

[ ORIGINAL ARTICLE ]

## The Mid-term Mortality and Mode of Death in Survivors with ST-elevation Myocardial Infarction

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### Abstract:

**Objective** The popularity of primary percutaneous coronary intervention (p-PCI) for ST-elevation myocardial infarction (STEMI) has increased over the past decades. Despite improvements in in-hospital mortality rates, it is clinically important to investigate the prognoses after discharge. However, data on the mode of death and prognostic factors are limited. We analyzed these factors in a Japanese cohort in the modern p-PCI era.

**Methods** Between January 2004 and December 2017, a total of 1,222 patients who underwent p-PCI within 24 hours from the onset of STEMI and were alive at discharge (mean age, 67.7 years old; men, 75.5%), were evaluated. The two-year mortality was analyzed using a Cox regression model, and the mode of death was evaluated.

**Results** The rate of mortality at 2 years was 5.7%. Non-cardiac death was more frequent than cardiac death (62.6% vs. 37.4%). A Cox multivariate analysis identified the following as independent predictors of the 2-year mortality: hemoglobin (log-transformed) [adjusted hazard ratio (HR), 0.048; 95% confidence interval (CI), 0.008-0.29;  $p < 0.001$ ], age above 80 years old (adjusted HR, 2.26; 95% CI, 1.30-3.91;  $p = 0.004$ ), Killip class  $\geq$  II (adjusted HR, 1.99; 95% CI, 1.17-3.39;  $p = 0.011$ ), brain natriuretic peptide level (log-transformed) (adjusted HR, 1.47; 95% CI, 1.09-2.01;  $p = 0.013$ ), and body mass index (log-transformed) (adjusted HR, 0.16; 95% CI, 0.030-0.84;  $p = 0.030$ ).

**Conclusion** This study demonstrated that the 2-year mortality was 5.7% in STEMI survivors after p-PCI. Non-cardiac death was more frequent than cardiac death. Compared to well-known clinical variables, angiographic findings did not have a significant influence on the mid-term mortality.

**Key words:** ST elevation myocardial infarction, survivors, mid-term mortality, predictors, cause of death

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### Introduction

ST-elevation myocardial infarction (STEMI) remains one of the leading causes of mortality worldwide (1). In recent decades however, the in-hospital mortality after STEMI has dramatically decreased because of the establishment of coro-

nary care units, improvements in medical therapy, and widespread use of early reperfusion therapy by primary percutaneous coronary intervention (p-PCI) (2, 3).

As the majority of patients with STEMI survive until discharge from the hospital in current clinical practice (4), it is important to investigate the cause of death and its correlation with the prognostic factors in these patients. Although

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several studies have reported the cause of death after PCI in patients with acute coronary syndrome (ACS) and stable angina (5-7), as well as significant prognostic factors after acute myocardial infarction (AMI) (8-10), these studies pre-date the p-PCI era and/or assessed the short-term outcome. No descriptive study on the mode of death or prognostic factors, including detailed angiography findings, during the mid-term has yet been conducted in survivors with STEMI after PCI.

The present study therefore assessed the details concerning the mode of death and evaluated the variables associated with the mid-term mortality in STEMI survivors after p-PCI from a single-center database.

## Materials and Methods

### Ethical statements

Written informed consent was obtained from each patient or their family before or after PCI. This study was approved by the medical ethics committees of our hospital and was conducted in accordance with the Declaration of Helsinki.

### Study design and population

Data of STEMI survivors who underwent PCI between January 2004 and December 2017 were retrieved from the Ogaki Municipal Hospital database. Patients were excluded if the onset-to-door time of STEMI was >24 hours, the time of the onset of STEMI was not clear, there were culprit lesions but PCI was not performed, coronary artery bypass grafting (CABG) was performed instead of PCI, the culprit lesions were within the bypass grafts, or they died during STEMI hospitalization. Furthermore, for patients with multiple occurrences of STEMI during the study period, follow-up data were used for the first STEMI event.

### Study endpoint

The two-year mortality and details of the cause of death were investigated. To analyze the differences in the cause of death according to the age, we divided the study population into 4 groups: <59 years old, 60-69 years old, 70-79 years old, and ≥80 years old. Furthermore, we analyzed the cause of death according to the time when the PCI was performed: first half (2004-2010) and second half (2011-2017) of the study period.

### Definitions and data collection

STEMI was diagnosed as previously reported (11). Hypertension was defined as current or previous treatment with antihypertensive medication. Diabetes mellitus was defined as current or previous treatment with antidiabetic medication (insulin or oral hypoglycemic drugs) or a hemoglobin A1c level ≥6.5%, in accordance with the National Glycohemoglobin Standardization Program (12). Dyslipidemia was defined as current or previous treatment with anti-dyslipidemic medication or a low-density lipoprotein cholesterol level of

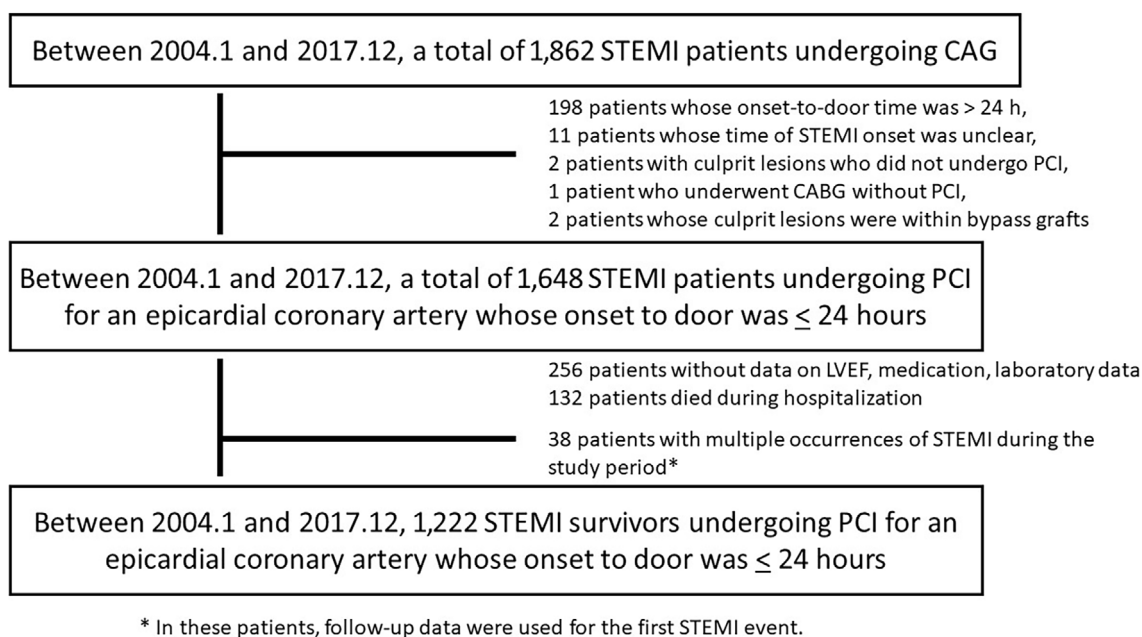
≥140 mg/dL, a high-density lipoprotein cholesterol level of <40 mg/dL, or a triglyceride level of ≥150 mg/dL, according to the Japan Atherosclerosis Society guidelines (13). Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m<sup>2</sup>. We calculated the eGFR according to the Japanese equation as follows:  $eGFR \text{ (mL/min/1.73 m}^2\text{)} = 194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287}$  ( $\times 0.739$  if a woman) (14). The left ventricular ejection fraction (LVEF) was measured by the Teichholz method between two weeks and two months after STEMI. If the patients had local asynergy, the LVEF was evaluated by Simpson's biplane method using two-dimensional apical, two-chamber, and four-chamber views. Coronary angiography findings were obtained from the STEMI database of Ogaki Municipal Hospital, chart review, and GOODNET<sup>®</sup> system (GOODMAN, Nagoya, Japan). The assessment of angiographic data was performed by at least two investigators in our institute, as previously mentioned (15, 16). Atrial fibrillation (AF) was defined as follows: (a) patients who had AF irrespective of the duration of arrhythmia at admission or (b) patients who developed AF during hospitalization. We collected clinical data at admission, the details of medication therapy, and laboratory data at discharge. Data after discharge were collected during a follow-up hospital visit or by telephonic contact.

The patient survival and time from p-PCI until death were ascertained. Causes of death were divided into two groups as follows: 1) cardiac for myocardial infarction, sudden cardiac death, congestive heart failure/structural heart disease, fatal arrhythmia, and obvious non-cardiac causes that could not be identified (17); and 2) non-cardiac for vascular (intracranial bleeding and ischemic stroke), cancer (solid organ, hematologic), infectious, and chronic diseases (neurological, pulmonary, renal failure, liver/multiorgan failure, and senile decay) (5).

### Statistical analyses

Continuous variables were expressed as means±standard deviations or median and interquartile range (IQR; 25-75%), while categorical covariates were expressed as numbers and percentages. Student's *t*-test was used for the analysis of continuous variables with a normal distribution, and the Mann-Whitney U test was used for the analysis of variables that were not normally distributed. Comparisons of categorical covariates were performed using the chi-square test. The event-free survival (Kaplan-Meier curves) was analyzed using the log-rank test.

The chi-square test was also used to assess the cause and distribution of death. A backward stepwise Cox regression analysis was performed to determine the independent predictors of all-cause mortality up to 2 years after STEMI-PCI, using the predictors associated with all-cause mortality ( $p < 0.05$ ) in a univariate analysis. Logarithmic transformation was performed for non-normally distributed variables for the Cox analysis. In the table, the variables were reverted from the logarithmic transformation.



**Figure 1. Study population. STEMI: ST-elevation myocardial infarction, CAG: coronary angiography, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, LVEF: left ventricular ejection fraction**

The results were reported as adjusted hazard ratios (HRs) with associated 95% confidence intervals (CIs). The SPSS software program, version 23 (SPSS, Chicago, USA) was used for all statistical analyses. All p-values were two-tailed, and results with  $p < 0.05$  were considered to be statistically significant for all analyses.

## Results

### Patients' characteristics

During the study period, a total of 1,222 STEMI survivors were identified for this study (Fig. 1). The baseline clinical and angiographic characteristics are shown in Table 1. The cohort had a mean age of  $67.7 \pm 12.1$  years, and 75.5% were men. A Killip class  $\geq$  II at admission was found in 21.9% of the patients. Diabetes mellitus and CKD were seen in 34.6% and 36.5% of the patients, respectively. Compared to the group without mortality, the mortality group was characterized by an older age, lower body mass index (BMI), and higher Killip class. Furthermore, patients in this group had a higher incidence of prior ischemic stroke, CKD, and AF.

### Lesion/Procedural characteristics

The most common culprit vessel was the left anterior descending artery in 47.8% of the patients followed by right coronary artery (41.2%), left circumflex artery (9.6%), and left main trunk (1.4%). Initial thrombolysis in myocardial infarction (TIMI) grade 0/1 was seen in 63.8% of the patients, and 78.6% of the patients had a final TIMI grade 3 after PCI. According to collateral channel, Rentrop grade 3

was seen in 7.4% of the patients. Intra-aortic balloon pumping (IABP) and the use of percutaneous cardiopulmonary support were seen in 27.7% and 1.7% of the patients, respectively. There were no significant differences in the location of the culprit lesion or initial TIMI grade between the two groups. However, a final TIMI grade of 0/1 was more frequently seen, IABP usage was more common, and the onset to balloon time was longer in patients in the mortality group than in those in the no mortality group.

### Findings at discharge

As shown in Table 2, compared to patients in the no mortality group, those in the mortality group were characterized by lower LVEF, lower hemoglobin, and higher brain natriuretic peptide (BNP) levels at discharge. Furthermore, these patients were less frequently treated with aspirin and thienopyridine and more frequently treated with diuretics.

### The mid-term prognosis, mode of death, and predictors of mortality

Data for the 1- and 2-year follow-up were available for 98.3% and 90.1% of patients, respectively. During the follow-up period, the rate of mortality at 1 and 2 years was 3.3% and 5.7%, respectively (Fig. 2). The proportions of the causes of death are shown in Fig. 3. Non-cardiac death, including cancer and infection, was more frequent than cardiac death (62.6% vs. 37.4%). The cohort was divided into four age categories to analyze the proportion, cause, and distribution of death according to age (Fig. 4A, B). With increasing age, the proportion of death increased significantly (Log-rank  $p < 0.001$ ), and the cause and distribution of death was significantly different among different age groups ( $p =$

**Table 1. Baseline Patient, Lesion, and Procedural Characteristics.**

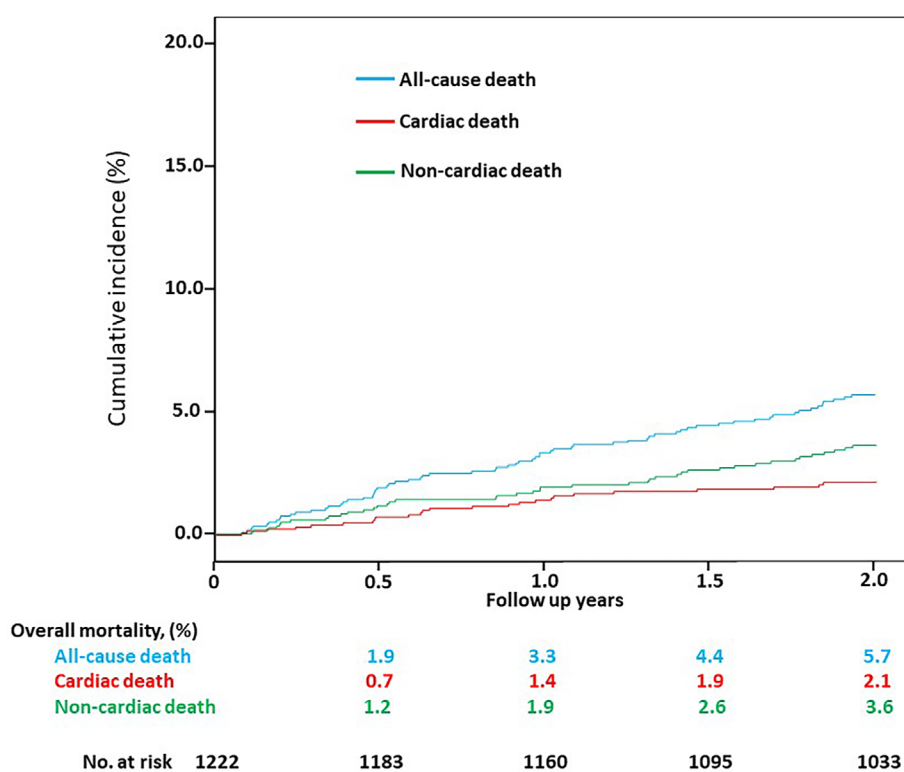
	Overall n=1,222	Without mortality n=1,155	With mortality n=67	p value
<b>-Patient clinical characteristics</b>				
Age, years	67.7±12.1	67.1±12.1	77.8±8.5	<0.001
Age ≥80 years, n (%)	227 (18.6)	192 (16.6)	35 (52.2)	<0.001
Male, n (%)	922 (75.5)	880 (76.2)	42 (62.7)	0.012
BMI, kg/m <sup>2</sup>	23.6 (21.4-25.9)	23.7 (21.5-26.0)	22.0 (18.6-24.2)	<0.001
BMI <18.5 kg/m <sup>2</sup> , n (%)	70 (5.8)	54 (4.7)	16 (24.2)	<0.001
Prior MI, n (%)	117 (9.6)	106 (9.2)	11 (16.4)	0.050
Prior CABG, n (%)	10 (0.8)	9 (0.8)	1 (1.5)	0.79
Prior ischemic stroke, n (%)	88 (7.2)	78 (6.8)	10 (14.9)	0.012
Prior intracranial bleeding, n (%)	18 (1.5)	17 (1.5)	1 (1.6)	0.96
Dyslipidemia, n (%)	888 (72.7)	845 (73.2)	43 (64.2)	0.11
Diabetes mellitus, n (%)	423 (34.6)	399 (34.5)	24 (35.8)	0.83
Hypertension, n (%)	1,036 (84.8)	975 (84.4)	61 (91.0)	0.14
Current smoking, n (%)	598 (48.9)	578 (50.4)	20 (29.9)	0.001
CKD, n (%)	446 (36.5)	404 (35.0)	42 (62.7)	<0.001
Atrial fibrillation, n (%)	165 (13.5)	146 (12.6)	19 (28.4)	<0.001
PAD, n (%)	49 (4.0)	46 (4.0)	3 (4.5)	0.84
<b>-Findings at presentation</b>				
<b>Killip class, n (%)</b>				
I, n (%)	955 (78.2)	922 (79.8)	33 (49.3)	<0.001
II, n (%)	156 (12.8)	138 (11.9)	18 (26.9)	
III, n (%)	51 (4.2)	47 (4.1)	4 (6.0)	
IV, n (%)	60 (4.9)	48 (4.2)	12 (17.9)	
≥II, n (%)	267 (21.8)	233 (20.2)	34 (50.7)	<0.001
<b>-Lesion characteristics</b>				
<b>Culprit vessel</b>				
LMT, n (%)	17 (1.4)	15 (1.3)	2 (3.0)	0.25
LAD, n (%)	584 (47.8)	557 (48.2)	27 (40.3)	0.21
LCx, n (%)	117 (9.6)	111 (9.6)	6 (9.0)	0.86
RCA, n (%)	504 (41.2)	472 (40.9)	32 (47.8)	0.27
<b>-Angiographical/Procedure data</b>				
<b>Initial TIMI grade, n (%)</b>				
0, n (%)	642 (52.5)	613 (53.1)	29 (43.3)	0.38
1, n (%)	138 (11.3)	130 (11.3)	8 (11.9)	
2, n (%)	334 (27.3)	310 (26.8)	24 (35.8)	
3, n (%)	108 (8.8)	102 (8.8)	6 (9.0)	
0/1, n (%)	780 (63.8)	743 (64.3)	37 (55.2)	0.13
<b>Final TIMI grade, n (%)</b>				
0, n (%)	4 (0.3)	3 (0.3)	1 (1.5)	0.034
1, n (%)	16 (1.3)	13 (1.3)	3 (4.5)	
2, n (%)	241 (19.7)	227 (19.7)	14 (20.9)	
3, n (%)	961 (78.6)	912 (79.0)	49 (73.1)	
0/1/2, n (%)	261 (21.4)	243 (21.0)	18 (26.9)	0.26
<b>Rentrop grade, n (%)</b>				
0, n (%)	658 (53.8)	623 (53.9)	35 (52.2)	0.072
1, n (%)	289 (23.6)	269 (23.3)	20 (29.9)	
2, n (%)	184 (15.1)	180 (15.6)	4 (6.0)	
3, n (%)	91 (7.4)	83 (7.2)	8 (11.9)	
3, n (%)	91 (7.4)	83 (7.2)	8 (11.9)	0.15
<b>Baseline angiography</b>				
3-vessel disease, n (%)	147 (12.0)	135 (11.7)	12 (17.9)	0.13
<b>PCI strategy</b>				
POBA, n (%)	113 (9.2)	106 (9.2)	7 (10.4)	0.24
BMS, n (%)	651 (53.3)	622 (53.9)	29 (43.3)	
DES, n (%)	458 (37.5)	427 (37.0)	31 (46.3)	
<b>Mechanical support</b>				
IABP use, n (%)	339 (27.7)	311 (26.9)	28 (41.8)	0.008
PCPS use, n (%)	21 (1.7)	18 (1.6)	3 (4.5)	0.074
<b>-Time to reperfusion</b>				
Onset to balloon time, h	3.6 (2.4-6.6)	3.5 (2.4-6.5)	4.4 (2.8-10.8)	0.039

Values are numbers (%) or mean±SD. Values are also presented as median (Q1-Q3). BMI: body mass index, MI: myocardial infarction, CABG: coronary artery bypass grafting, CKD: chronic kidney disease, PAD: peripheral artery disease, LMT: left main trunk, LAD: left anterior descending artery, LCx: left circumflex artery, RCA: right coronary artery, TIMI: thrombolysis in myocardial infarction, POBA: plain old balloon angioplasty, BMS: bare metal stent, DES: drug eluting stent, IABP: Intra-aortic balloon pumping, PCPS: percutaneous cardiopulmonary support

**Table 2. Laboratory Data, Echocardiographic Findings and Medications at Discharge.**

	Overall n=1,222	Without mortality n=1,155	With mortality n=67	p value
<b>-Findings at discharge</b>				
peak CK, IU/L	2,086.5 (998.8-3,715.5)	2,104.0 (1,012.0-3,739.0)	1,793.0 (853.0-3,075.0)	0.12
LVEF, %	57.0 (49.0-64.3)	58.0 (49.0-65.0)	50.0 (40.0-61.0)	<0.001
LVEF <40%, n (%)	95 (7.8)	80 (6.9)	15 (22.4)	<0.001
Hemoglobin, g/dL	12.5 (11.1-13.7)	12.6 (11.3-13.8)	10.7 (9.4-11.8)	<0.001
BNP, pg/mL	115.2 (54.5-253.4)	109.7 (52.2-236.4)	267.5 (161.1-496.9)	<0.001
<b>-Medication at discharge</b>				
Aspirin use, n (%)	1,183 (96.8)	1,122 (97.1)	61 (91.0)	0.006
Thienopyridine use, n (%)	1,146 (93.8)	1,090 (94.4)	56 (83.6)	<0.001
Warfarin use, n (%)	73 (6.0)	66 (5.7)	7 (10.4)	0.11
DOAC use, n (%)	42 (3.4)	38 (3.3)	4 (6.0)	0.24
Statin use, n (%)	1,185 (97.0)	1,122 (97.1)	63 (94.0)	0.15
ACE-I use, n (%)	780 (63.8)	743 (64.3)	37 (55.2)	0.13
ARB use, n (%)	227 (18.6)	220 (19.6)	7 (10.6)	0.070
CCB use, n (%)	213 (17.4)	206 (17.8)	7 (10.4)	0.12
$\beta$ -blocker use, n (%)	900 (73.6)	857 (74.2)	43 (64.2)	0.070
Diuretic use, n (%)	305 (25.0)	272 (23.6)	33 (49.3)	<0.001
OHA use, n (%)	289 (23.6)	273 (23.7)	16 (23.9)	0.97
Insulin use, n (%)	40 (3.3)	37 (3.2)	3 (4.5)	0.57
PPI use, n (%)	1,112 (91.0)	1,052 (91.2)	60 (89.6)	0.65

Values are numbers (%) or median (Q1-Q3). CK: creatine kinase, LVEF: left ventricular ejection fraction, BNP: brain natriuretic peptide, DOAC: direct oral anticoagulants, ACE-I: angiotensin-converting enzyme inhibitor, ARB: angiotensin II receptor blocker, CCB: calcium channel blocker, OHA: oral hypoglycemic agent, PPI: proton pump inhibitor

**Figure 2. Results of a Kaplan-Meier analysis of the cumulative mortality over two years.**

0.042).

A Cox multivariate regression analysis identified the following as independent predictors of all-cause mortality at 2

years: hemoglobin (log-transformed) [adjusted hazard ratio (HR), 0.048; 95% confidence interval (CI), 0.008-0.29; p<0.001], age above 80 years old (adjusted HR, 2.26; 95% CI,

1.30-3.91;  $p=0.004$ ), Killip class  $\geq$ II (adjusted HR, 1.99; 95% CI, 1.17-3.39;  $p=0.011$ ), BNP level (log-transformed) (adjusted HR, 1.47; 95% CI, 1.09-2.01;  $p=0.013$ ), and BMI (log-transformed) (adjusted HR, 0.16; 95% CI, 0.030-0.84;  $p=0.030$ ) (Table 3).

### The mid-term prognosis, cause of death, and PCI strategy and medication according to the period when PCI was performed

As shown in Table 4, there was a significant change in the PCI strategy over the years. Furthermore, thienopyridine, direct oral anticoagulants, statin, angiotensin-converting enzyme inhibitor, and proton pump inhibitor were more frequently used in the second half than in the first half. There was no significant difference in the proportion of death between the first and second halves (Fig. 5A). Despite no statistical significance, the percentage of non-cardiac death seemed to increase in the second half compared to the first half. Among the causes of non-cardiac death, the distribu-

tion did not change significantly between the PCI periods (Fig. 5B).

## Discussion

Three important findings were obtained in this study. First, the rate of all-cause mortality at 2 years was 5.7% in STEMI patients who had been treated with p-PCI and were alive at discharge. Second, non-cardiac death was more frequent than cardiac death, and the distribution of cause of death significantly differed according to the age. Third, a lower hemoglobin level, age over 80 years old, higher Killip class, higher BNP level, and lower BMI were associated with an increased risk of mid-term mortality. However, angiography findings, such as the location of the culprit lesion, initial/final TIMI grade, and Rentrop grade, did not have a significant influence on the mid-term mortality.

Data concerning the accurate assessment of STEMI survivors who have undergone p-PCI are limited because most previous reports have included STEMI patients who died during hospitalization. The reported all-cause mortality at 1 year ranged from 3.8% (18) to 10% (4) in STEMI patients who were alive at discharge. However, these reports did not reveal details about the cause of death, and the rate of p-PCI was low (46%) in the latter report (4). The present study clearly demonstrated the mid-term mortality and cause of death in STEMI survivors who underwent p-PCI. Our finding of a 2-year mortality of 5.7% in STEMI survivors (mean age, 67.7 years old) with a high rate of follow-up is comparable to findings in previous reports (4, 18).

Some investigators have reported that the cause of death after STEMI differs between the early and chronic phases and that cardiac death is more frequent in the early phase than in the chronic phase. Patients who survived STEMI had a good prognosis (cardiac death rate: 1.0-2.0% per year). However, non-cardiac death was the major cause among late deaths (17, 19). Indeed, our present data also showed that

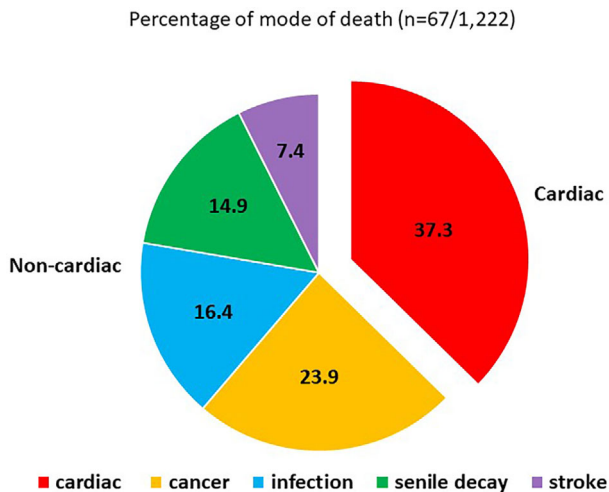


Figure 3. Proportions of the causes of death.

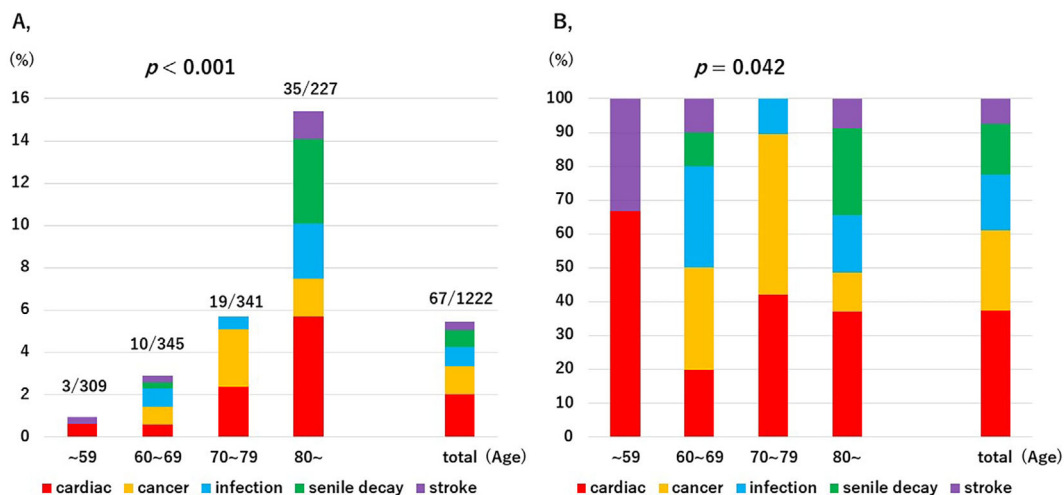


Figure 4. A: Details of the causes of death according to age. B: Distribution of death according to age.

**Table 3. Univariate and Multivariate Regression Analysis for the Association between 2-year All-cause Mortality and Clinical Findings.**

Factors for predicting	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
Age: over 80 years	5.22	3.23-8.44	<0.001	2.66	1.30-3.91	0.004
Male	0.53	0.32-0.87	0.013			
BMI (log)	0.015	0.003-0.068	<0.001	0.16	0.030-0.84	0.030
Prior MI	1.89	0.99-3.60	0.054			
Prior CABG	0.53	0.072-3.94	0.54			
Prior ischemic stroke	2.34	1.19-4.59	0.013			
Prior intracranial bleeding	1.04	0.14-7.45	0.97			
Dyslipidemia	0.67	0.41-1.10	0.11			
Diabetes mellitus	1.06	0.64-1.74	0.83			
Hypertension	1.81	0.78-4.19	0.17			
Current smoking	0.43	0.25-0.72	0.001			
CKD	3.01	1.83-4.94	<0.001			
Atrial fibrillation	2.64	1.55-4.48	<0.001			
PAD	1.09	0.34-3.46	0.89			
Killip class ≥II	3.49	1.99-6.11	<0.001	1.99	1.17-3.39	0.011
LMT	2.37	0.58-9.67	0.23			
LAD	0.73	0.45-1.20	0.21			
LCx	0.89	0.39-2.07	0.79			
RCA	1.32	0.82-2.14	0.25			
Initial TIMI 0/1	0.69	0.43-1.12	0.13			
Final TIMI grade 0/1/2	1.35	0.78-2.31	0.28			
Rentrop 3	1.72	0.82-3.60	0.15			
3-vessel disease	1.59	0.85-2.98	0.14			
POBA	1.17	0.53-2.55	0.70			
IABP use	1.91	1.18-3.10	0.009			
PCPS use	2.98	0.94-9.47	0.065			
Onset to balloon time (log)	1.39	1.03-1.89	0.032			
peak CK (log)	0.82	0.64-1.04	0.10			
LVEF (log)	0.11	0.048-0.24	<0.001	0.42	0.16-1.09	0.075
Hemoglobin (log)	0.003	0.001-0.014	<0.001	0.048	0.008-0.29	0.001
BNP (log)	2.38	1.88-3.02	<0.001	1.47	1.09-2.01	0.013
Aspirin use	0.33	0.14-0.76	0.009			
Thienopyridine use	0.31	0.16-0.59	<0.001			
Warfarin use	1.84	0.84-4.02	0.13			
DOAC use	1.76	0.64-4.85	0.27			
Statin use	0.48	0.17-1.31	0.15			
ACE-I use	0.69	0.43-1.12	0.14			
ARB use	0.49	0.22-1.07	0.073			
CCB use	0.55	0.25-1.20	0.14			
β-blocker use	0.63	0.38-1.04	0.071			
Diuretics use	3.05	1.89-4.93	<0.001			
OHA use	1.02	0.58-1.79	0.94			
Insulin use	1.45	0.46-4.63	0.53			
PPI use	0.84	0.39-1.84	0.67			

Covariates introduced into the multivariate model were: Age, sex, BMI, prior ischemic stroke, current smoking, CKD, atrial fibrillation, Killip class, final TIMI grade 0/1/2, onset to balloon time, LVEF, hemoglobin, BNP, aspirin use, and diuretic use.

HR: hazard ratio, CI: confidence interval

Abbreviations as in Tables 1 and 2.

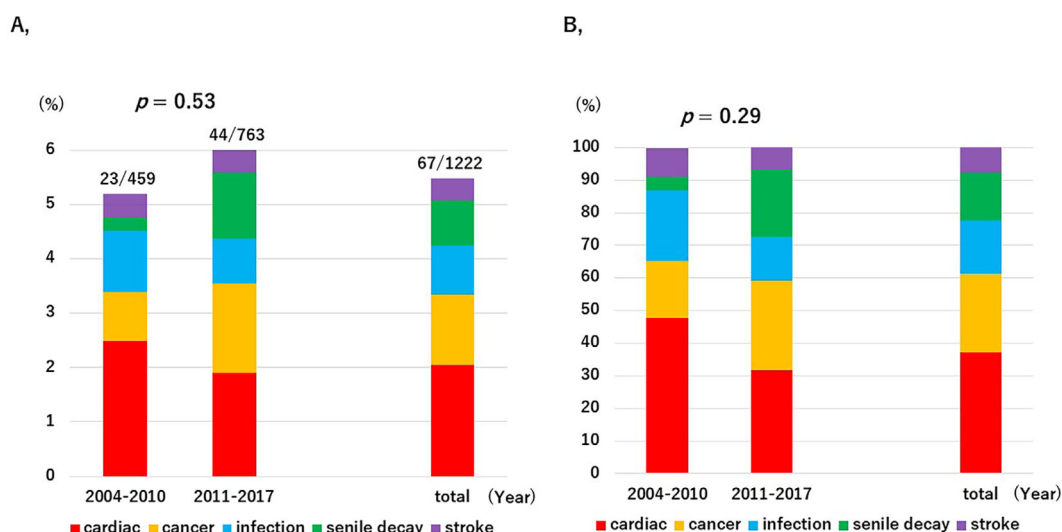
the 2-year cardiac mortality was 2.1%, which was lower than the rate of non-cardiac mortality (3.6%). Although previous reports showed that non-cardiac deaths exceeded car-

diac deaths at roughly six years after PCI in STEMI patients (7, 19), these results included in-hospital mortality. When the data were limited to survivors, the incidence of

**Table 4. PCI Strategy and Medication at Discharge according to PCI Era.**

	Overall n=1,222	2004-2010 n=459	2011-2017 n=763	p value
<b>PCI strategy</b>				
POBA, n (%)	113 (9.2)	55 (12.0)	58 (7.6)	<0.001
BMS, n (%)	651 (53.3)	388 (84.5)	263 (34.5)	
DES, n (%)	458 (37.5)	16 (3.5)	442 (57.9)	
<b>Medication at discharge</b>				
Aspirin use, n (%)	1,183 (96.8)	452 (98.5)	731 (95.8)	0.010
Thienopyridine use, n (%)	1,146 (93.8)	421 (91.7)	725 (95.0)	0.021
Warfarin use, n (%)	73 (6.0)	39 (8.5)	34 (4.5)	0.004
DOAC use, n (%)	42 (3.4)	0 (0.0)	42 (5.5)	<0.001
Statin use, n (%)	1,185 (97.0)	438 (95.4)	747 (97.9)	0.014
ACE-I use, n (%)	780 (63.8)	234 (51.0)	546 (71.6)	<0.001
ARB use, n (%)	227 (18.6)	111 (25.4)	116 (15.5)	<0.001
CCB use, n (%)	213 (17.4)	73 (15.9)	140 (18.3)	0.28
$\beta$ -blocker use, n (%)	900 (73.6)	338 (73.6)	562 (73.7)	0.99
Diuretic use, n (%)	305 (25.0)	115 (25.1)	190 (24.9)	0.96
OHA use, n (%)	289 (23.6)	101 (22.0)	188 (24.7)	0.29
Insulin use, n (%)	40 (3.3)	16 (3.5)	24 (3.2)	0.75
PPI use, n (%)	1,112 (91.0)	394 (85.8)	718 (94.2)	<0.001

Abbreviations as in Tables 1 and 2.



non-cardiac death was more frequent than that of cardiac death in the early phase, as seen in our study. According to the detailed mode of non-cardiac death, our study showed that malignant disease and infectious disease, which were predominant non-cardiac causes of death, were the main causes of death in sexagenarians and septuagenarians. In contrast, senile decay was the main cause of non-cardiac death in octogenarians.

The comparison of the periods when PCI was performed showed that the rate of cardiac death decreased while that of non-cardiac death increased in the second half compared to that in the first half, although the difference was not statistically significant. This might have been due to progress in

PCI devices and techniques. Furthermore, the frequent usage of medications such as statins and angiotensin-converting enzyme inhibitors might have led to a lower rate of cardiac death in the second half than in the first.

Several reports have studied the significant predictors of death after AMI. However, most of those studies predate the p-PCI era and assessed only the short-term outcomes (9, 10). Therefore, these results might not be applicable in modern clinical practice for assessing the mid-term prognosis. Our study is clinically relevant because we assessed the prognostic factors, including angiographic findings, in STEMI survivors who underwent p-PCI with a high rate of follow-up.



A higher Killip class and higher BNP level are well-known predictive factors of death in STEMI patients, as previously reported (20, 21). In our study, anemia was also associated with an increased risk of mid-term mortality in STEMI survivors, which is in line with previous reports (22). Recently, anemia was reported to lead to a high bleeding risk in patients with ACS who underwent PCI (23). Patients who had bleeding events had a dramatic increase in mortality because of the bleeding itself and thrombotic complications (24).

Lower BMI was also one of the significant predictors of all-cause mortality in this study. Obesity is usually associated with cardiovascular risk factors, such as hypertension, diabetes mellitus, and dyslipidemia (25). However, the present study showed that a markedly lower BMI was related to a poor outcome following PCI in patients with STEMI. This finding might support the “obesity paradox”, a concept that states that being underweight has a possible negative effect on short- and long-term outcomes after PCI (26, 27). One of the potential reasons for this phenomenon is that patients with a low BMI have a higher risk of non-cardiac death due to chronic diseases because of cachexia, malnutrition, depression, immunodeficiency (28-30), and malignant diseases. Both anemia and a low BMI have been identified as surrogate markers of frailty (29, 31) in the elderly. Therefore, our findings may highlight the impact of frailty on the mid-term mortality, especially non-cardiac death, as previously reported by us (32).

Notably, our study showed that angiographic findings have no significant influence on the mid-term mortality in STEMI survivors. If the patients are alive at discharge, the angiographic findings might not have a significant influence on the mid-term mortality. However, these findings should be interpreted with caution. In general, anterior wall infarction is a significant predictive index in STEMI patients (17) and results in a reduced LVEF and increased risk of heart failure (33). However, our study did not show the same trend. Therefore, further studies with a larger cohort and longer follow-up periods are needed in order to assess the impact of culprit lesions and the LVEF.

### Limitations

Several limitations associated with the present study warrant mention. First, the study had a single-center, retrospective design. Second, we did not include the “use of thienopyridine at discharge” or “IABP” in the final Cox multivariate regression models. This was because the prescription of thienopyridine was left to the physicians’ discretion, and the type of thienopyridine used differed based on the year in which the procedure had been performed. The use of IABP was also left to each PCI operators’ discretion and could result in potential procedure bias. Third, our study lacked a systemic quantitative coronary analysis at an independent institute, and we did not collect data on the coronary artery dominance and details concerning the PCI procedure. Fourth, the study population was relatively small, which

might have resulted in low statistical power, with a particularly strong influence of angiographic findings on the prognosis. Further investigations are necessary to determine the independent predictors of mid-term mortality and cause of death in STEMI patients in a larger cohort with a longer follow-up period.

### Conclusion

This study showed that the mortality at 2 years was 5.7% among STEMI survivors after p-PCI. During the follow-up period, the rate of non-cardiac death was higher than the rate of cardiac death. The angiographic findings did not significantly influence the mid-term mortality compared to well-known clinical variables and the hemodynamic status.

**The authors state that they have no Conflict of Interest (COI).**

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