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Impact of time to revascularization on outcomes in patients after out-of-hospital cardiac arrest with STEMI

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ABSTRACT

Background: International guidelines recommend emergency coronary angiography in patients after out-of-hospital cardiac arrest (OHCA) with ST-segment elevation on 12-lead electrocardiography. However, the association between time to revascularization and outcomes remains unknown. This study aimed to evaluate the association between time to revascularization and outcomes in patients with OHCA due to ST-segment-elevation myocardial infarction (STEMI) who underwent percutaneous coronary intervention (PCI).
Methods: This multicenter, retrospective, nationwide observational study included patients aged ≥18 years with OHCA due to STEMI who underwent PCI between 2014 and 2020. The time of the first return of spontaneous circulation (ROSC) was defined as the time of first ROSC during resuscitation, regardless of the pre-hospital or in-hospital setting. The primary outcome was a 1-month favorable neurological outcome, defined as cerebral performance category 1 or 2. Multivariable logistic regression analysis was used to assess the association between the time to revascularization and favorable neurological outcomes.
Results: A total of 547 patients were included in this analysis. The multivariable logistic regression analysis showed that a shorter time from the first ROSC to revascularization was associated with 1-month favorable neurological outcomes (63/86 [73.3%] in the time from the first ROSC to revascularization ≤60 min group versus 98/193 [50.8%] in the >120 min group; adjusted OR, 0.26; 95% CI, 0.11–0.56; *P* for trend, 0.015).
Conclusions: Shorter time to revascularization was significantly associated with 1-month favorable neurological outcomes in patients with OHCA due to STEMI who underwent PCI.

1. Introduction

Acute myocardial infarction is a major cause of out-of-hospital cardiac arrests (OHCA) worldwide [1-3]. OHCA due to acute myocardial infarction has a high mortality rate following successful resuscitation and hospitalization [4-8]. The electrical and mechanical dysfunction associated with myocardial ischemia leads to an increased risk of atrial or ventricular arrythmia, bradyarrhythmia, valve malfunction, heart failure, and sudden death [9]. The establishment of a resuscitation care strategy may improve clinical outcomes in patients with OHCA due to acute myocardial infarction.

Percutaneous coronary intervention (PCI) reduces mortality and morbidity in patients with acute myocardial infarction [10]. Previous studies showed that shorter time to revascularization was significantly associated with reduced mortality in patients with ST-segment-elevation myocardial infarction (STEMI) [11,12]. Additionally, shorter time to revascularization was also associated with better outcomes in patients after STEMI with severe complications such as cardiogenic shock [13,14]. Therefore, earlier revascularization may have the potential to improve outcomes among patients with OHCA due to STEMI who underwent primary PCI.

Abbreviations: CI, confidence interval; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; JAAM-OHCA, Japanese Association for Acute Medicine - out-of-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; STEMI, ST-segment-elevation myocardial infarction.

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Recent international guidelines for cardiopulmonary resuscitation (CPR) recommend emergency coronary angiography to perform a goal of PCI in patients with suspected cardiac causes of arrest and ST-segment elevation on electrocardiography after OHCA [15,16]. Previous studies showed outcomes in patients with OHCA due to STEMI [8,17,18]. However, these studies did not evaluate the association between outcomes and time to revascularization. Another previous study evaluated the association between in-hospital mortality and time to revascularization for patients with OHCA due to STEMI who underwent primary PCI [19]. However, that previous study performed the univariate analysis that did not adjust for confounding factors such as patient characteristics and resuscitation time course. Therefore, further statistical analyses adjusting for these confounding factors is needed to assess the association between time to revascularization and neurological outcomes in patients with OHCA due to STEMI who underwent primary PCI.

To assess the association between the time to revascularization and neurological outcomes in patients with OHCA due to STEMI who underwent primary PCI, we analyzed data from a nationwide hospital-based retrospective registry.

2. Methods

2.1. Study design, setting, and population

In this retrospective, nationwide, observative study, we identified patients with OHCA utilizing data from the Japanese Association for Acute Medicine - out-of-hospital cardiac arrest (JAAM-OHCA) registry. This registry is a nationwide hospital-based retrospective data registry. The details of the methodology and data collected by this registry have been described previously [20].

This study included adult patients (aged ≥18 years) after OHCA due to STEMI who underwent primary PCI from June 1, 2014, to December 31, 2020, in Japan. Patients were excluded if there were declared as death without resuscitation by physicians after hospital arrival, no available prehospital data, received extracorporeal cardiopulmonary resuscitation, time from emergency medical services (EMS) call to revascularization >360 min, missing data, or unsuccessful PCI.

The study protocol was approved by the Ethics Committee of Kyoto Prefectural University of Medicine (ERB-C-650-1), and each participating institution approved the JAAM-OHCA Registry protocol.

2.2. Pre-hospital, in-hospital data collection, and quality control

The JAAM-OHCA registry includes both pre-hospital and in-hospital data. In-hospital data were collected via web sheets by the attending physicians or medical staff of each participating institution. The anonymized collected data were confirmed by members of the JAAM-OHCA registry committee. In-hospital data were combined with pre-hospital data collected from the All-Japan Utstein Registry of the Fire and Disaster Management Agency based on the Utstein style [21].

The following data were collected: sex, age, cause of cardiac arrest, witness status, presence of a bystander who performed CPR, shock by a public access automated external defibrillator, first documented rhythm at EMS arrival (ventricular fibrillation/pulseless ventricular tachycardia, pulseless electrical activity, asystole, or others), annual numbers of patients with OHCA transported by EMS to hospital, presence of a pre-hospital physician, pre-hospital intravenous fluid, pre-hospital adrenaline administration, pre-hospital advanced airway management, first documented rhythm at hospital arrival (ventricular fibrillation/pulseless ventricular tachycardia, pulseless electrical activity, asystole, or return of spontaneous circulation (ROSC)), 12-lead electrocardiography after ROSC, arterial blood gases at hospital arrival, coronary angiography, PCI, intra-aortic balloon pumping, extracorporeal membrane oxygen, targeted temperature management, time course of resuscitation, survival status 1-month after cardiac arrest, and neurological status 1-month after cardiac arrest. In this registry, revascularization was defined as balloon dilation, thrombus aspiration, or stent implantation for lesions of stenosis. Based on the annual number of patients with OHCA transported by EMS to hospital, participants were divided into three groups: low volume hospital (≤139 patients per year), middle volume hospital (140–279 patients per year), and high volume hospital (≥280 patients per year).

The time course of resuscitation was collected as follows: time of EMS call, hospital arrival, revascularization, and ROSC. We collected the time of ROSC in detail. ROSC in the pre-hospital setting was defined as the Utstein style [21,22]. ROSC in the in-hospital setting was defined as the resumption of a sustained heart rhythm and continuous palpable pulse for >30 s. The time of the first ROSC was defined as the time of first ROSC during resuscitation, regardless of the pre-hospital or in-hospital setting. Door-to-balloon time was used to measure the time to revascularization in patients with STEMI [10,11,23,24]. Traditionally, the time of “door” was defined as the time at which the patient arrived at the hospital [23]. However, with the development of pre-hospital emergency medicine, the definition of the term “door” has become ambiguous. The international guideline for STEMI recommended that the clock to revascularization be started at the time of STEMI diagnosis using 12-lead electrocardiography [25]. Furthermore, the international guideline for CPR strongly recommended that 12-lead electrocardiography should be performed immediately after ROSC [15]. Therefore, the time of the first ROSC and that of the 12-lead electrocardiography were approximately the same. We used the time of the first ROSC as the starting point for our measurement.

The attending physician followed up all patients with OHCA and described their survival status and neurological outcome 1-month after cardiac arrest. Neurological outcomes were defined using a cerebral performance category (CPC) scale: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; and category 5, dead/brain-dead [26].

2.3. Primary and secondary outcome

The primary outcome of this study was 1-month survival with favorable neurological outcomes. A favorable neurological outcome was defined as a CPC score of 1 or 2 [26]. The secondary outcome was the 1-month survival.

2.4. Statistical analysis

Based on the time from the first ROSC to revascularization, we divided patients into four groups: (a) time from the first ROSC to revascularization ≤60 min, (b) 61–90 min, (c) 91–120 min, or (d) >120 min. Patient characteristics, pre-hospital information, in-hospital information, and resuscitation time courses were statistically analyzed between groups with the use of $\chi 2$ test for categorical variables and Kruskal-Wallis test for continuous variables.

The primary and secondary outcomes were analyzed using multivariable logistic regression analysis to calculate the unadjusted odds ratio (OR), adjusted OR, 95% confidence interval (CI), and *P* for trends. Based on previous studies [11,27], the multivariable logistic regression analysis was adjusted for several factors, including age (continuous variables), sex (male or female), bystander witness (yes or no), bystander CPR (yes or no), first documented rhythm at EMS arrival (ventricular fibrillation/pulseless ventricular tachycardia, pulseless electrical activity, asystole, or other), hospital volume (low, middle, or high), the presence of a pre-hospital physician (presence or absence), time from EMS call to hospital arrival (continuous variables), time from EMS call to the first ROSC (continuous variables), lactate at hospital arrival (continuous variables), pH at hospital arrival (continuous variables), and targeted temperature management (yes or no). We described the nonlinear relationship between the predictive probability of a 1-month favorable neurological outcome and the time from the first ROSC to revascularization using a restricted cubic spline with univariable logistic regression models.

We also performed multivariable logistic regression analysis to estimate the association between the probability of a 1-month favorable neurological outcome and the time from EMS call to revascularization or time from hospital arrival to revascularization.

All statistical analyses were performed using EZR version 1.54 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), R Statistical software (version 4.2.1; The R Foundation for Statistical Computing, Vienna, Austria), and JMP version 14.2 software (SAS, Cary, NC). EZR is a graphical user interface for the R Statistical software [28]. All tests were two-sided, and P values <0.05 were defined as statistically significant.

3. Results

3.1. Study population and characteristics

From June 1, 2014, to December 31, 2020, 68,110 patients with OHCA were registered in the JAAM-OHCA registry. After applying the exclusion criteria, 547 patients who experienced OHCA due to STEMI and underwent primary PCI were included in the study (Fig. 1).

Table 1 presents the patient characteristics and pre/in-hospital information. We divided the 547 patients into the following four groups according to the time from the first ROSC to revascularization: (a) time from the first ROSC to revascularization ≤60 min (n = 86), (b) 61–90 min (n = 147), (c) 91–120 min (n = 121), or (d) >120 min (n = 193).

3.2. Resuscitation time courses

Table 2 presents the resuscitation time course. The median time from the first ROSC to revascularization in the study population was 100 min (IQR: 74–142 min). The median time from EMS call to revascularization and time from hospital arrival to revascularization differed significantly among the groups ($P < 0.001$).

3.3. Primary and secondary outcomes

Table 3 presents the primary and secondary outcomes according to the time from the first ROSC to revascularization. The proportion of 1-month favorable neurological outcomes was 63/86 (73.3%) in the time from the first ROSC to revascularization ≤60 min group, 96/147 (65.3%) in the 61–90 min group, 66/121 (54.5%) in the 91–120 min

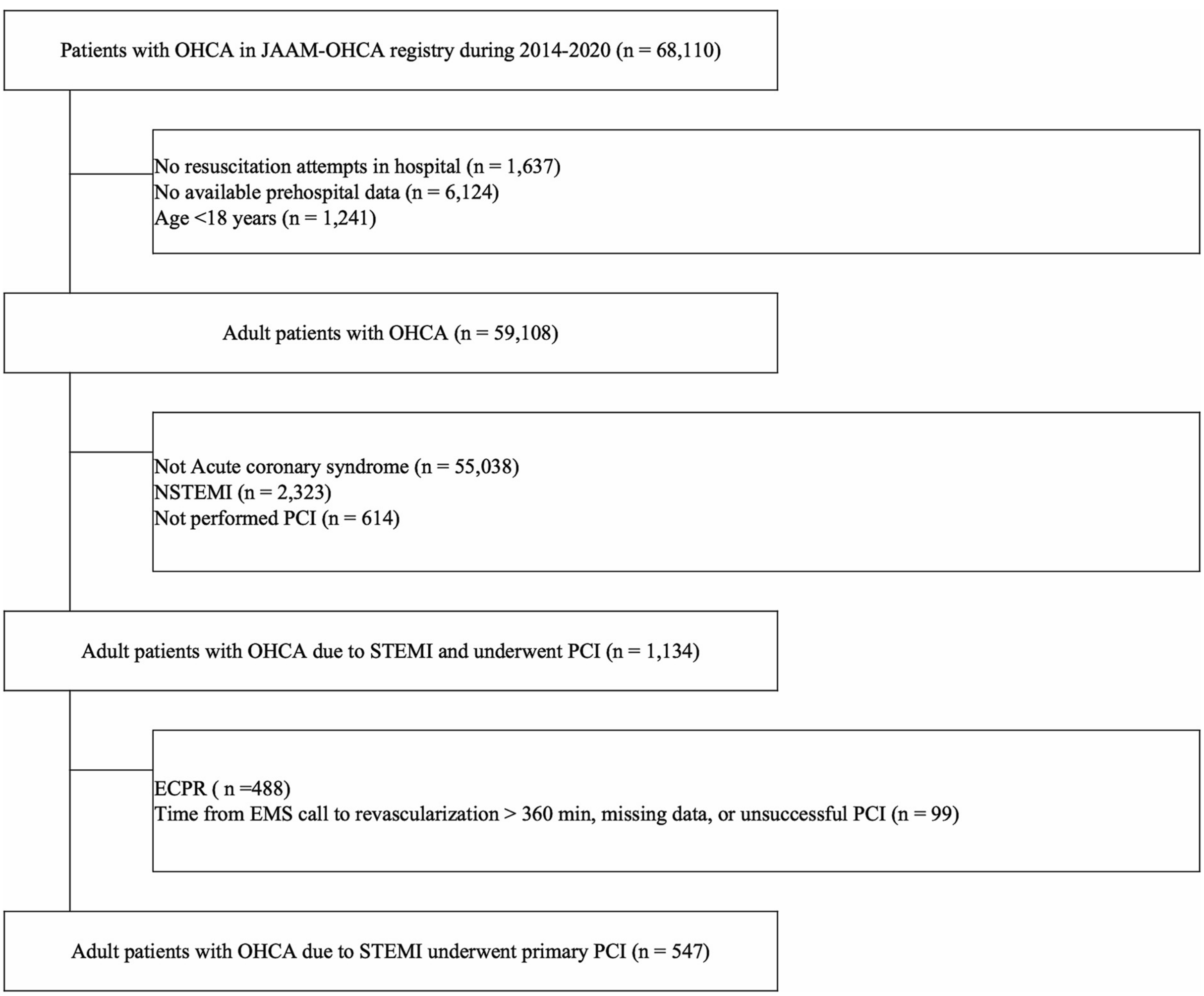

Fig. 1. Flowchart of patient inclusion in this study.
The diagram shows all enrolled patients from the Japanese Association for Acute Medicine - out-of-hospital cardiac arrest (JAAM-OHCA) registry between June 1, 2014, and December 31, 2020, in Japan.
ECPR = extracorporeal cardiopulmonary resuscitation; JAAM-OHCA = Japanese Association for Acute Medicine - out-of-hospital cardiac arrest; NSTEMI = non-ST-segment-elevation myocardial infarction; OHCA = out-of-hospital cardiac arrest; PCI = percutaneous coronary intervention; STEMI = ST-segment-elevation myocardial infarction.

Table 1
Patient characteristics.

	Total	Time from the first ROSC to revascularization				*P* value
		≤60 min	61–90 min	91–120 min	>120 min	
	n = 547	*n* = 86	*n* = 147	*n* = 121	*n* = 193	
Age, median (Q1-Q3)	67 (57–75)	65 (53–73)	68 (56–76)	67 (59–74)	67 (58–77)	0.115
Male, n (%)	456 (83.4)	78 (90.7)	120 (81.6)	101 (83.5)	157 (81.3)	0.239
Pre-hospital information						
Bystander witness, n (%)	435 (79.5)	67 (77.9)	122 (83.0)	88 (72.7)	158 (81.9)	0.151
Bystander CPR, n (%)	284 (51.9)	45 (52.3)	74 (50.3)	64 (52.9)	101 (52.3)	0.976
Shocked by public-accessed AED, n (%)	89 (16.3)	14 (16.3)	19 (12.9)	15 (12.4)	41 (21.2)	0.109
First documented rhythm at EMS arrival, n (%)						0.016
VF/pVT	340 (62.2)	56 (65.1)	99 (67.3)	81 (66.9)	104 (53.9)	
PEA	74 (13.5)	8 (9.3)	22 (15.0)	10 (8.3)	34 (17.6)	
Asystole	39 (7.1)	4 (4.7)	4 (2.7)	9 (7.4)	22 (11.4)	
Other	94 (17.2)	18 (20.9)	22 (15.0)	21 (17.4)	33 (17.1)	
Pre-hospital physician presence, n (%)	124 (22.7)	26 (30.2)	31 (21.1)	29 (24.0)	38 (19.7)	0.250
Advanced airway management, n (%)	171 (31.3)	24 (27.9)	37 (25.2)	49 (40.5)	61 (31.6)	0.050
Intravenous fluid, n (%)	177 (32.4)	21 (24.4)	46 (31.3)	34 (28.1)	76 (39.4)	0.048
Adrenaline, n (%)	111 (20.3)	9 (10.5)	30 (20.4)	19 (15.7)	53 (27.5)	0.005
In-hospital information						
First documented rhythm at hospital arrival, n (%)						0.081
VF/pVT	66 (12.1)	19 (22.1)	15 (10.2)	14 (11.6)	18 (9.3)	
PEA	89 (16.3)	9 (10.5)	24 (16.3)	19 (15.7)	37 (19.2)	
Asystole	50 (9.1)	10 (11.6)	11 (7.5)	8 (6.6)	21 (10.9)	
ROSC	342 (62.5)	48 (55.8)	97 (66.0)	80 (66.1)	117 (60.6)	
TTM, n (%)	297 (54.3)	49 (57.0)	74 (50.3)	66 (54.5)	108 (56.0)	0.707
IABP, n (%)	185 (33.8)	31 (36.0)	45 (30.6)	44 (36.4)	65 (33.7)	0.749
Arterial blood gases data at hospital arrival, median (Q1-Q3)						
pH	7.22 (7.05–7.32)	7.22 (7.03–7.30)	7.24 (7.08–7.33)	7.24 (7.12–7.32)	7.17 (7.02–7.31)	0.091
Lactate (mg/dL)	80.1 (51.0–106.9)	69.8 (47.8–101.7)	82.8 (54.0–101.3)	76.5 (47.0–104.4)	84.6 (51.9–109.9)	0.519
Institution information						
Hospital volume according to annual number of patients with OHCA, n (%)						0.281
Low volume ≤139 patients per year	202 (36.9)	31 (36.0)	55 (37.4)	35 (28.9)	81 (42.0)	
Middle volume 140–279 patients per year	161 (29.4)	29 (33.7)	40 (27.2)	43 (35.5)	49 (25.4)	
High volume ≧280 patients per year	184 (33.6)	26 (30.2)	52 (35.4)	43 (35.5)	63 (32.6)	

AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; EMS = emergency medical services; IABP = intra aortic balloon pumping; OHCA = out-of-hospital cardiac arrest; PEA = pulseless electric activity; pVT = pulseless ventricular tachycardia; ROSC = return of spontaneous circulation; TTM = targeted temperature management; VF = ventricular fibrillation.

group, and 98/193 (50.8%) in the >120 min group. In the univariable and multivariable analyses, a shorter time from the first ROSC to revascularization was significantly associated with an increased probability of 1-month favorable neurological outcomes (i.e., patients in the time from the first ROSC to revascularization ≤60 min vs. patients in the time from the first ROSC to revascularization >120 min; adjusted OR, 0.26; 95% CI, 0.11–0.56; *P* for trend, 0.015) (Table 3 and Fig. 2).

Table 4 presents the association between the 1-month neurological outcomes and the time from EMS call to revascularization and time from hospital arrival to revascularization. In the multivariable logistic regression analyses, a decrease in the proportion of 1-month favorable neurological outcomes was significantly associated with a longer time from EMS call to revascularization and time from hospital arrival to revascularization.

4. Discussion

In this retrospective analysis of a nationwide registry in Japan, we found that a shorter time from the first ROSC to revascularization was significantly associated with an increase in the probability of 1-month favorable neurological outcomes. Our findings imply that physicians may increase the probability of 1-month favorable neurological outcomes by minimizing the time to revascularization among patients with OHCA due to STEMI, even among those treated in accordance with the guidelines.

Recent international guidelines for CPR recommend emergency coronary angiography to perform immediate PCI in patients after OHCA with a suspected cardiac cause of arrest and ST-segment elevation on 12-lead electrocardiography [15,16]. A previous retrospective study

Table 2
Resuscitation times.

	Total	Time from the first ROSC to revascularization				*P* value
		≤60 min	61–90 min	91–120 min	>120 min	
	n = 547	*n* = 86	*n* = 147	*n* = 121	*n* = 193	
Resuscitation times						
Time from EMS call to hospital arrival (min), median (Q1-Q3)	30 (24–37)	28 (23–35)	30 (24–37)	30 (24–37)	30 (25–39)	0.229
Time from EMS call to the first ROSC (min), median (Q1-Q3)	22 (14–32)	24 (17–34)	21 (15–32)	20 (12—30)	22 (14–32)	0.232
Time from EMS call to revascularization (min), median (Q1-Q3)	126 (95–166)	72 (64–81)	100 (92–110)	127 (115–135)	180 (161–221)	<0.001
Time from hospital arrival to revascularization (min), median (Q1-Q3)	91 (63–134)	43 (36–50)	70 (59–80)	95 (85–104)	147 (126–182)	<0.001
Time from the first ROSC to revascularization (min), median (Q1-Q3)	100 (74–142)	49 (40–54)	77 (69–84)	105 (97–112)	157 (140–186)	<0.001

EMS = emergency medical services; ROSC = return of spontaneous circulation.

Table 3
Primary and secondary outcome.

	Number of cases, n (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
1-month favorable neurological outcome (CPC 1 or 2)			
Time from the first ROSC to revascularization ≤60 min	63/86 (73.3)	Ref	Ref
Time from the first ROSC to revascularization 61–90 min	96/147 (65.3)	0.69 (0.38–1.23)	0.50 (0.22–1.11)
Time from the first ROSC to revascularization 91–120 min	66/121 (54.5)	0.44 (0.24–0.80)	0.21 (0.09–0.50)
Time from the first ROSC to revascularization >120 min	98/193 (50.8)	0.38 (0.21–0.66)	0.26 (0.11–0.56)
P for trend[b]		0.001	0.015
1-month survival			
Time from the first ROSC to revascularization ≤60 min	71/86 (82.6)	Ref	Ref
Time from the first ROSC to revascularization 61–90 min	116/147 (78.9)	0.79 (0.39–1.58)	0.52 (0.20–1.32)
Time from the first ROSC to revascularization 91–120 min	99/121 (81.8)	0.95 (0.46–1.96)	0.74 (0.26–2.06)
Time from the first ROSC to revascularization >120 min	141/193 (73.1)	0.57 (0.30–1.09)	0.41 (0.16–0.98)
P for trend[b]		0.050	0.074

CI = confidence interval; CPC = cerebral performance category; CPR = cardiopulmonary resuscitation; EMS = emergency medical services; OR = odds ratio; ROSC = return of spontaneous circulation.

[a] Adjusted for Age, Sex, Bystander witness, Bystander CPR, First documented rhythm at EMS arrival, Hospital volume, Pre-hospital physician presence, Time from EMS call to hospital arrival, Time from EMS call to the first ROSC, Lactate at hospital arrival, pH at hospital arrival, Targeted temperature management.

[b] Time from the first ROSC to revascularization as continuous variable.

reported that the time from the onset of symptoms or cardiac arrest to revascularization was significantly higher in patients with OHCA due to STEMI with primary PCI who died than in those who survived [27]. However, the previous study included only a small number of patients and did not adjust for confounding factors. Thus, we enrolled enough patients to gain statistical power to detect significant differences. Another retrospective study showed the effect of the time from medical contact to revascularization in patients with STEMI presenting with cardiogenic shock and/or OHCA [19]. This previous study reported that a shorter time from medical contact to revascularization was associated with fewer adverse outcome. However, this study may have confounding factors that affected the outcomes. First, this study did not examine the time from ROSC to revascularization but from medical contact to revascularization. A longer time to ROSC was significantly associated with decreased favorable neurological outcomes and survival rates among patients with OHCA [29,30]. To minimize the effect of this confounding factor, we assessed the association between outcomes and the time from the first ROSC to revascularization. Second, this study did not adjust for the time to ROSC, which was an important confounding factor. Therefore, we adjusted for the time from EMS call to the first ROSC in the multivariable logistic regression analysis. Our study was based on these previous studies and extended them by demonstrating the impact of earlier revascularization, adjusting for confounding factors in a multivariable logistic analysis in a large cohort of patients with OHCA due to STEMI.

The decreased probability of 1-month survival associated with a longer time to revascularization among patients after OHCA due to STEMI was consistent with the pathophysiological models of acute myocardial infarction. The importance of early revascularization in patients with STEMI is based on the concept that a shorter time to revascularization may reduce impaired cardiac function, ventricular arrhythmias, comorbidities, and mortality [9,31]. In animal models of myocardial infarction, a longer time to revascularization may result in large myocardial necrosis because of the longer time of cardiac ischemia [32]. A previous study on patients with STEMI showed that the myocardial infarct size was associated with a longer time to revascularization [33]. Larger myocardial necrosis can lead to impaired cardiac function, arrhythmias, and increased mortality [31]. Using these findings on rapid revascularization for acute myocardial infarction without cardiac arrest, rapid revascularization could have potential for pathophysiological benefits in acute

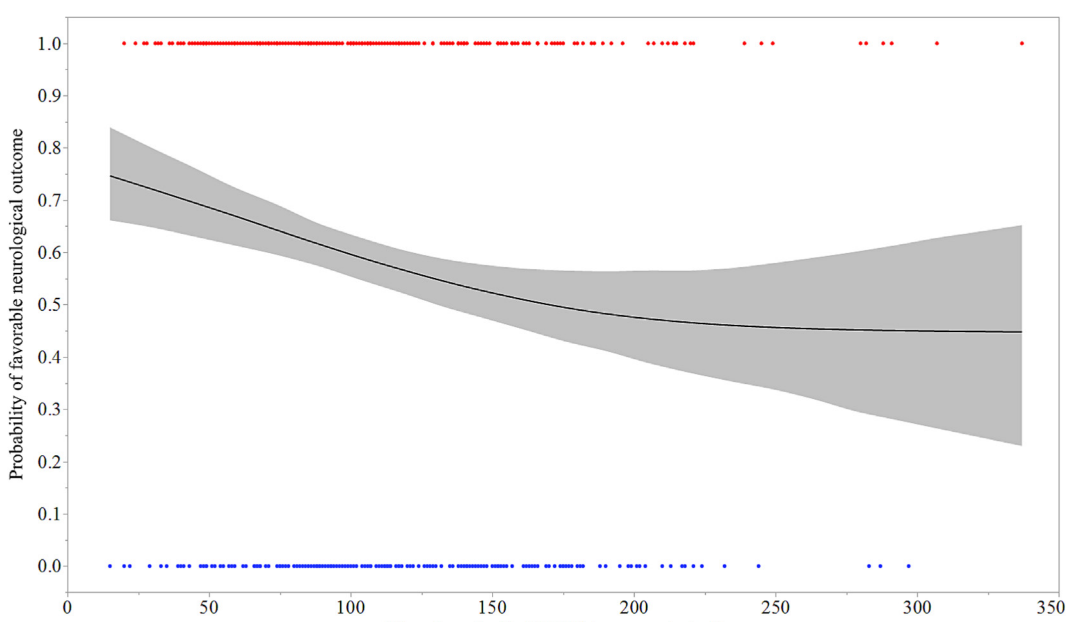

Fig. 2. Probability of favorable neurological outcomes by time to revascularization.

Table 4
1-month favorable neurological outcome according to resuscitation time.

	Number of cases, n (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Time from EMS call to revascularization			
1-month favorable neurological outcome (CPC 1 or 2)			
Time from EMS call to revascularization ≤90 min	93/117 (79.5)	Ref	Ref
Time from EMS call to revascularization 91–120 min	94/139 (67.6)	0.54 (0.30–0.96)	0.49 (0.23–1.02)
Time from EMS call to revascularization 121–150 min	62/116 (53.4)	0.30 (0.16–0.53)	0.33 (0.15–0.71)
Time from EMS call to revascularization >150 min	74/175 (42.3)	0.19 (0.11–0.33)	0.23 (0.11–0.48)
P for trend[b]		<0.001	0.015
1-month survival			
Time from EMS call to revascularization ≤90 min	103/117 (88.0)	Ref	Ref
Time from EMS call to revascularization 91–120 min	116/139 (83.5)	0.69 (0.33–1.40)	0.69 (0.28–1.71)
Time from EMS call to revascularization 121–150 min	92/116 (79.3)	0.52 (0.25–1.07)	0.79 (0.30–2.05)
Time from EMS call to revascularization >150 min	116/175 (66.3)	0.27 (0.14–0.51)	0.42 (0.18–0.98)
P for trend[b]		<0.001	0.074
Time from hospital arrival to revascularization			
1-month favorable neurological outcome (CPC 1 or 2)			
Time from hospital arrival to revascularization ≤60 min	100/130 (76.9)	Ref	Ref
Time from hospital arrival to revascularization 61–90 min	92/139 (66.2)	0.59 (0.34–1.01)	0.58 (0.27–1.19)
Time from hospital arrival to revascularization 91–120 min	61/114 (53.5)	0.35 (0.19–0.60)	0.31 (0.14–0.66)
Time from hospital arrival to revascularization >120 min	70/164 (42.7)	0.22 (0.13–0.38)	0.31 (0.15–0.63)
P for trend[b]		<0.001	0.015
1-month survival			
Time from hospital arrival to revascularization ≤60 min	112/130 (86.2)	Ref	Ref
Time from hospital arrival to revascularization 61–90 min	116/139 (83.5)	0.81 (0.41–1.58)	1.02 (0.42–2.44)
Time from hospital arrival to revascularization 91–120 min	89/114 (78.1)	0.57 (0.29–1.11)	0.75 (0.30–1.85)
Time from hospital arrival to revascularization >120 min	110/164 (67.1)	0.33 (0.18–0.60)	0.60 (0.27–1.33)
P for trend[b]		<0.001	0.074

CI = confidence interval; CPC = cerebral performance category; CPR = cardiopulmonary resuscitation; EMS = emergency medical services; OR = odds ratio; ROSC = return of spontaneous circulation.

[a] Adjusted for Age, Sex, Bystander witness, Bystander CPR, First documented rhythm at EMS arrival, Hospital volume, Pre-hospital physician presence, Time from EMS call to hospital arrival, Time from EMS call to the first ROSC, Lactate at hospital arrival, pH at hospital arrival, Targeted temperature management.

[b] Time from the first ROSC to revascularization as continuous variable.

myocardial infarction with cardiac arrest. In animal models of cardiac arrest due to acute myocardial infarction, early revascularization has been associated with a smaller myocardial infarct size and better cardiac function [34]. Among patients with OHCA, myocardial dysfunction may contribute to increased mortality [35]. Thus, our findings imply that immediate revascularization have the potential to prevent myocardial ischemia and improve clinical outcomes in patients with OHCA caused by STEMI. This hypothesis is consistent with the results of a previous observational study showing that a higher percentage of TIMI 3 flow grade was associated with reduced mortality among patients with OHCA due to STEMI and those who underwent primary PCI [27].

Our findings highlight the importance of reducing the time to revascularization in patients with OHCA due to STEMI. The increased probability of 1-month favorable neurological outcomes associated with a shorter time to revascularization among patients with OHCA due to STEMI in our study is consistent with the results of previous studies [11,24,36]. Among patients with STEMI without OHCA, door-to-balloon time was used as a measure of time to revascularization. Particularly, the 90 min door-to-balloon time has traditionally been the benchmark target time for revascularization as a quality measurement [37]. Achieving a door-to-balloon time < 90 min contributes to improved mortality in patients with STEMI. Although we did not demonstrate a benchmark time as a door-to-balloon time of 90 min, we described the nonlinear relationship between a longer time to revascularization and the reduced predictive probability of 1-month favorable neurological outcomes. Our nonlinear relationships are consistent with those reported in a previous study on patients with STEMI [11]. Moreover, our study estimated the association between clinical outcomes and several resuscitation times, including the time from the EMS call to revascularization, and time from hospital arrival to revascularization. We found an association between 1-month favorable neurological outcomes and a shorter time to revascularization, regardless of the starting time to revascularization. Our findings suggest the necessity to shorten the time to revascularization by even one minute at every moment during resuscitation among patients with OHCA due to STEMI. This strategy of shortening the time to revascularization may have the potential to improve clinical outcomes in patients with OHCA due to STEMI.

Our results showed the differences of approximately 20% between the probability of 1-month favorable neurological outcome and survival. The differences were much larger than the results of previous studies about OHCA due to STEMI in western countries [8,18]. The larger differences in our study were consistent with the results of previous studies among patients with OHCA underwent invasive treatment using the JAAM-OHCA registry [38-40]. There were several reasons for this finding. First, the overall CPR duration in Japan was much longer than other countries [29]. This study showed that the longer CPR duration was associated with worse neurological outcomes in patients with OHCA. Second, Japanese physicians often continued treatment for patients with OHCA predicting survival expected but worse neurological outcomes. Previous study described that Japanese physician did not tend to prefer to withhold or withdraw life-sustaining treatment in patients, although Japanese guidelines for end-of-life care described the decision-making process for withholding or withdrawing life-sustaining treatment [41].

This study had some limitations. First, this study did not include patient information such as medical history, medications, and social history. In addition, this study did not have cardiovascular data such as angiography findings, types of devices, procedural duration, and sites of infarction, which might affect mortality and favorable neurological outcomes. Second, 12-lead electrocardiography was recorded immediately after ROSC in not all patients. Third, the JAAM-OHCA registry included only patients who received treatment at participating institutions in Japan. Our findings may not be applicable to other countries.

5. Conclusions

Using a multicenter nationwide registry in Japan, we demonstrated that a shorter time to revascularization was associated with a decreased proportion of the 1-month survival with favorable neurological outcomes among patients with OHCA due to STEMI who underwent primary PCI. This strategy of ensuring a shorter time to revascularization has the potential to improve clinical outcomes in patients with OHCA and STEMI.

Institutional review board statement

This study protocol was approved by the Institutional Review Board of each participating hospital.

Informed consent statement

The study protocol was approved by the institutional review board of each participating hospital. Patient consent was waived due to the observational study and de-identification of personal data.

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CRediT authorship contribution statement

Satoshi Nakajima: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tasuku Matsuyama:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Kenji Kandori:** Writing – review & editing, Methodology. **Asami Okada:** Writing – review & editing, Methodology. **Yohei Okada:** Writing – review & editing, Methodology. **Tetsuhisa Kitamura:** Writing – review & editing, Methodology. **Bon Ohta:** Supervision, Project administration.

Data availability

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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