



# Clinical Characteristics and In-Hospital Mortality According to Left Main and Non-Left Main Culprit Lesions — Report From the Japan Acute Myocardial Infarction Registry (JAMIR) —

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**Background:** Acute coronary syndrome (ACS) due to an unprotected left main coronary artery (LMCA) lesion is a critical condition, but there are limited data available on in-hospital outcomes of percutaneous coronary intervention (PCI).

**Methods and Results:** The Japan Acute Myocardial Infarction Registry is a nationwide, real-world database. The clinical data on 13,548 ACS patients hospitalized between January 2011 and December 2013 were retrospectively collected from 10 representative regional ACS registry groups. We compared the 404 patients (3.0%) with LMCA ACS with the remaining 13,144 patients with non-LMCA ACS. The LMCA group was characterized by older age, lower rate of ST-segment elevation myocardial infarction, and higher rate of advanced Killip class. In-hospital mortality was significantly higher in patients with LMCA ACS than in those with non-LMCA ACS (23.3% vs. 5.5%, respectively;  $P < 0.001$ ). Primary PCI for non-LMCA lesions was associated with lower in-hospital mortality (OR, 0.48; 95% CI: 0.34–0.66), but that for LMCA lesions was not (OR, 2.89; 95% CI: 1.13–7.40). Longer door-to-balloon time was associated with Killip class  $\geq 2$  and higher in-hospital mortality in the non-LMCA group but not in the LMCA group.

**Conclusions:** Primary PCI in patients with LMCA ACS is still challenging; therefore, effective strategies are needed.

**Key Words:** Acute coronary syndrome; Left main; Multicenter registry; Percutaneous coronary intervention

Acute coronary syndrome (ACS) involving occlusion of the unprotected left main coronary artery (LMCA) is a critical condition, often leading to abrupt and severe circulatory failure, lethal arrhythmia, and sudden cardiac death.<sup>1–3</sup> Percutaneous coronary intervention (PCI) is advantageous in that it achieves rapid reperfusion in critically ill patients.<sup>4</sup> The 2017 European Society of Cardiology ST-segment elevation myocardial infarction (STEMI) guidelines state that cardiogenic shock is a class I indication for PCI, while coronary artery bypass grafting (CABG) is a class I indication if the coronary anatomy is not suitable for PCI.<sup>5</sup> The optimal revascularization strategy

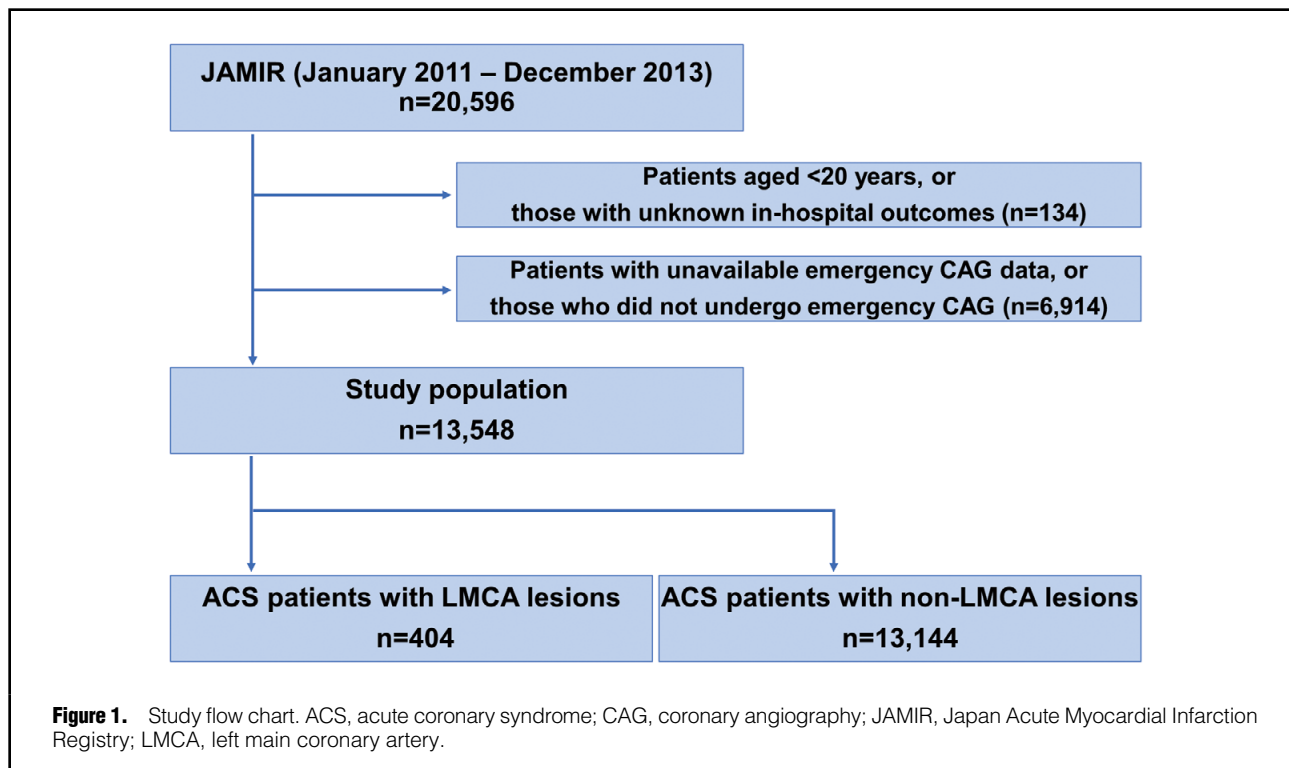
for patients with ACS due to an unprotected LMCA culprit lesion in acute situations, however, is still unclear, because only small cohorts have been reported. Therefore, to better understand the current status of revascularization strategies, we analyzed the clinical characteristics, in-hospital outcomes, and impact of primary PCI on in-hospital mortality in patients with ACS due to an unprotected LMCA lesion in the Japan Acute Myocardial Infarction Registry (JAMIR), a nationwide, real-world database of patients with ACS in Japan.<sup>6</sup>

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## Methods

### Subjects

JAMIR is a nationwide, large-scale registry. Clinical data were retrospectively collected from 10 regional registries or institutions and analyzed regarding medical practices and emergency care for ACS in Japan. The aims and protocols of this registry have been published elsewhere.<sup>6</sup>

Initially, 20,596 consecutive patients with type 1 myocardial infarction (MI) who were hospitalized  $\leq 24$  h after MI onset between January 2011 and December 2013 were enrolled. ACS was diagnosed according to the universal definition of MI proposed by the Joint European Society of Cardiology/American Heart Association/World Heart Federation Task Force.<sup>7</sup> The criteria for ACS according to the World Health Organization Monitoring of Trends and Determinants in Cardiovascular Disease (WHO MONICA) Project were also used when troponin was difficult to assess.<sup>8</sup> The JAMIR study did not include patients with ACS associated with PCI or CABG (universal classification types 4 and 5). Of the 20,596 patients with ACS, 134 aged  $<20$  years or with unknown in-hospital outcome and 6,914 in whom detailed emergency coronary angiography data were not available or who had not undergone coronary angiography, were excluded. All patients in this study underwent emergency coronary angiography, and culprit lesions were confirmed. Ultimately, the study population consisted of 13,548 patients (Figure 1).

### Definitions and Endpoints

STEMI was defined as ST elevation  $\geq 1$  mm in at least 2 contiguous leads on the index or qualifying electrocardiogram, when new left bundle branch block was presumed, or when new pathological Q waves accompanied by chest pain or a rise in cardiac biomarkers was observed. In the

absence of ST-segment elevation, patients meeting the diagnostic criteria for MI were classified as non-STEMI (NSTEMI).<sup>7</sup> The detailed definitions of risk factors for cardiovascular disease (hypertension, diabetes mellitus, dyslipidemia, and current smoking) have been described previously.<sup>6</sup> Primary PCI was defined as procedures performed  $\leq 24$  h after symptom onset, and door-to-balloon (DTB) time was defined as the time from arrival at the hospital to first balloon inflation during PCI. Final coronary flow in the infarct-related artery was graded using the Thrombolysis in Myocardial Infarction (TIMI) flow classification. In the JAMIR study, the decision to reperfuse was made by the individual cardiologist in charge. The major outcome in this study was in-hospital mortality. This study was conducted in accordance with the tenets of the Declaration of Helsinki. The institutional review boards or ethics committees at all participating centers approved the study protocol.

### Statistical Analysis

Categorical variables are presented as n (%). Continuous variables are presented as median (IQR). Continuous variables were compared using the t-test or Mann-Whitney U-test, as appropriate. Categorical variables were analyzed using the chi-squared test. Logistic regression models were used to evaluate the impact of primary PCI on in-hospital mortality. In addition, logistic regression was used to identify indications for primary PCI in patients with ACS due to an unprotected LMCA lesion, and to evaluate predictors of in-hospital mortality in this population. Odds ratios (OR) and 95% confidence interval (CI) were calculated. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA), and all were 2-tailed, with  $P < 0.05$  considered statistically significant.

Table 1. ACS Patient Characteristics				
	Overall (n=13,548)	LMCA lesion (n=404)	Non-LMCA lesion (n=13,144)	P-value
Age (years)	69 (59–78)	71 (63–79)	69 (59–78)	<0.001
Sex (male)	76.1	80.9	75.9	0.020
CAD				
STEMI	80.3	67.8	81.2	<0.001
Killip classification				
1	74.0	37.6	75.3	<0.001
2	11.5	13.8	11.5	
3	5.8	15.3	5.4	
4	8.7	33.3	7.9	
Multivessel disease	47.8	78.6	46.8	<0.001
Risk factors				
Hypertension	64.0	60.5	64.1	0.148
Diabetes	32.7	36.0	32.6	0.158
Dyslipidemia	47.0	37.9	47.3	<0.001
Current smoking	36.0	29.3	36.2	0.006
IABP use	16.8	59.4	15.4	<0.001
PCPS use	2.8	12.2	2.4	<0.001
Transportation				
Ambulance	81.4	83.8	81.3	0.193
Self	15.9	14.1	15.9	
In-hospital onset	2.8	2.1	2.8	
Primary PCI	93.3	75.8	93.8	<0.001
Final TIMI flow				
Grade 0	1.7	2.1	1.7	0.002
Grade 1	1.2	2.1	1.1	
Grade 2	5.0	11.6	4.9	
Grade 3	92.1	84.3	92.3	
DTB time (min)	82 (50–153)	100 (60–161)	82 (50–153)	0.338
In-hospital death	6.1	23.3	5.5	<0.001

Data given as % or median (IQR). ACS, acute coronary syndrome; CAD, coronary artery disease; DTB, door-to-balloon; IABP, intra-aortic balloon pump; LMCA, left main coronary artery; PCI, percutaneous coronary intervention; PCPS, percutaneous cardiopulmonary support; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

## Results

### Characteristics and In-Hospital Mortality

The study flow chart is shown in **Figure 1**. In the JAMIR study, 404 (3.0%) of 13,548 patients had an unprotected LMCA culprit lesion. Patient characteristics according to LMCA ACS status are summarized in **Table 1**, and comparison between JAMIR and other ACS registries is given in **Supplementary Table**. JAMIR was characterized by older age and a higher rate of advanced Killip class than other ACS registries. Compared with patients with a non-LMCA lesion, those with an unprotected LMCA lesion were older and more likely to be male; had a lower rate of STEMI, dyslipidemia, and current smoking; and had a higher rate of multivessel disease and advanced Killip class. The rate of ambulance use did not differ between the 2 groups. In patients with LMCA ACS, intra-aortic balloon pump (IABP) assist and percutaneous cardiopulmonary support (PCPS) were significantly more frequent than in patients with non-LMCA ACS, whereas PCI and final TIMI grade 3 were significantly less common. In-hospital mortality was approximately 4-fold higher in the LMCA ACS group compared with the non-LMCA ACS group

(23.3% vs. 5.5%, respectively;  $P<0.001$ ; **Table 1**).

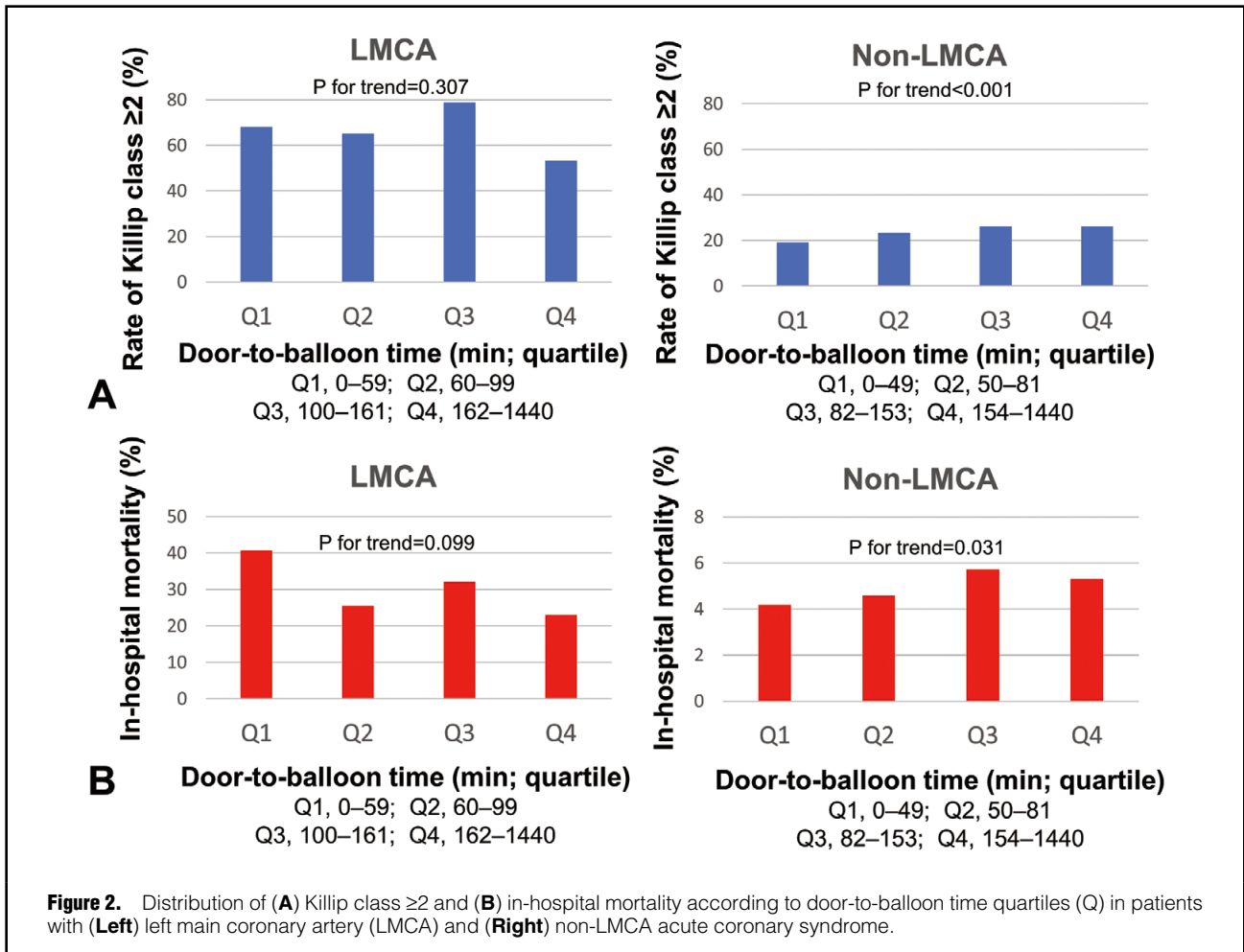
### Impact of Primary PCI on In-Hospital Mortality

The impact of primary PCI on in-hospital mortality in patients with an unprotected LMCA lesion and those with a non-LMCA lesion is shown in **Table 2**, **Supplementary Figure 1**. In patients with a non-LMCA lesion, in-hospital mortality was significantly lower for those who underwent PCI than for those who did not (5.0% vs. 13.9%, respectively;  $P<0.001$ ), whereas the inverse was true in patients with an unprotected LMCA lesion (27.3% vs. 10.4%, respectively;  $P<0.001$ ; **Supplementary Figure 1**). The results of multivariate logistic regression modeling to evaluate the impact of primary PCI on in-hospital mortality are shown in **Table 2**. Even after adjustment, primary PCI for a non-LMCA lesion was significantly associated with improved in-hospital mortality (model 1, OR, 0.33; 95% CI: 0.27–0.41,  $P<0.001$ ; model 2, OR, 0.35; 95% CI: 0.28–0.44,  $P<0.001$ ; and model 3, OR, 0.48; 95% CI: 0.34–0.66,  $P<0.001$ ), whereas PCI for an unprotected LMCA lesion was significantly associated with worse in-hospital mortality (model 1, OR, 3.23; 95% CI: 1.60–6.53,  $P=0.001$ ; model 2, OR, 3.28; 95% CI: 1.62–6.65,  $P=0.001$ ; and model 3, OR,

**Table 2. Multivariate Predictors of In-Hospital Mortality in ACS Patients After Primary PCI**

Variables	Model 1 (crude)	P-value	Model 2 (age, sex-adjusted)	P-value	Model 3 (fully adjusted) <sup>†</sup>	P-value
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
LMCA lesions	3.23 (1.60–6.53)	0.001	3.28 (1.62–6.65)	0.001	2.89 (1.13–7.40)	0.027
Non-LMCA lesions	0.33 (0.27–0.41)	<0.001	0.35 (0.28–0.44)	<0.001	0.48 (0.34–0.66)	<0.001

<sup>†</sup>Adjusted for age, sex, ST-segment elevation myocardial infarction, Killip class, hypertension, diabetes, dyslipidemia, and smoking habit. CI, confidence interval; OR, odds ratio. Other abbreviations as in Table 1.



**Figure 2.** Distribution of (A) Killip class  $\geq 2$  and (B) in-hospital mortality according to door-to-balloon time quartiles (Q) in patients with (Left) left main coronary artery (LMCA) and (Right) non-LMCA acute coronary syndrome.

2.89; 95% CI: 1.13–7.40,  $P=0.027$ ).

In the JAMIR study, data on DTB time were available for 210 patients with an unprotected LMCA lesion and for 8,875 patients with a non-LMCA lesion. Median DTB time did not significantly differ between the 2 groups (LMCA, 100 min; IQR, 60–161 min vs. non-LMCA, 82 min; IQR, 50–153 min;  $P=0.338$ ; **Table 1**). In the non-LMCA ACS group, a longer DTB time was associated with Killip class  $\geq 2$  ( $P$  for trend $<0.001$ ) and higher in-hospital mortality ( $P$  for trend=0.031). These associations, however, were not observed in the LMCA ACS group (Killip class  $\geq 2$ ,  $P$  for trend=0.307; in-hospital mortality,  $P$  for trend=0.099; **Figure 2**). When limiting to analysis of STEMI patients, DTB time was associated with Killip class  $\geq 2$  and in-hospital mortality in the non-LMCA STEMI group (Killip

class  $\geq 2$ ,  $P$  for trend $<0.001$ ; in-hospital mortality,  $P$  for trend=0.030) but not in the LMCA STEMI group (Killip class  $\geq 2$ ,  $P$  for trend=0.523; in-hospital mortality,  $P$  for trend=0.230; **Supplementary Figure 2**).

#### LMCA ACS and Survivor Status

Clinical characteristics according to survivor status in the LMCA ACS group are listed in **Table 3**. Compared with the survivors, the patients who died in the hospital had a higher rate of STEMI and advanced Killip class, and a higher rate of use of ambulance, IABP, and PCPS. Moreover, the rate of primary PCI was significantly higher in non-survivors than in survivors (89.1% vs. 71.7%, respectively;  $P=0.001$ ). Median DTB time was slightly shorter in non-survivors than in survivors, but the difference was not

Table 3. LMCA ACS Clinical Characteristics vs. Survivor Status, Clinical Presentation, and PCI Status									
	Died	Survived	P-value	STEMI	NSTEMI	P-value	PCI (+)	PCI (-)	P-value
Age (years)	71 (62–82)	71 (63–79)	0.770	70 (62–78)	71 (64–78)	0.335	71 (63–79)	70 (63–78)	0.561
Sex (male)	80.9	81	0.980	80.5	79.5	0.820	82.3	76.0	0.173
CAD									
STEMI	78.7	64.8	0.023	100	0	–	72.3	55.6	0.005
Killip classification									
1	10.3	45.3	<0.001	36.6	41.2	0.203	34.9	45.9	0.001
2	7.7	15.6		14.1	15.5		10.7	22.4	
3	11.5	16.3		14.1	17.5		16.1	11.8	
4	70.5	22.8		35.2	25.8		38.3	20.0	
Multivessel disease	83.3	77.5	0.345	76.1	77.3	0.834	80.3	73.1	0.186
Risk factors									
Hypertension	60.4	60.5	0.994	60.2	63.3	0.584	60.4	61.5	0.859
Diabetes	34.1	36.6	0.655	35.3	38.2	0.607	36.2	37.5	0.820
Dyslipidemia	33.3	39.3	0.307	39.6	38.0	0.783	39.9	33.3	0.257
Current smoking	28.4	29.5	0.842	27.9	30.2	0.662	30.0	28.4	0.766
IABP use	77.4	54.3	<0.001	57.9	54.0	0.512	62.8	49.5	0.023
PCPS use	35.7	5.5	<0.001	11.3	8.0	0.366	13.4	9.7	0.352
Transportation									
Ambulance	98.9	79.3	<0.001	87.5	76.0	0.007	87.3	75.27	0.002
Self	1.1	18		11.6	21.2		11.7	19.35	
In-hospital onset	0	2.7		0.9	2.9		1.1	5.38	
Primary PCI	89.1	71.7	0.001	80.7	66.7	0.005	100	0	
DTB time (min)	90 (54–150)	105 (65–200)	0.086	90 (57–157)	140 (76–273)	0.012	100 (60–161)		
In-hospital death	100	0	–	25.0	14.3	0.023	27.3	10.4	<0.001

Data given as % or median (IQR). NSTEMI, non-ST-segment elevation myocardial infarction. Other abbreviations as in Table 1.

significant (90 min; IQR, 54–150 min vs. 105 min, IQR, 65–200 min, respectively;  $P=0.086$ ). On multivariate analysis of the variables in model 3 (Table 2), advanced Killip class (OR, 5.93; 95% CI: 2.35–14.99,  $P<0.001$ ), in addition to primary PCI, was an independent predictor of in-hospital death.

### LMCA ACS and STEMI Status

Clinical characteristics according to STEMI and NSTEMI status in the LMCA ACS group are also listed in Table 3. Age, sex, Killip class, and risk factors for cardiovascular disease did not differ significantly between the 2 groups. Patients with STEMI had a significantly higher rate of ambulance use than those with NSTEMI (STEMI, 87.5% vs. NSTEMI, 76.0%, respectively;  $P=0.007$ ), more commonly underwent primary PCI (STEMI, 80.7% vs. NSTEMI, 66.7%, respectively;  $P=0.005$ ), and had a shorter median DTB time (STEMI, 90 min; IQR, 57–157 min vs. NSTEMI, 140 min; IQR, 76–273 min, respectively;  $P=0.012$ ). Additionally, DTB time quartiles were associated with the proportion of patients with STEMI (first quartile: 0–59 min, 81.8%; second quartile: 60–99 min, 80.0%; third quartile: 100–161 min, 64.6%; fourth quartile: 162–1,440 min, 61.2%;  $P$  for trend=0.009). In-hospital mortality was significantly higher in patients with STEMI than in those with NSTEMI (25.0% vs. 14.3%, respectively;  $P=0.023$ ).

### Factors Associated With Primary PCI in LMCA ACS

To clarify the characteristics of patients with LMCA ACS who underwent primary PCI, subgroup analysis according to the presence or absence of a primary PCI procedure was performed (Table 3). Patients with primary PCI were

characterized by a significantly higher rate of STEMI and advanced Killip class, and a higher rate of ambulance and IABP use, compared to those without primary PCI. On multivariate logistic regression analysis, age  $\geq 80$  years (vs. age  $< 60$  years: OR, 2.92; 95% CI: 1.08–7.89,  $P=0.034$ ), Killip class 4 (vs. class 1: OR, 2.60; 95% CI: 1.24–5.46,  $P=0.012$ ), and STEMI (OR, 1.91; 95% CI: 1.06–3.44,  $P=0.032$ ) were independent factors associated with primary PCI in patients with LMCA ACS (Table 4; model 1). Even after adjusting for sex, multivessel disease, and Killip class, age  $\geq 80$  years (vs. age  $< 60$  years: OR, 2.88; 95% CI: 1.03–8.03,  $P=0.043$ ) and STEMI (OR, 2.22; 95% CI: 1.17–4.20,  $P=0.014$ ) were significantly associated with treatment allocation to primary PCI (Table 4; model 2).

### Predictors of In-Hospital Mortality in After Primary PCI

We focused on patients with LMCA ACS undergoing primary PCI, and evaluated predictors of in-hospital mortality in this population. On multivariate logistic regression analysis, Killip class 4 (OR, 5.17; 95% CI: 2.44–10.95,  $P<0.001$ ), IABP or PCPS use (OR, 6.61; 95% CI: 2.06–21.23,  $P=0.002$ ), and final TIMI grade  $< 3$  (OR, 4.90; 95% CI: 1.94–12.33,  $P<0.001$ ) were independent predictors of in-hospital mortality in patients with LMCA ACS after primary PCI (Table 5).

### Discussion

The major findings in the present analysis of the nationwide real-world JAMIR database with 13,548 ACS patients are as follows: (1) JAMIR included 404 patients (3.0%) who had an unprotected LMCA culprit lesion; (2) in-hospital



Variables	OR	95% CI	P-value
<b>Model 1</b>			
Men	1.86	0.93–3.70	0.077
Age, 60–69 years (vs. <60 years)	2.12	0.89–5.07	0.092
Age, 70–79 years (vs. <60 years)	2.10	0.89–4.96	0.092
Age, ≥80 years (vs. <60 years)	2.92	1.08–7.89	0.034
Killip class 2 (vs. class 1)	0.77	0.35–1.68	0.511
Killip class 3 (vs. class 1)	1.85	0.77–4.48	0.172
Killip class 4 (vs. class 1)	2.60	1.24–5.46	0.012
Hypertension	0.67	0.36–1.25	0.207
Diabetes	0.80	0.43–1.48	0.473
Dyslipidemia	1.57	0.84–2.92	0.155
Current smoking	1.21	0.60–2.42	0.599
STEMI	1.91	1.06–3.44	0.032
<b>Model 2</b>			
Men	2.09	0.996–4.40	0.051
Age, 60–69 years (vs. <60 years)	2.18	0.87–5.38	0.090
Age, 70–79 years (vs. <60 years)	1.80	0.74–4.37	0.195
Age, ≥80 years (vs. <60 years)	2.88	1.03–8.03	0.043
Multivessel disease	1.48	0.74–2.98	0.272
Killip class 2 (vs. class 1)	0.52	0.22–1.23	0.138
Killip class 3 (vs. class 1)	1.17	0.43–3.16	0.757
Killip class 4 (vs. class 1)	1.55	0.72–3.34	0.267
STEMI	2.22	1.17–4.20	0.014

Abbreviations as in Tables 1,2.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Men	0.84 (0.44–1.62)	0.608	–	–
Age, per 1-year increase	1.00 (0.98–1.02)	0.891	–	–
Hypertension	0.95 (0.56–1.61)	0.840	–	–
Diabetes	1.03 (0.60–1.77)	0.912	–	–
Dyslipidemia	0.79 (0.46–1.36)	0.400	–	–
Current smoking	1.02 (0.57–1.81)	0.960	–	–
STEMI	1.96 (0.98–3.94)	0.058	–	–
Killip class 4	7.47 (4.03–13.87)	<0.001	5.17 (2.44–10.95)	<0.001
Multivessel disease	1.26 (0.54–2.94)	0.599	–	–
IABP or PCPS use	3.78 (1.92–7.45)	<0.001	6.61 (2.06–21.23)	0.002
Final TIMI flow <3	4.15 (2.01–8.58)	<0.001	4.90 (1.94–12.33)	<0.001

Multivariate logistic regression model was adjusted for variables with P<0.05 on univariate analysis. Abbreviations as in Tables 1,2.

mortality was significantly higher in patients with LMCA ACS than in those with non-LMCA ACS; (3) primary PCI for an unprotected LMCA culprit lesion was more frequently performed in high-risk populations (e.g., elderly, STEMI, or patients with Killip class 4) but was not closely related to better in-hospital outcome; and (4) Killip class 4 and final TIMI grade <3 were independent predictors of in-hospital mortality in patients with LMCA ACS after primary PCI.

JAMIR is the largest collection of nationwide ACS data in Japan, and was established to integrate 10 regional registries containing clinical data on medical treatment and emergency care. We recently showed that the 20,462

ACS patients in the JAMIR study were characterized by advanced age (24% of patients were aged ≥80 years) and a high rate of ambulance use (78.9%) and primary PCI (87.9%).<sup>6</sup> Overall in-hospital mortality and cardiac mortality were 8.3% and 6.6%, respectively.<sup>6</sup> Clinical characteristics in the JAMIR study were similar to those in a Japanese nationwide claim-based database, suggesting that the JAMIR data closely reflect the status of current ACS patients in Japan.<sup>6,9</sup> This large-scale registry enables the assessment of real-world medical practices and emergency care in patients with LMCA ACS.

ACS due to an unprotected LMCA lesion is a critical condition characterized by a high risk of cardiogenic shock

and in-hospital mortality.<sup>1-3</sup> There have been very limited data, however, on the incidence, clinical characteristics, and short-term outcomes after primary PCI in this population, and existing results are mainly derived from small registries consisting of between 48 and 348 patients, except for the Global Registry of Acute Coronary Events (GRACE; n=1,799).<sup>10-16</sup> In these small registries, the incidence of LMCA ACS was approximately 5% in patients undergoing coronary angiography.<sup>10,11</sup> Additionally, in most studies, especially those involving randomization or comparison of matched cohorts, patients with LMCA ACS were excluded due to their high risk. Therefore, the optimal revascularization strategy in this population is the subject of ongoing debate, and current consensus guidelines do not state specific treatment recommendations. JAMIR included a relatively large number of patients with LMCA ACS compared with previous reports,<sup>10,12-16</sup> with a prevalence of 3.0%. Importantly, the in-hospital mortality of patients with LMCA ACS was 23.3%, which was approximately 4-fold higher than that of patients with non-LMCA ACS (5.5%). Regarding hemodynamic status, according to JAMIR, one-third of patients with LMCA ACS presented with cardiogenic shock (i.e., Killip class 4), and many patients received mechanical support with IABP (59.4%) or PCPS (12.2%).

A wide range of in-hospital mortality rates in subjects with LMCA ACS has been reported, varying between 7.7% and 50.0%.<sup>10,11,13,14,16</sup> In the GRACE registry, one of the largest cohorts of ACS, the overall in-hospital mortality in patients with ACS due to an unprotected LMCA lesion was 7.7%,<sup>11</sup> which was much lower than in the present study (23.3%). In the GRACE registry, only 35% and 1.8% of patients had STEMI and Killip class 4, respectively, indicating that that registry included more low-risk patients than the JAMIR study.<sup>11</sup> The Korea Acute Myocardial Infarction Registry (n=256; mean age, 66 years) showed that the prevalence of STEMI, Killip class 4, and in-hospital mortality in patients with LMCA ACS were 44.1%, 14.1%, and 16.0%, respectively.<sup>12</sup> Such disparities in in-hospital mortality may be related in part to the presentation and severity of ACS (**Supplementary Table**).

In the JAMIR study, 93.3% of patients with ACS underwent primary PCI, a higher rate than in registries in Western countries.<sup>17,18</sup> For instance, in the Myocardial Ischaemia National Audit Project (MINAP) and the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry, only 56.7% and 78% of STEMI patients, respectively, underwent primary PCI.<sup>17,18</sup> Moreover, in the present study, primary PCI was performed not only in most patients with a non-LMCA lesion (93.8%), but also in a relatively high proportion of those with an unprotected LMCA lesion (75.8%). In general, timely performance of primary PCI for the infarct-related coronary artery contributes to reducing infarct size, preserving left ventricular (LV) function, and decreasing mortality.<sup>4-6,18</sup> Several observational studies have reported that primary PCI is now the most common revascularization strategy for an unprotected LMCA culprit lesion, especially in higher risk patients, and its benefits include achieving more rapid and less invasive reperfusion than CABG, with acceptable short- and long-term outcomes.<sup>1,10-12</sup> The optimal revascularization strategy for patients with LMCA ACS, however, is still unknown because no prospective randomized studies have compared

primary PCI and CABG. Acharya et al demonstrated that acute MI (AMI) patients with shock who underwent CABG as a salvage procedure had a high operative mortality of 53.3%.<sup>19</sup> In contrast, other small-scale registries failed to demonstrate the superiority of primary PCI over CABG in patients with LMCA ACS.<sup>14,15</sup> Caggegi et al reported that PCI had a similar safety profile (death and MI) as CABG, but was associated with a higher risk of repeat revascularization in patients with LMCA disease and ACS.<sup>20</sup> The GRACE registry showed that CABG was often performed with delayed timing in more stable patients, and that both types of revascularization improved 6-month survival in comparison with an initial conservative medical strategy.<sup>11</sup> In the present study, in-hospital mortality was worse when primary PCI was performed for an unprotected LMCA lesion than when it was not, whereas PCI for a non-LMCA lesion was correlated with improved in-hospital mortality. Additionally, the JAMIR study showed that primary PCI for an unprotected LMCA lesion was more frequently performed in the elderly, in patients with STEMI, and in those with Killip class 4, and that Killip class 4, use of mechanical circulatory supports, and final TIMI grade <3 were independent predictors of in-hospital mortality.<sup>10-13,16</sup> In the present study primary PCI was found to be a reasonable treatment option, but it did not lead to improved in-hospital outcomes because it was performed in patients with LMCA ACS whose condition was particularly serious and unstable.

One of the unique features of the present study is that it contains data on DTB time. Shorter DTB time was previously associated with lower mortality in STEMI patients,<sup>21-25</sup> and in the American Heart Association's Mission: Lifeline® program (since 2010),<sup>26,27</sup> DTB time <90 min was an important performance measure for STEMI treatment. Current guidelines recommend that hospitals providing primary PCI for patients with STEMI should treat patients in ≤120 min after contact with the medical system or hospital admission.<sup>5</sup> A shorter DTB time was found to be associated with improved short- and long-term mortality in patients with cardiogenic shock, out-of-hospital cardiac arrest, or advanced Killip class,<sup>24,25</sup> but few studies have examined the effect of DTB time on clinical outcomes in patients who underwent primary PCI for ACS due to an unprotected LMCA lesion. Interestingly, in the present study, despite the high rate of ambulance use, a large number of patients with LMCA ACS died early, and the DTB time tended to be shorter in non-survivors than in survivors. One small-scale study described a paradoxical effect with regard to time from initial presentation to treatment and 30-day survival, with a longer door-to-treatment time associated with higher survival.<sup>15</sup> This may be due to the fact that those who presented more rapidly were often more critically ill, and suggests the need for other therapeutic strategies as well as efforts to shorten DTB time. Recently, small-scale studies showed that use of Impella 2.5 or Impella CP, 2 new percutaneous LV assist devices, prior to as compared with after primary PCI, improved survival both in patients with AMI complicated by cardiogenic shock and in those with LMCA AMI.<sup>28,29</sup> This evidence suggests that early active unloading of the LV and hemodynamic stabilization to maintain organ perfusion, as achieved with these devices, may be more effective than reducing DTB time for improving outcomes in these critically ill patients.

## Study Limitations

This study had several limitations. First and most importantly, the study population was relatively large compared with previous studies, but may still be too small to reach definitive conclusions. Second, given that this was a retrospective observational all-comer study, the enrolled patients were heterogeneous and residual confounding or selection bias cannot be completely excluded.<sup>30,31</sup> Additionally, given that 10 regional ACS registries were integrated in this study, standardization of treatment may be insufficient. JAMIR, however, as a real-world data source, enrolled all consecutive patients diagnosed with ACS, including elderly people and patients with comorbidities, who are often excluded from randomized clinical trials. Therefore, this study facilitates understanding of the outcomes of LMCA ACS, for which the performing of randomized clinical trials ethically is difficult in practice. Third, we could not assess the impact of CABG on in-hospital mortality because data on CABG were unavailable. Many patients who were not treated with primary PCI may have undergone CABG. Fourth, patients with LMCA ACS who had out-of-hospital cardiac arrest/life-threatening arrhythmia and were not resuscitated were excluded from this study. Finally, although JAMIR provides data on multivessel disease, the precise anatomical distribution of the lesions and coronary artery dominance are unknown. It would have been of interest to know how LMCA lesions were distributed anatomically, for instance whether or not they included the bifurcation, and if additional lesions were located on the right coronary artery vs. the left anterior descending and/or the circumflex coronary artery.

## Conclusions

Based on the nationwide JAMIR registry, primary PCI for an unprotected LMCA culprit lesion is still challenging; therefore, effective strategies need to be developed.

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## Disclosures

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## Appendix

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### Supplementary Files

Please find supplementary file(s);  
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