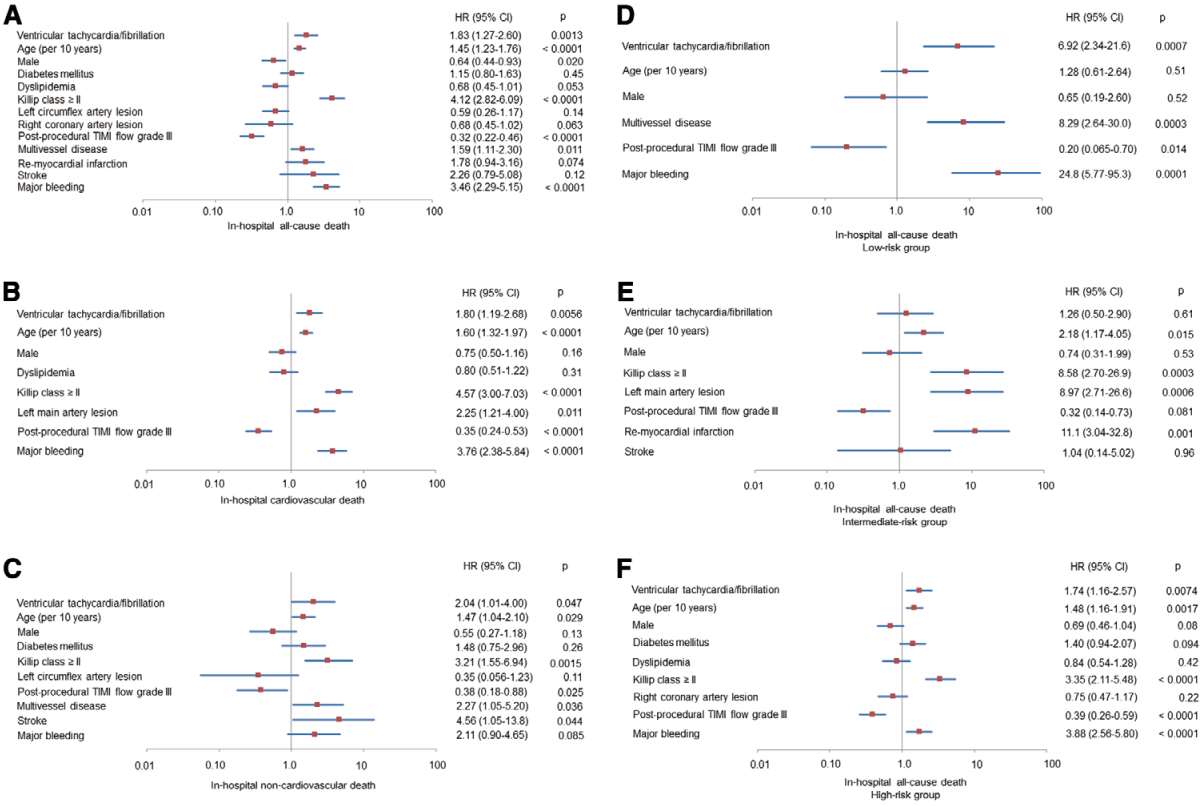

Figure 2. Forest plots of the independent determinants of in-hospital death. (**A**) In-hospital all-cause death, (**B**) in-hospital cardiovascular death, (**C**) in-hospital non-cardiovascular death, (**D**) in-hospital all-cause death in the low-risk group, (**E**) in-hospital all-cause death in the intermediate-risk group, and (**F**) in-hospital all-cause death in the high-risk group.

phase VT/VF were diabetes mellitus (adjusted odds ratio (OR) 0.65, 95% confidence interval (CI) 0.55–0.77, P<0.0001), Killip class ≥II (adjusted OR 1.98, 95% CI 1.62–2.40, P<0.0001), culprit lesion of the left main coronary artery (adjusted OR 3.16, 95% CI 1.96–5.15, P<0.0001), right coronary artery (adjusted OR 1.49, 95% CI 1.27–1.76, P<0.0001), and peak creatine kinase >3,000 IU/L (adjusted OR 2.14, 95% CI 1.82–2.51, P<0.0001).

In-Hospital Outcomes

Among all patients, the numbers of in-hospital deaths for all, cardiovascular, and non-cardiovascular causes were 287 (6.7%), 214 (5.0%), and 67 (1.6%), respectively (**Figure 1**). Cause of death could not be determined for 6 patients (0.1%). In-hospital mortality rates were significantly higher in patients with acute-phase VT/VF (14.6%) than in those without (4.3%, **Table 3**). Multivariate analysis revealed that patients with acute-phase VT/VF had 1.8-, 1.8-, and 2.0-fold higher incidences of in-hospital deaths from all, cardiovascular, and non-cardiovascular causes, respectively, compared with patients without acute-phase VT/VF (**Figures 2A–C**).

Furthermore, as compared with patients without VT/VF, the in-hospital mortality rate remained higher in patients with acute-phase VT/VF when patients were divided into groups according to baseline risk (**Table 3**). After adjustment for variables related to acute-phase VT/VF, the effect of acute-phase VT/VF on in-hospital all-cause death was most prominent in patients with low baseline risk and remained significant in those with high baseline risk, but became insignificant in the intermediate-risk group (**Figures 2D–F**). Diagnostic significance of VT/VF on in-hospital mortality stratified according to baseline risk is shown in **Table S3**.

5-Year Mortality Rate

Among the 3,996 STEMI patients who were discharged alive, 240 died during the 5-year follow-up period (73 cardiovascular deaths; 97 non-cardiovascular deaths; 70 deaths of unknown cause, **Figure 1**). Time-to-event curves for 5-year deaths among patients who were discharged alive are depicted in **Figure 3**. The incidence of 5-year all-cause death was significantly higher in patients with acute-phase VT/VF than in those without, but only for the high-risk group. After adjustment for other correlated factors, acute-phase VT/VF was found not to be an independent predictor of 5-year all-cause, cardiovascular, or non-cardiovascular death (**Figures 4A–C**) in the overall population and the intermediate- and low-risk groups (**Figures 4D,E**, respectively), but was related to increased all-cause 5-year mortality in the high-risk group (**Figure 4F**). Diagnostic significance of VT/VF on 5-year mortality stratified according to baseline risk is shown in **Table S3**.

Discussion

Among 4,283 STEMI patients who were hospitalized within

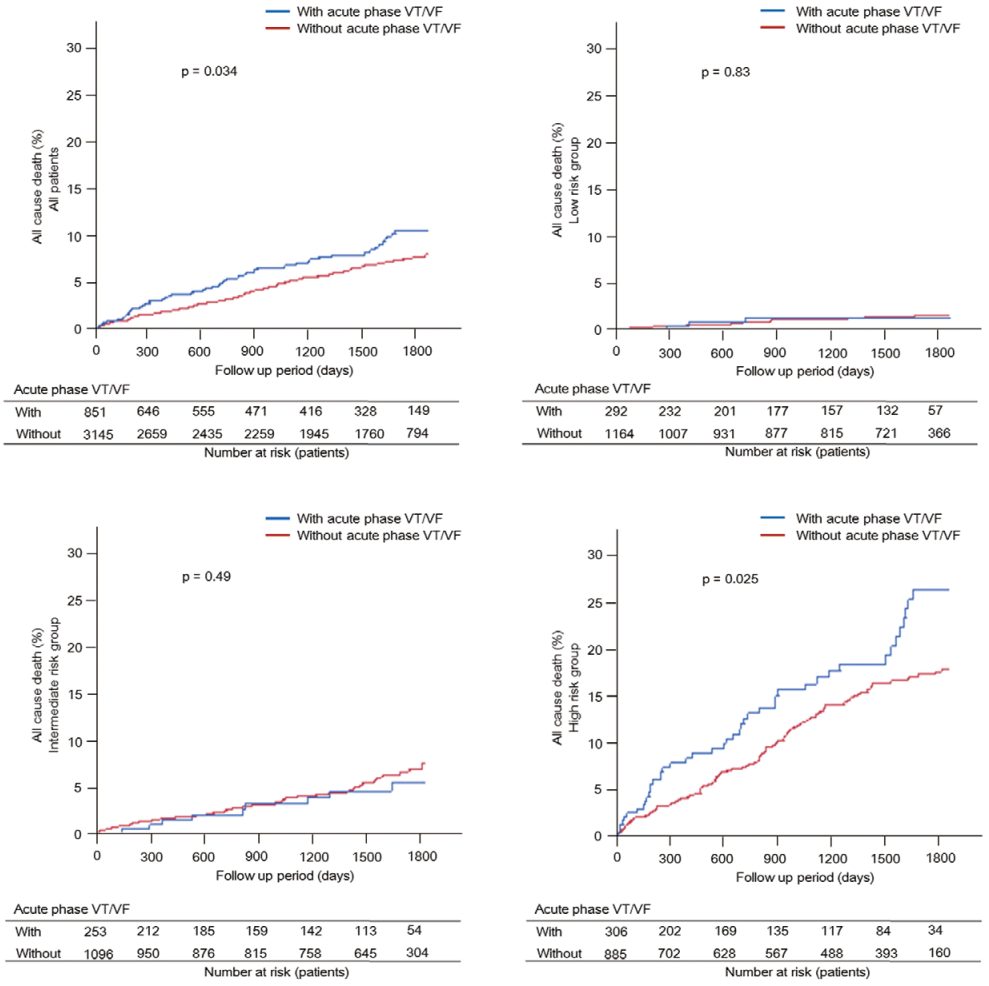

Figure 3. Kaplan-Meier cumulative event rates for 5-year all-cause mortality rates among patients stratified according to baseline risk. Mortality rates in patients with and without acute-phase ventricular tachycardia and fibrillation (VT/VF) were compared.

12 h of symptom onset and underwent primary PCI, the incidence of acute-phase VT/VF was 23.3%. Notably, although acute-phase VT/VF was associated with an increased risk of in-hospital death, it was only associated with increased 5-year mortality rate after hospital discharge among patients with high baseline risk. Because this was an observational study in which participating physicians were encouraged to register all consecutive patients, the study population comprised a broad spectrum of AMI patients, including those who would have been excluded in previously reported randomized controlled trials. Thus, the present study population is considered to closely reflect the real-world, clinical practice setting of post-AMI patients.

Various Definitions of Acute-Phase VT/VF

As our definition of acute-phase VT/VF included non-sustained VT/VF, the 23% incidence rate of acute-phase VT/VF in the present study population was markedly higher than that reported in other PCI-era studies, including the APEX-AMI (5.7%)[17] and HORIZONS-AMI trials (5.2%),[18] in which acute-phase VT/VF was defined as VT/VF that was sustained for >30s. In general, ventricular tachyarrhythmias of various duration and timing can occur during the acute-phase of AMI and would therefore have different hemodynamic influences, underlying mechanisms, and consequently, different prognostic effects. For example, patients with sustained acute-phase VT are reported to have higher in-hospital cardiac mortality rates, but had similar 1-year rates after discharge than those with non-sustained VT.[2] In addition, the 90-day mortality rate was higher if acute-phase VT/VF occurred after PCI than before PCI.[17] Thus, acute-phase VT/VF, as defined in the present study, may have had low prognostic significance.

Factors Associated With the Occurrence of Acute-Phase VT/VF

The main factors associated with acute-phase VT/VF in the present study population were Killip class ≥II, culprit lesion in the left main artery, and peak creatine kinase >3,000 IU/L, indicating that acute-phase VT/VF was associated with large infarct and severe heart failure. These factors were previously identified as potential determinants of acute-phase VT/VF.[18,19] In addition to these factors, lesions in the right coronary artery were also associated with acute-phase VT/VF, as was found in the APEX-AMI study.[17] Notably, diabetes mellitus was associated

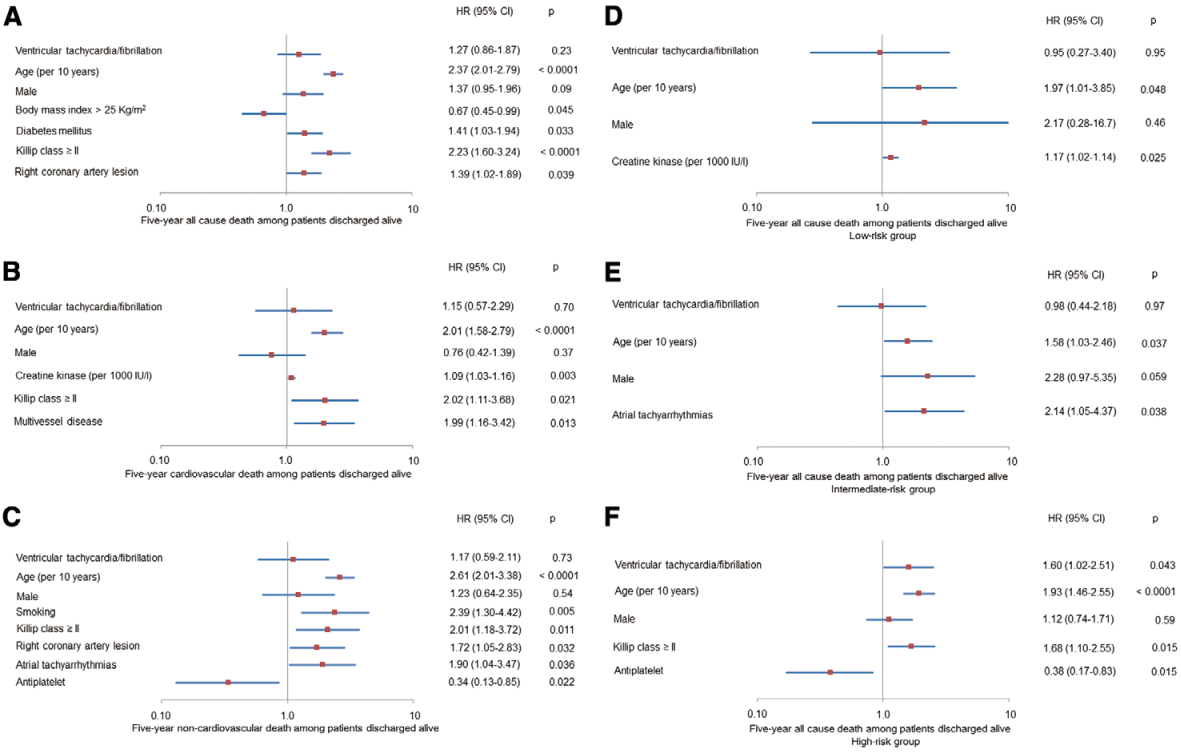

Figure 4. Forest plots displaying independent determinants of 5-year mortality rates: (**A**) all-cause death, (**B**) cardiovascular death, (**C**) non-cardiovascular death, (**D**) all-cause death among patients discharged alive in the low-risk group, (**E**) all-cause death among patients discharged alive in the intermediate-risk group, and (**F**) all-cause death among patients discharged alive in the high-risk group. CI, confidence interval; HR, hazard ratio.

with a decreased incidence of acute-phase VT/VF, which was also observed in previous studies.[18,19] A possible explanation is that sulfonylurea medications play an antiarrhythmic role through inhibition of cardiac adenosine triphosphate-sensitive potassium (K-ATP) channels, although the number of patients taking this type of drug is unknown in the current study.

In-Hospital Prognostic Significance of Acute-Phase VT/VF

There are several possible explanations for why STEMI patients with acute-phase VT/VF had worse outcomes than those without, even in the PCI era. Failure to control various causes of acute-phase VT/VF, such as myocardial ischemia and heart failure, could lead to life-threatening consequences. It is also possible that pulseless VT and VF could have resulted in death without spontaneous conversion or efficacious therapeutic intervention, such as electrocardioversion.

Multivariate analyses revealed that acute-phase VT/VF was also associated with an increased risk of in-hospital death from non-cardiovascular causes. The coexistence of acute-phase VT/VF with severe cardiac diseases and the consequent intensive care required for the treatment of these conditions may have led to life-threatening complications, such as infection, bleeding, and renal failure. However, it is also possible that acute-phase VT/VF developed as a complication of severe non-cardiovascular conditions.

The association between acute-phase VT/VF and in-hospital death was significant in patients with high baseline risk, but not in those with intermediate baseline risk. This discordance might be explained by the relatively preserved cardiac function and general conditions in the intermediate-risk group compared with the high-risk group, because the intermediate group would, therefore, be expected to have a lower incidence of life-threatening complications following VT/VF.

The incidence of acute-phase VT/VF was the lowest among patients with low baseline risk; however, the effect of acute-phase VT/VF on in-hospital death was the highest among these patients (Figures 2D–F). This split finding may imply that more in-hospital deaths were caused by VT/VF related to acute myocardial ischemia, transient electrolytes and autonomic imbalance in the low-risk group than in the intermediate- and high-risk groups, whereas the number of life-threatening events from cardiovascular causes other than VT/VF or non-cardiovascular origins was relatively low in the low-risk group, thereby increasing the relative prognostic effect of acute-phase VT/VF. Consistent with this speculation, the prevalence of non-cardiovascular death among all-cause deaths was lower in the low-risk group (15.0%) than in the intermediate- and high-risk groups (27.7% and 25.2%, respectively).

Long-Term Prognostic Significance of Acute-Phase VT/VF

Acute-phase VT/VF is considered to occur mainly because of electrical instability resulting from damage, such as progressive myocardial damage from a deficiency in the blood supply and reperfusion injury, caused by acute myocardial ischemia. In addition, the extent of myocardial ischemia, cardiac function, and non-cardiac general condition influences the devel-

opment of acute-phase VT/VF. In the present study population, the patients in the high-risk group were more likely to have a larger myocardial infarct (higher peak creatinine kinase and higher frequency of left main artery disease), poorer cardiac function (more severe Killip class and decreased left ventricular ejection fraction), and poorer non-cardiac-related general condition (higher age, poorer renal function, higher frequency of concomitant hypertension, and higher blood glucose on admission). Therefore, it is conceivable that the occurrence of acute-phase VT/VF is representative of these life-threatening cardiac and non-cardiac general conditions, and thus was predictive of a poor long-term prognosis in the high-risk group. In contrast, patients in the low- and intermediate-risk groups had a relatively small infarct, preserved cardiac function, and favorable non-cardiac general condition. Therefore, it is likely that acute-phase VT/VF is predominantly induced by acute myocardial ischemia, transient electrolytes and autonomic nerve imbalance; and that the prognostic effect of acute-phase VT/VF would disappear in the chronic phase of AMI after hospital discharge. For this reason, it is reasonable to consider that acute-phase VT/VF in low- and intermediate-risk patients is not necessarily indicative of poor long-term prognosis.

In the pre-PCI era, Eldar et al showed that 1-year mortality rates were similar between patients with and without primary VT/VF, which was defined as ≥3 ventricular complexes occurring within 48 h of AMI onset and without hemodynamic compromise (Killip class I).[2] This definition of VT/VF was very similar to that used in the present study, and the conclusion from their study was consistent with our present findings. Thus, we may conclude that the prognostic effect of acute-phase VT/VF including ≥3 ventricular complexes on long-term mortality rates remain limited after the introduction of PCI as a primary strategy for treating AMI patients.

Most other studies conducted in the pre-PCI era have compared long-term prognoses between patients with and without sustained VT/VF during the acute phase of AMI.[1–4] In those studies, both poorer[1] and similar outcomes[2–4] in patients with sustained VT/VF were reported. In the PCI era, only 2 major studies have evaluated the effect of sustained VT/VF during the acute phase of AMI on mid- to long-term outcomes. In the APEX-AMI trial,[17,20] sustained VT/VF in the acute phase was associated with an increased 90-day mortality rate (23.2% vs. 3.6%; adjusted hazard ratio (HR) 3.63, 95% CI 2.59–5.09, P<0.001). Notably, 84.5% of deaths occurred within the first 30 days, suggesting that the 90-day mortality rate is a comparable outcome measure to the in-hospital mortality rate in the present study. In the HORIZONS-AMI trial,[18] no significant differences in the 3-year mortality rate were detected between patients with and without acute-phase VT/VF (4.6% vs. 6.7%; adjusted HR 0.73; 95% CI 0.30–1.79, P=0.27). Despite the use of differing definition of acute-phase VT/VF, the in-hospital and long-term prognostic effects of acute-phase VT/VF in the APEX-AMI and HORISONS-AMI trials were similar to those found in the present study. In addition, even though less severe VT/VF (including ≥3 consecutive ventricular complexes) patients were included in the present study population, patients with acute-phase VT/VF in the high baseline risk group demonstrated poorer long-term outcomes than those without acute-phase VT/VF, suggesting that the prognostic effect of acute-phase VT/VF depends on the severity of the patient's general condition, rather than the duration of VT/VF.

Clinical Perspectives

Even in the PCI era, acute-phase VT/VF complicating STEMI is associated with worse in-hospital outcomes. Therefore, careful observation and treatment of STEMI patients is needed if VT/VF occurs during hospitalization.

An important finding of this study was that the prognostic significance of acute-phase VT/VF on long-term survival after discharge was limited to STEMI patients who had high baseline risk. However, following hospital discharge, therapeutic strategies, including the use of implantable cardioverter-defibrillators, need to be cautiously determined, even in high-risk patients. The randomized controlled trials DINAMIT and IRIS showed that implanted cardioverter-defibrillators used early after MI did not improve all-cause mortality rates.[21,22] Furthermore, secondary analysis of the DINAMIT trial revealed that factors associated with ventricular arrhythmias also correlated with a high risk of non-sudden death, thereby potentially negating the benefits of a implantable cardioverter-defibrillator.[23] In addition, recent guidelines do not definitely state the indication of implanted cardioverter defibrillator for the secondary prevention of VT/VF developed during the acute phase of MI.[24] These observations suggest that less invasive and removable prophylactics, such as wearable cardioverter-defibrillator, are needed to improve outcomes in patients with VT/VF following AMI.[25]

Study Limitations

This study has several limitations that warrant mention. First, acute-phase VT/VF events, as defined in the present study, were relatively conclusive and may have limited prognostic significance. Second, we did not collect data on late ventricular arrhythmias that occurred beyond 7 days of AMI onset. It is possible that clinical significance differs between acute and late ventricular arrhythmias, and further investigations are needed to examine the influence of these arrhythmias on outcomes. Third, left ventricular ejection fraction assessed by echocardiography or left ventriculography during hospitalization, which is known as one of most important prognostic factors in AMI patients, was not included in the multivariate analyses because of missing data in a substantial number of patients. Finally, not all data related to specific treatments for arrhythmia, such as intravenous and oral antiarrhythmic drug usage during hospitalization and implantation of cardioverter-defibrillators, were available, despite the possibility that these treatments may have influenced the occurrence of acute-phase VT/VF and death.

Conclusions

Even in the PCI era, episodes of acute-phase VT/VF in STEMI patients were associated with higher in-hospital mortality rates in the present study. However, the prognostic significance of acute-phase VT/VF on long-term survival after discharge was limited to high-risk patients. Therefore, appropriate treatment strategies for discharged STEMI patients with VT/VF events may need to be determined on the basis of individual risk.

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Supplementary Files

Supplementary File 1

Table S1. Other clinical characteristics of patients with STEMI on admission

Table S2. Determinants of acute-phase VT/VF in patients with STEMI on admission

Table S3. Diagnostic significance of VT/VF among STEMI patients stratified according to baseline risk

Please find supplementary file(s);
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