

## Outcomes of survivors of ST-segment elevation myocardial infarction complicated by out-of-hospital cardiac arrest: a single-center surveillance study

### Hastane dışı kardiyak arrest ile komplike olmuş sağ kalan ST-segment yükselmeli miyokart enfarktüsü hastalarının sonuçları: Tek merkezli sağkalım çalışması

Yalçın Velibey, M.D., Emre Can Parsova, M.D., Ufuk Sadık Ceylan, M.D., Özge Güzelburc, M.D., Koray Demir, M.D., Ufuk Yıldız, M.D., Aylın Şafak, M.D., Evliya Akdeniz, M.D., Tolga Sinan Güvenç, M.D., Emrah Bozbeyoğlu, M.D., Ahmet İlker Tekkeşin, M.D.

Department of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery, Training and Research Hospital, İstanbul, Turkey

#### ABSTRACT

**Objective:** The aim of the present study was to evaluate in-hospital and long-term outcomes of ST-segment elevation myocardial infarction (STEMI) survivors who experienced out-of-hospital cardiac arrest (OHCA) and underwent primary percutaneous coronary intervention (PCI) at a high-volume center within the STEMI network.

**Methods:** The records of 2681 consecutive STEMI patients who underwent primary PCI between January 2009 and December 2014 at a single center in the STEMI network were retrospectively analyzed. Patients with STEMI complicated by OHCA were compared with a reference group of STEMI patients who did not experience OHCA.

**Results:** Compared with STEMI survivors without OHCA (n=2587, 96.5%), the frequency of anterior myocardial infarction, duration of hospitalization, rate of in-hospital major adverse cardiovascular and cerebrovascular events, and the incidence of ischemic cerebrovascular disease and major bleeding during in-hospital follow-up were significantly greater in those with OHCA (n=94, 3.5%). The distribution of age and gender was similar between the 2 groups. The primary PCI success rate was high and was similar in both groups. In-hospital mortality was significantly higher (18.1% vs. 1.5%; p<0.001) and survival at the 12<sup>th</sup> and 60<sup>th</sup> months was lower (74.5% vs. 96.5%; p<0.001 and 71.3% vs. 93.7%; p<0.001) in STEMI survivors with OHCA. OHCA was an independent predictor for in-hospital mortality (Odds ratio [OR]: 3.413; 95% confidence interval [CI]: 1.534–7.597; p=0.003) and all-cause mortality at 60 months (OR: 3.285; 95% CI: 2.020–5.340; p<0.001).

**Conclusion:** Mortality was high in patients with STEMI complicated by OHCA, even though PCI was performed with the same success rate seen in patients without OHCA.

#### ÖZET

**Amaç:** Bu çalışma hastane dışında kardiyak arrest olmuş (HDKA) ve yüksek volümlü tek bir merkezin ST-segment yükselmeli miyokart enfarktüsü (STYME) ağı içerisinde primer perkütan koroner girişim (PKG) yapılmış STYME hastalarından sağ kalanların hastane içi ve uzun dönem sonuçlarını araştırmayı amaçlamıştır.

**Yöntemler:** Ocak 2009 ile Aralık 2014 arasında tek bir merkezin STYME ağı içerisinde STYME ile hastaneye başvurmuş ve primer PKG uygulanmış 2681 hastayı geriye dönük olarak inceledik. HDKA ile komplike olmuş STYME hastaları ile HDKA olmamış referans STYME hasta grubu karşılaştırıldı.

**Bulgular:** Hastane dışında kardiyak arrest olan STYME sağ kalanlarında (2587, %96.5), HDKA olmayanlara (94, %3.5) göre anterior miyokart enfarktüsü, hastanede yatış süresi, hastane içi majör istenmeyen kardiyovasküler ve serebrovasküler olay (MACCE) oranları, hastane içi takipte iskemik serebrovasküler hastalık ve majör kanama belirgin olarak yüksek saptandı. Yaş ve cinsiyet dağılımı her iki grupta benzerdi. Primer PKG başarı oranı her iki grupta da benzer ve yüksek bulundu. HDKA olan STYME hastalarında hastane içi mortalite belirgin olarak yüksek (%18.1'e karşı %1.5, p<0.001) iken 12. ve 60. aylardaki sağ kalım oranı düşük (%74.5 ve %96.5, p<0.001 ile %71.3 ve %93.7, p<0.001) saptandı. HDKA'nın hastane içi mortalitenin (Odds oranı [OO]: 3.413, Güven aralığı [GA] %95: 1.534–7.597, p=0.003) ve 60. aydaki tüm nedenlere bağlı mortalitenin (OO: 3.285, %95 GA: 2.020–5.340, p<0.001) bağımsız bir öngördürücüsü olduğu saptanmıştır.

**Sonuç:** Hastane dışında kardiyak arrest ile komplike olmuş STYME hastalarında, HDKA olmayanlarla aynı başarı oranı ile PKG yapılmış olsa da, mortalite fazladır.

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Correspondence: Dr. Yalçın Velibey. Dr. Siyami Ersek Göğüs Kalp ve Damar Cerrahisi Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İstanbul, Turkey.

Tel: +90 216 - 542 44 44 e-mail: yalchinvelibey@gmail.com

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Each year, 360,000–400,000 people have an out-of-hospital cardiac arrest (OHCA) in the United States.<sup>[1,2]</sup> Acute myocardial infarction (MI) is a common precipitant of OHCA, with nearly 50% of resuscitated OHCA patients having an acutely occluded coronary vessel on coronary angiography.<sup>[3]</sup> Acute ST-segment elevation MI (STEMI) is a major manifestation of coronary artery disease (CAD) that constitutes approximately two-thirds of all acute coronary events.<sup>[3]</sup> Primary percutaneous coronary intervention (pPCI) is the preferred treatment modality for STEMI patients, but the hospital must be capable of performing pPCI or it must be possible to transfer the patient to a pPCI-capable hospital within 60 to 90 minutes.<sup>[4,5]</sup> Recent advances in the care of STEMI patients with OHCA include a more liberal consideration of emergent coronary angiography and pPCI and early initiation of targeted temperature management.<sup>[6–9]</sup> Data on the long-term prognosis of patients with acute STEMI complicated by an OHCA are limited because these patients are most often excluded from large interventional trials.<sup>[10–12]</sup> A few studies have evaluated the outcomes of patients with STEMI and OHCA treated with contemporary PCI approaches and they indicate that early reperfusion strategies may be associated with better survival. Most of these studies are retrospective and have suggested that patients with STEMI resuscitated in the emergency department should be seriously considered for emergent angiography and revascularization, regardless of neurological status.<sup>[13–18]</sup>

The aim of this retrospective analysis was to study short and long-term outcomes of STEMI survivors with OHCA who underwent pPCI at a single center within the STEMI network in Turkey and to compare the results with those of earlier studies.

## METHODS

### Study design and patient selection

Clinical parameters, in-hospital data, 1-year and 5-year outcomes of all consecutive patients treated with pPCI after a witnessed OHCA (i.e., occurring in the presence of a bystander) or OHCA that had not been witnessed, were analyzed. The results were compared with those of other patients who presented during the same time period without cardiac arrest and underwent pPCI for STEMI at our center. A total of 2700 patients diagnosed with STEMI at a single institution

between January 2009 and December 2014 were scanned retrospectively. None of the patients had received pre-hospital thrombolysis. The time delay from cardiac arrest until the initiation of advanced cardio-pulmonary life support was

#### Abbreviations:

CAD	Coronary artery disease
CI	Confidence interval
CPC	Cerebral Performance Category
ECG	Electrocardiogram
MACCE	Major adverse cardiac and cerebrovascular events
MI	Myocardial infarction
OHCA	Out-of-hospital cardiac arrest
OR	Odds ratio
PCI	Percutaneous coronary intervention
pPCI	Primary percutaneous coronary intervention
ROSC	Return of spontaneous circulation
STEMI	ST-segment elevation MI
TIMI	Thrombolysis In Myocardial Infarction

not determined due to the inclusion of unwitnessed OHCA cases in the study population. All ambulances are staffed with trained paramedics. A return of spontaneous circulation (ROSC) was obtained in all of the patients before performance of pPCI. Patient records and electrocardiograms (ECGs) were carefully reviewed by cardiologists to confirm the diagnosis of STEMI, which was defined as: *i*) recorded prolonged (>30 minutes) symptoms, such as chest pain or dyspnea at presentation compatible with STEMI; *ii*) typical ECG changes consistent with new ST segment elevation; *iii*) a troponin value greater than the 99th upper reference limit. The criteria for ECG patterns consistent with ST elevation were a new ST elevation at the J point in 2 contiguous leads using the cut-points of  $\geq 0.1$  mV in all leads, with the exception of V2–V3, where the following cut-points were applied:  $\geq 0.2$  mV in men  $\geq 40$  years of age and  $\geq 0.25$  mV in men  $< 40$  years; or  $\geq 0.15$  mV in women or new or presumed new onset left bundle branch block.<sup>[19]</sup> The patients included in the present analysis underwent percutaneous angioplasty, with or without stent implantation, to examine at least one major coronary artery. As an institutional protocol, all STEMI patients underwent pPCI within the first 12 to 24 hours after the onset of persistent chest pain and all patients received 300 mg acetyl salicylic acid and a 300–600 mg oral loading dose of clopidogrel or an equivalent loading dose of prasugrel/ticagrelor (loading doses of antiplatelet drugs were administered by nasogastric tube to patients who had OHCA), along with standard weight-adjusted intravenous bolus unfractionated heparin (70–100 U/kg for those who were treated with glycoprotein IIb/IIIa inhibitors 50–60 U/kg) before the coronary intervention. The addition of a glycoprotein

IIb-IIIa inhibitor (12.5 mg/50 mL tirofiban [Aggrastat; Medicure Pharma, Inc., Somerset, NJ, USA]) to the antiplatelet regimen was not standard and was left to the surgeon's discretion per institutional protocol, and these data were also recorded. Statin therapy was not provided as a loading dose before the procedure, but was initiated within 24 hours after the procedure. The exclusion criteria were: patients aged <18 years, and those who were pregnant or were breastfeeding, patients who died before emergency coronary angiography, those who received fibrinolytics and did not undergo pPCI, those who were managed medically or not treated with balloon angiography or stenting after emergency angiography, and those with an ST-segment elevation not due to myocardial infarction. In all, 19 patients were excluded, and the data of 2681 patients were eligible for analysis. The demographic, clinical, echocardiographic, angiographic, and laboratory data, as well as the time of initial admission, time of intervention, and in-hospital outcomes were retrieved from institutional electronic medical records and recorded for statistical analysis. All of the data regarding hospital outcomes were verified either by calling each patient by phone or by personal interview. This study was carried out according to the principles of the Declaration of Helsinki, and was approved by the institutional ethics committee.

### Definitions

Patients with OHCA were identified after evaluation by trained paramedics of 112 emergency medical services or emergency department personnel as either: 1) having received attempts at external defibrillation (by lay responders or emergency personnel) or chest compressions by organized emergency medical services or emergency department personnel, or 2) being pulseless, but not having received attempts at defibrillation or cardiopulmonary resuscitation by trained paramedics in the ambulance or emergency medical services personnel. The records of routine biochemical analyses and complete blood counts (if available) that were obtained on admission and every day after pPCI were retrieved from the medical record system. The patients were divided into 2 groups based on the experience of OHCA: STEMI patients with OHCA and STEMI patients without OHCA. Anemia was defined as a baseline hemoglobin value below 13 g/dL for men and 12 g/dL for women.<sup>[20]</sup> The presence of diabetes mellitus was defined as a previous diag-

nosis of diabetes or the use of antidiabetic agents at admission or having at least 2 fasting blood sugar measurements >126 mg/dL during hospitalization. Hypertension was defined as a previous diagnosis of hypertension, previous use of antihypertensive medications, or a systolic pressure  $\geq$ 140 mm Hg and/or a diastolic pressure  $\geq$ 90 mm Hg on at least 2 separate measurements during hospitalization 48 hours after the index event.<sup>[21,22]</sup> Left ventricular ejection fraction was measured as a part of a 2-dimensional echocardiographic examination performed regularly for all patients hospitalized with STEMI using the biplane Simpson method according to the recommendations of the American Society of Echocardiography.<sup>[23]</sup> Per institutional policy, echocardiography was performed for all STEMI patients within 48 hours after the initial hospitalization. A 2.5–3.5 MHz phased-array transducer and a GE Vivid 7 system (GE Healthcare, Inc. Chicago, IL, USA) were used. Systolic dysfunction was defined as left ventricular ejection fraction <40%. The Thrombolysis In Myocardial Infarction (TIMI) flow grade rate of the infarct-related artery was assessed visually by the operator and classified accordingly. Multi-vessel disease was defined as at least >50% stenosis in 2 or more major coronary arteries. The occurrence of cardiac free-wall rupture, ventricular septal rupture, or acute mitral regurgitation during in-hospital follow-up after pPCI was considered a mechanical complication. Major bleeding was defined according to the TIMI bleeding classification.<sup>[24]</sup> A composite of in-hospital mortality, nonfatal MI, and cerebrovascular accident was defined as an in-hospital major adverse cardiac and cerebrovascular events (MACCE). A cerebrovascular accident was defined as a new motor or sensory loss in a part of the body that could be transient or permanent. Hemorrhagic and ischemic stroke were classified based on computed tomography and diffusion magnetic resonance imaging findings. The outcomes of in-hospital MACCE rate, in-hospital mortality, and all-cause mortality at 1 year and 5 years post discharge were analyzed.

### Statistical analysis

IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) software was used to perform the statistical analysis. Continuous variables were presented as mean $\pm$ SD while categorical data were expressed as a percentage of the total. A one-way Kolmogorov-Smirnov test was used to determine

the pattern of distribution for continuous variables. An independent samples test (Student's t-test) was used for group comparisons of normally distributed continuous variables, and if the distribution was not normal, the Mann-Whitney U test was used. For categorical variables, comparisons were performed with a chi-square test and Fisher's exact test, as required. Kaplan-Meier charts were constructed for the in-hospital MACCE rate, in-hospital mortality, and the 12- and 60-month survival rate, and a log-rank test was used to assess whether the differences between curves was coincidental. Cox regression was used to determine independent predictors for in-hospital mortality and mortality at 60 months. All parameters with a significance level of 0.1 or less in the univariate analysis, or parameters that were  $p > 0.1$  and had been determined as predictive for mortality according to previous studies were included in a multivariate logistic regression

model. A 2-sided  $p < 0.05$  was considered significant in all comparisons. All of the data provided were within a 95% confidence interval (95% CI).

## RESULTS

### Patient characteristics

Baseline demographic and clinical data, and laboratory measurements of the whole study population are provided in Table 1. Renal function was poorer, and the levels of blood urea nitrogen, creatinine, and glucose, as well as the white blood cell and neutrophil counts were significantly higher in the OHCA group compared with the group without OHCA. Age and gender distributions were similar between the 2 groups. The history of PCI was significantly greater in patients without OHCA than in patients with OHCA; however,

**Table 1. Baseline demographics and laboratory measurements stratified in patients with ST-segment elevation myocardial infarction with and without out-of-hospital cardiac arrest**

Parameter	With OHCA (n=94, 3.5%)			Without OHCA (n=2587, 96.5%)			p
	n	%	Mean±SD	n	%	Mean±SD	
Demographic and clinical variables							
Age, years			56.3±13.1			56.9±11.6	0.659
Male gender	78	83		2157	83.4		0.919
Diabetes mellitus	19	20.2		531	20.5		0.941
Hypertension	28	29.8		734	28.4		0.765
Anemia*	22	23.4		629	24.3		0.840
Smoking	36	38.3		1011	39.1		0.879
Prior stroke	3	3.2		32	1.2		0.003
Prior CABG	1	1.1		71	2.7		0.322
Prior PCI	5	5.3		335	12.9		0.029
Laboratory findings							
White blood cell ( $\times 10^3 \text{ mm}^3$ )			17.6±8.0			12.0±3.8	<0.001
Hemoglobin (g/L)			13.7±1.9			13.7±1.7	0.924
Platelet ( $\times 10^3 \mu\text{L}$ )			259.1±73.4			239.9±71.2	0.002
Neutrophil ( $\times 10^3 \mu\text{L}$ )			14.5±7.6			9.3±3.6	<0.001
Monocyte ( $\times 10^3 \mu\text{L}$ )			0.8±0.5			0.7±0.5	0.003
Glucose (mg/dL)			210.0±118.2			155.5±77.3	<0.001
Blood urea nitrogen (mg/dL)			18.6±7.6			16.6±6.0	0.007
Creatinine (mg/dL)			1.1±0.5			0.9±0.3	<0.001
eGFR (mL/min/1.73 m <sup>2</sup> )			80.2±27.0			92.1±23.9	<0.001

\*: Haemoglobin <13 g/dL for men, <12 g/dL for women. OHCA: Out-of-hospital cardiac arrest; eGFR: Estimated glomerular filtration rate; CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention.

**Table 2.** Periprocedural characteristics and postprocedural in-hospital outcomes stratified by the presence of an out-of-hospital cardiac arrest in patients with ST-segment elevation myocardial infarction

Parameter	With OHCA (n=94, 3.5%)			Without OHCA (n=2587, 96.5%)			p
	n	%	Mean±SD	n	%	Mean±SD	
Procedural characteristics							
Anterior wall MI	58	61.7		1135	43.9		<0.001
Multivessel disease	16	17		494	19.1		0.615
Contrast media use (mL)			276.1±104.9			245.6±86.2	0.005
DES	7	7.4		178	6.9		0.832
BMS	80	85.1		1990	76.9		0.063
Stent length (mm)			3.2±0.4			3.1±0.7	0.160
Stent diameter (mm)			22.5±6.4			21.3±6.3	0.087
PTCA only	7	7.4		419	16.2		0.071
Postprocedural TIMI flow							
TIMI 3 flow	88	93.6		2422	93.6		
TIMI 0-2 flow	6	6.4		165	6.4		0.998
In-hospital outcomes							
Acute stent thrombosis	1	1.1		37	1.4		1.000
Duration of hospitalization (days)			11.0±15.7			7.4±5.4	0.004
LVEF (%)*			42.0±11.2			47.3±9.9	<0.001
Bleeding	7	7.4		28	1.1		
Major bleeding†	8	8.5		2	0.1		0.046
LVEF at 6 months			45.7±12.7			50.5±10.7	0.021
In-hospital MACCE rate	25	26.6		102	3.9		<0.001
In hospital mortality	17	18.1		39	1.5		<0.001
Post MI mechanical complication‡	1	1.1		10	0.4		0.325
Stroke following pPCI	3	3.2		8	0.3		0.006
Ischemic stroke following pPCI	3	3.2		6	0.2		0.003
Hemorrhagic stroke following pPCI	0	0		2	0.1		1.000

\*: Measured 48 hours after primary percutaneous coronary intervention.

†: Any intracranial bleeding (excluding microhemorrhage <10 mm evident only on gradient-echo magnetic resonance imaging), or clinically overt signs of hemorrhage associated with a drop in hemoglobin of ≥5 g/dL or a ≥15% absolute decrease in hematocrit, or fatal bleeding (bleeding that directly results in death within 7 days).

‡: The occurrence of cardiac free-wall rupture, ventricular septal rupture, or acute mitral regurgitation during in-hospital follow-up after primary percutaneous coronary intervention.

OHCA: Out-of-hospital cardiac arrest; MI: Myocardial infarction; DES: Drug-eluting stent; BMS: Bare-metal stent; PTCA: Percutaneous transluminal coronary angioplasty; TIMI: Thrombolysis in myocardial infarction; LVEF: Left ventricular ejection fraction; MACCE: Major adverse cardiac and cerebrovascular event; pPCI: Primary percutaneous coronary intervention.

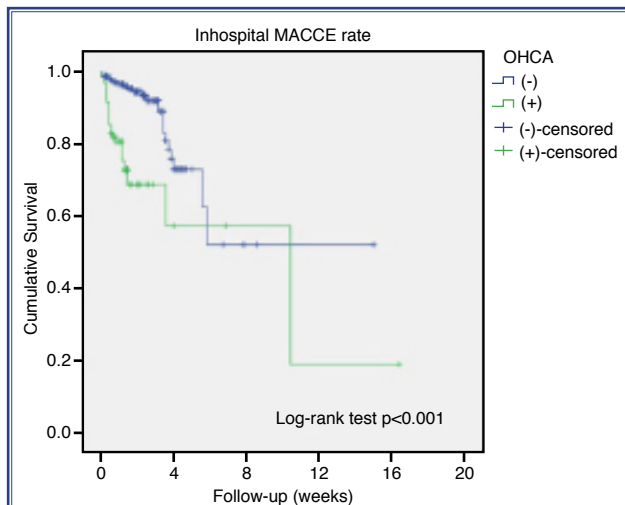
there were no differences concerning atherosclerotic risk factors between the groups. On the other hand, the stroke history was significantly higher in patients with OHCA than in patients without OHCA. Table 2 summarizes the periprocedural characteristics and in-hospital outcomes of the study groups. The rate of anterior MI, in-hospital MACCE, ischemic cerebrovascular disease, and major bleeding during in-hospital

follow-up, as well as the amount of contrast media used during pPCI and the duration of hospitalization were significantly higher in OHCA group. Importantly, no difference was noted in the postprocedural rate of TIMI 3 flow and acute stent thrombosis between groups. Ejection fraction following pPCI and at the sixth month were also significantly lower in patients with OHCA.

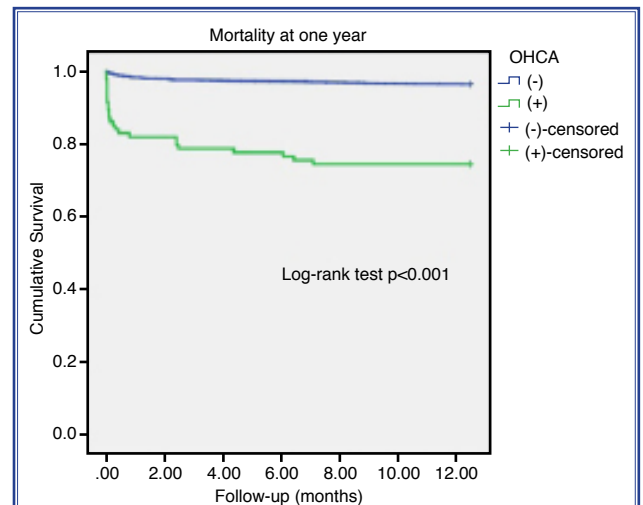
### Survival analysis and determinants of in-hospital mortality and long-term mortality

The Kaplan-Meier curves for the in-hospital MACCE rate, and the in-hospital and long-term survival expectations for the groups are shown in Figures 1-4. As shown in Figures 1 and 2, the rates of in-hospital MACCE and in-hospital mortality were significantly higher (26.6% vs. 3.9%,  $p<0.001$  for in-hospital MACCE rate; 18.1% vs. 1.5%,  $p<0.001$

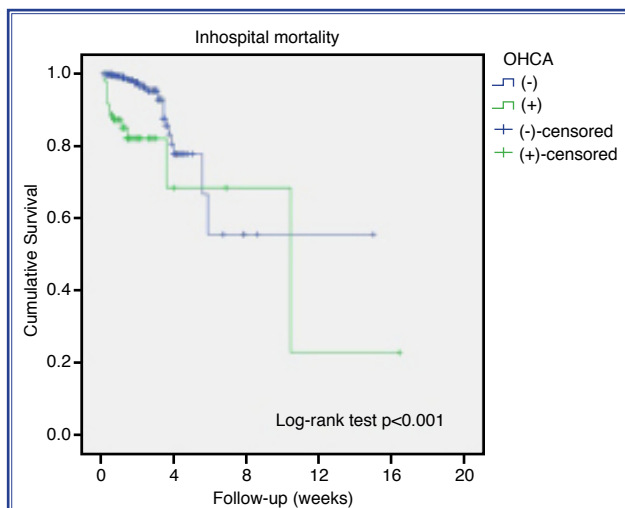
for in-hospital mortality) in the OHCA group. At 12 and 60 months, survival was also significantly lower (74.5% vs. 96.5%,  $p<0.001$  for 12 months; 71.3% vs. 93.7%,  $p<0.001$  for 60 months) in the OHCA group (Tables 3 and 4, Figs. 3 and 4). The median duration of long-term follow-up was  $46.1\pm 19.8$  months. Multivariate determinants of in-hospital mortality and mortality at 60 months are provided in Table 5. After adjustment for other variables, OHCA was determined to be an independent predictor for



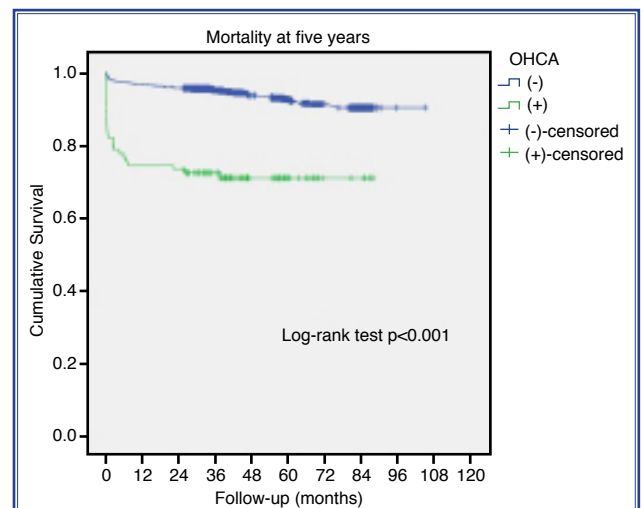
**Figure 1.** Kaplan-Meier plots indicating that the in-hospital major adverse cardiac and cerebrovascular (MACCE) rate curve for the out-of-hospital cardiac arrest (OHCA) group was significantly higher than that of the control group.



**Figure 3.** Kaplan-Meier plots indicating that the 12-month survival curve for the out-of-hospital cardiac arrest (OHCA) group was significantly lower than that of the control group.



**Figure 2.** Kaplan-Meier plots indicating that the in-hospital mortality rate curve for the out-of-hospital cardiac arrest (OHCA) group was significantly higher than that of the control group.



**Figure 4.** Kaplan-Meier plots indicating that the 60-month survival curve for the out-of-hospital cardiac arrest (OHCA) group was significantly lower than that of the control group.

**Table 3. Comparison of 12-month survival between ST-segment elevation myocardial infarction patients with and without out-of-hospital cardiac arrest**

	n	Exitus (n)	Survived (n)	Survival rate (%)	Mean survival time (month)
With OHCA	94	24	70	74.5	9.64±0.51
Without OHCA	2587	91	2496	96.5	12.13±0.37
Overall	2681	115	2566	95.7	12.04±0.41

OHCA: Out-of-hospital cardiac arrest; STEMI: Segment elevation myocardial infarction.

**Table 4. Comparison of 60-month survival between ST-segment elevation myocardial infarction patients with and without out-of-hospital cardiac arrest**

	n	Exitus (n)	Survived (n)	Survival rate (%)	Mean survival time (month)
With OHCA	94	27	67	71.3	63.72±3.94
Without OHCA	2587	163	2424	93.7	98.02±0.55
Overall	2681	190	2491	92.9	97.23±0.56

OHCA: Out-of-hospital cardiac arrest; STEMI: Segment elevation myocardial infarction.

**Table 5. Predictors of in-hospital mortality and mortality at 60 months**

Parameter	Predictors of in-hospital mortality		Parameter	Predictors of mortality at 60 months	
	OR (95% CI)	p		OR (95% CI)	p
Age (years)	1.077 (1.046–1.109)	<0.001	Age (years)	1.058 (1.042–1.074)	<0.001
Diabetes mellitus	0.795 (0.396–1.594)	0.518	Diabetes mellitus	0.991 (0.719–1.366)	0.955
Hypertension	2.565 (1.308–5.030)	0.006	Hypertension	1.137 (0.788–1.640)	0.493
Smoking	1.155 (0.595–2.242)	0.669	Smoking	1.211 (0.879–1.669)	0.242
Prior CABG	0.826 (0.513–1.754)	0.652	Prior CABG	0.909 (0.415–1.991)	0.812
Prior PCI	1.008 (0.385–2.637)	0.988	Prior PCI	1.670 (1.139–2.448)	0.009
Prior stroke	3.804 (1.375–10.525)	0.010	Prior stroke	2.446 (1.294–4.622)	0.006
OHCA (+)	3.413 (1.534–7.597)	0.003	OHCA (+)	3.285 (2.020–5.340)	<0.001
Anterior wall MI	1.619 (0.864–3.031)	0.132	Anterior wall MI	1.209 (0.899–1.626)	0.210
Hyperlipidemia	0.407 (0.157–1.056)	0.065	Hyperlipidemia	0.769 (0.534–1.106)	0.156
WBC (x10 <sup>3</sup> mm <sup>3</sup> )	1.080 (0.888–1.315)	0.440	WBC, x10 <sup>3</sup> mm <sup>3</sup>	1.136 (1.035–1.248)	0.007
Hemoglobin (g/L)	1.032 (0.882–1.208)	0.694	Hemoglobin, g/L	1.024 (0.937–1.119)	0.597
Platelet (x10 <sup>3</sup> μL)	1.000 (0.996–1.005)	0.836	Platelet, x10 <sup>3</sup> μL	1.001 (0.999–1.003)	0.215
Neutrophil (x10 <sup>3</sup> /μL)	0.992 (0.803–1.226)	0.944	Neutrophil, x10 <sup>3</sup> /μL	0.931 (0.846–1.024)	0.141
Glucose (mg/dL)	1.002 (1.000–1.005)	0.064	Glucose, mg/dL	1.004 (1.003–1.006)	<0.001
BUN (mg/dL)	1.036 (1.008–1.065)	0.011	BUN, mg/dL	1.039 (1.019–1.059)	<0.001

CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention; OHCA: Out-of-hospital cardiac arrest; MI: Myocardial infarction; WBC: White blood cell; BUN: Blood urea nitrogen; MI: Myocardial infarction; CAD: Coronary artery disease; PPI: Primary percutaneous intervention.

in-hospital mortality (Odds ratio [OR]: 3.413, 95% CI: 1.534–7.597; p=0.003) and all-cause mortality at 60 months (OR: 3.285, 95% CI: 2.020–5.340; p<0.001).

## DISCUSSION

OHCA is one of the leading public health issues and continues to be a major cause of death. The return of spontaneous circulation in a person with OHCA

mandates the immediate need to identify and treat the underlying cause, thereby preventing cardiac arrest.<sup>[25]</sup> Almost 50% of resuscitated patients with OHCA have an acutely occluded coronary vessel visible on coronary angiography that precipitated acute MI.<sup>[3]</sup> Acute STEMI constitutes a substantial proportion of acute coronary events and is a major manifestation of coronary artery disease. Immediate heart catheterization with PCI is advised for patients whose post-arrest electrocardiogram reveals STEMI or for those presenting with a shockable rhythm.<sup>[26]</sup> Poor clinical outcomes for OHCA patients presenting with STEMI have been revealed in a number of studies.<sup>[14,27–31]</sup> Few data exist regarding prognostic factors in cases of STEMI complicated by OHCA. This is primarily because factors influencing the efficiency of resuscitation, and hence affecting prognosis on an individual basis, are difficult to quantify. Various challenges include determining the exact time point of an OHCA, the start and duration of cardiopulmonary resuscitation (CPR) until the return of spontaneous circulation (ROSC), and the quality of bystander CPR.<sup>[14,27,32,33]</sup> In addition, another factor that is not sufficiently understood is the role of early coronary reperfusion in cases of OHCA caused by MI.<sup>[17,34,35]</sup> Above all, as suggested by recent data, clinical and electrocardiographic findings often cannot reliably diagnose an acute coronary occlusion in OHCA survivors,<sup>[13]</sup> and this may lead to delayed or omitted causal treatment. Furthermore, these patients have typically been excluded from large interventional trials. There few studies in the literature that only include witnessed OHCA patients (homogenous group). As in most other studies,<sup>[4,9,21]</sup> we included patients with witnessed and unwitnessed cardiac arrest. While some other authors also included in-hospital cardiac arrests,<sup>[3,15,18,36]</sup> we exclusively focused on OHCA because a well-organized hospital environment is not comparable to the setting outside a medical institution. Recent cardiopulmonary resuscitation (CPR) guidelines of the European Resuscitation Council recommend immediate angiography and PCI (as a preferred reperfusion strategy) or fibrinolysis (as a possible alternative) in STEMI patients who have ROSC after OHCA, and a probable positive effect on survival of out-of-hospital thrombolysis during CPR is supported by some data. None of the patients in this study received prehospital or in-hospital thrombolysis therapy because PCI is our standard treatment strategy in STEMI cases. Consistent with the results of previ-

ous studies,<sup>[29]</sup> we observed no differences concerning atherosclerotic risk factors between the OHCA group and the non-OHCA reference group. Our analysis also revealed a higher proportion of prior stroke and anterior wall MI in the OHCA group. It is interesting that the history of PCI was significantly higher in patients without OHCA than in patients with OHCA. We did not observe multi-vessel disease in the OHCA group, whereas other authors have reported a significantly higher proportion of multivessel disease in patients with OHCA.<sup>[29]</sup>

The procedural success of PCI was high in both groups but, as demonstrated in other studies, the in-hospital and long-term mortality of STEMI patients with OHCA was markedly higher than that of the reference group, with varying figures in different studies. In a retrospective study by Garot et al.,<sup>[14]</sup> 186 patients with STEMI and OHCA who had undergone PCI were evaluated. The in-hospital mortality and the 6-month mortality was 45% and 46%, respectively. In 18% of patients included in the study, mild therapeutic hypothermia was induced. In another retrospective study that included patients with STEMI and OHCA who had undergone PCI, the 6-month mortality was exceedingly low at 18%, and 68% of the surviving patients had a good neurological outcome, defined as a Cerebral Performance Category (CPC) score of 1 or 2. The main issues differentiating this study from others were that all of the patients underwent therapeutic hypothermia and only patients with an initial arrest rhythm of ventricular fibrillation were included. The cardiac arrest was witnessed in 94% of the patients.<sup>[27]</sup> In another study, which analyzed patients who were comatose after an initial arrest rhythm of ventricular fibrillation with STEMI and who had undergone PCI, the in-hospital mortality was only 25%.<sup>[28]</sup> Zimmerman et al.<sup>[29]</sup> retrospectively analyzed the clinical and procedural data as well as 1-year outcomes of 72 consecutive patients who underwent primary PCI after a witnessed OHCA and STEMI and compared the results with 695 patients with STEMI and PCI but without OHCA. They found that the overall mortality rate after 30 days and 1 year was significantly higher in the OHCA-group than in the non-OHCA group: 26.4% vs. 5.6% ( $p < 0.001$ ) and 34.7% vs. 9.5% ( $p < 0.001$ ), respectively. Witnessed and unwitnessed arrest cases were included in a retrospective study conducted by Shavelle et al.,<sup>[30]</sup> which found that in-hospital mortality was greater in patients who experienced STEMI



and OHCA compared with STEMI alone (38% vs. 6%; OR: 6.3, 95% CI: 5.3–7.4;  $p < 0.0001$ ). Ventricular fibrillation was the presenting rhythm in 74% of the arrest cases. Among the OHCA survivors, 193 (73%) were discharged with a CPC score of 1 or 2.

In conclusion, the results of the present study demonstrated that OHCA was associated with in-hospital and long-term cardiovascular death. Therefore OHCA and related risk characteristics can be used in a risk-stratification system for STEMI patients and at-risk patients can benefit from further support and rehabilitation. Our findings add to the collective understanding of risk characteristics for cardiopulmonary arrest and mortality in the setting of STEMI, which may provide important prognostic information to clinicians. These observations can guide emergency staff and interventional cardiologists in the identification of patients with a high risk of arrest and mortality.

### Study limitations

This study has some limitations. First of all, though it included a large patient cohort, our analysis was retrospective, and therefore causality cannot be determined. Additional prospective studies are needed to evaluate the prognostic role of OHCA in STEMI with greater accuracy. Our study also focused on a heterogeneous group, particularly composed of patients with OHCA due to STEMI, and included cases with witnessed and unwitnessed cardiac arrest. None of our patients received prehospital or in-hospital thrombolysis therapy because PCI is our standard treatment strategy in cases of STEMI. In addition, none of the patients included in the study underwent therapeutic hypothermia. Neurological recovery after OHCA was not assessed using the CPC scale due to incomplete medical records. Finally, several other clinical factors that might influence the outcome after resuscitation, such as hemodynamics, seizure treatment, and partial pressure of carbon dioxide were not taken into account. Additional investigation with standardized treatment protocols is therefore needed.

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**Keywords:** Out-of-hospital cardiac arrest; primary percutaneous coronary intervention; short- and long-term survival; ST-segment elevation myocardial infarction.

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