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CLINICAL RESEARCH **Acute Myocardial Infarction**

Survival and Neurologic Recovery in Patients With ST-Segment Elevation Myocardial Infarction Resuscitated From Cardiac Arrest

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Objectives We examined outcomes of patients resuscitated from cardiac arrest owing to ST-segment elevation myocardial infarction (STEMI) and predictors of survival and neurologic recovery.

Background Immediately after resuscitation from cardiac arrest owing to STEMI, many patients show signs of neurologic impairment, and benefits of percutaneous coronary intervention and subsequent prognosis are not well defined.

Methods Between January 1, 2002, and December 31, 2006, we retrospectively identified consecutive patients resuscitated from cardiac arrest, regardless of time to return of spontaneous circulation (ROSC) and neurologic status, and reviewed the outcomes of those who had STEMI. Mortality and neurologic recovery at discharge and long-term mortality were assessed by individual chart review for those who underwent emergent angiography.

Results Our study population consisted of 98 patients; 64% survived to discharge, and 92% had a full neurologic recovery. Predictors of survival were shorter time to ROSC, younger age, neurologic status post-resuscitation (alert or minimally responsive), and male sex. Predictors of neurologic recovery included shorter time to ROSC, neurologic status post-resuscitation (alert or minimally responsive), and younger age. Ninety-six percent of patients who were alert post-resuscitation survived. Ninety-three percent of patients who were minimally responsive post-resuscitation survived. Fifty-nine patients were unresponsive post-resuscitation, with 44% survival, of whom 88% had full neurologic recovery. In the unresponsive group, unwitnessed arrest, prolonged ROSC, and older age were associated with increased risk of death, and older age and prolonged ROSC predicted poor neurologic recovery.

Conclusions When resuscitated patients with STEMI are being evaluated in the emergency department, serious consideration should be given to emergent angiography and revascularization, regardless of neurologic status. (J Am Coll Cardiol 2009;53:409–15) © 2009 by the American College of Cardiology Foundation

In the U.S., 325,000 coronary heart disease deaths occur annually out of hospital or in emergency departments (EDs) (1). ST-segment elevation myocardial infarction (STEMI) is frequent in cardiac arrest survivors. American College of Cardiology/American Heart Association guidelines recommend emergent percutaneous coronary intervention (PCI) or lytic therapy for patients with STEMI, but traumatic or prolonged cardiopulmonary resuscitation (CPR) >10 min is a relative contraindication to thrombolytics (2).

Emergent PCI has been suggested to be the preferred treatment method of patients suffering from out-of-hospital cardiac arrest owing to MI (3–8). A recent retrospective study (9) concluded that "adequate pre-hospital management, early revascularization, and specific care in dedicated intensive care units should be strongly considered in resuscitated patients after cardiac arrest complicating acute myocardial infarction." However, after resuscitation, a number of patients show signs of neurologic impairment before primary PCI. The prognosis of these patients and benefits after PCI, compared with patients without significant neurologic impairment after cardiac arrest, are not well defined. There is often a dilemma regarding whether to proceed emergently for angiography and possible revascularization. Garot et al. (9) and several smaller studies (3–5,7,10) suggest the benefit of PCI in this group of patients.

Our study examined outcomes of patients with STEMI, resuscitated after cardiac arrest, who underwent emergent coronary angiography in a single U.S. medical center. We

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Abbreviations and Acronyms

CABG = coronary artery bypass graft

CPR = cardiopulmonary resuscitation

DTBT = door-to-balloon time

ECG = electrocardiograph

ED = emergency department

PCI = percutaneous coronary intervention

ROSC = return of spontaneous circulation

STEMI = ST-segment elevation myocardial infarction

reviewed the records of all patients who survived arrest and had STEMI, regardless of time to return of spontaneous circulation (ROSC) and neurologic status.

Methods

Our facility is a large, community-based, tertiary care referral center with catheterization laboratory capabilities that provide around-the-clock emergency PCI for patients with acute STEMI. With approval of the Institutional Review Board, we retrospectively queried our internal database of 2,290 consecutive patients who were suspected of having an acute coronary syndrome between January 1, 2002, and December 31, 2006. We identified 1,149 patients with STEMI who underwent emergent PCI, and 33 additional patients had thrombolytic therapy. Patients with cardiac arrest were identified and electrocardiographs (ECGs) reviewed. There were 114 patients who had STEMI (ST-segment elevation >1 mm in 2 contiguous leads) on post-resuscitation ECG. We excluded 16 patients: 5 cases for which the family refused permission or the patient had previously refused catheterization, 10 patients who died in the ED before catheterization, and 1 patient who received thrombolytic therapy. These 16 patients did not undergo coronary angiography. Our study population comprised 98 patients who had STEMI and cardiac arrest, either out of hospital (n = 67) or within the ED (n = 31), and underwent emergent angiography.

Further data were obtained from electronic hospital records, ED records, and the institutional American College of Cardiology–National Cardiovascular Data Registry-compatible cardiac catheterization database. Three physicians extensively examined all records. Information was collected on patients' past medical histories, time to ROSC, witnessed arrest, bystander CPR, neurologic status post-resuscitation in the ED, hypothermia protocol use, use of vasopressors, door-to-balloon time (DTBT), and angiographic findings/interventions. End points were mortality at discharge, neurologic recovery at discharge, and long-term mortality. Long-term mortality was determined through the Social Security Index.

Data analysis. Predictors of death and neurologic recovery were analyzed by multivariable logistic regression. Predictive models were developed by a backward elimination strategy comparing reduced models with the full model by the likelihood ratio test. This statistic is equal to −2 times the difference in log likelihoods of the 2 models and is distributed as a chi-square with degrees of freedom equal to the difference in the number of parameters in the models. Models were validated by bootstrap methods (a random sample with replacement of the original data). A model was calculated for each bootstrap replicate and applied to the

Table 1 Patient Characteristics

	No. of Patients (%)
Total population	98
Age, yrs	
Mean	61.9 ± 14.9
Median	61.4
Medical history	
Male	69 (70.4%)
Hypertension	54 (55.1%)
Diabetes	21 (21.4%)
Prior MI	23 (23.5%)
Prior VT/VF arrest	7 (7.1%)
CHF	15 (15.3%)
Prior CABG	13 (13.3%)
Known CAD	29 (29.6%)
CRI	11 (11.2%)
PVD	6 (6.1%)
Dyslipidemia	27 (27.6%)
COPD	9 (9.2%)
Location of arrest	
Field	64
In presence of EMS	3
ED	31
Witnessed arrest	88 (89.8%)
Immediate CPR	66 (67.3%)
EMS dispatch to arrival time, min	5
Time to ROSC, min	14.6 ± 14.5
Neurologic status post-arrest	
Alert	25 (25.5%)
Minimally responsive to pain and stimuli	14 (14.3%)
Unresponsive to pain and stimuli	59 (60.25%)
Hypothermia protocol	3 (3.1%)
DTBT, min	104.1 ± 52.4
Before angiography	
Mechanically ventilated	73 (74.5%)
On sedatives	0 (0%)
On vasopressors	29 (29.6%)
Angiographic findings	
Angiographically normal	4
Nonobstructive disease	6
Culprit lesion	70
Multivessel disease without culprit lesion	18
Location of culprit lesions	
RCA	22
LAD	31
Circumflex	12
Graft	3
Left main	1
Ramus	1

CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CPR = cardiopulmonary resuscitation; CRI = chronic respiratory insufficiency; DTBT = door-to-balloon time; ED = emergency department; EMS = emergency medical services; LAD = left anterior descending artery; MI = myocardial infarction; PVD = peripheral vascular disease; RCA = right carotid artery; ROSC = return of spontaneous circulation; VF = ventricular fibrillation; VT = ventricular tachycardia.

original sample. The accuracy index of the model from the original data was subtracted from the index of the bootstrap model to obtain an estimate of bias (model overfitting). The bias estimates were averaged over 200 bootstrap replicates to obtain bias-corrected c-statistics to assess model discrimination. Harrell's Design and Hmisc libraries in S-Plus (Insightful, Inc., Seattle, Washington) were used for these analyses (11). The Kaplan-Meier product-limit method was used to estimate both in-hospital and out-of-hospital survival. We analyzed the complete cohort of patients. In addition, the same analysis was applied to the pre-specified group of unresponsive patients, because this group is associated with the greatest confusion and uncertainty regarding management and clinical outcomes.

Results

Baseline characteristics for all 98 patients are summarized in Table 1. The patients with STEMI and cardiac arrest had a mean DTBT of 104 min, whereas those with STEMI alone had a mean DTBT of 80 min during the same time period.

Survival to discharge was 64% in the whole group. Ninety-six percent of the alert patients, 93% of the minimally responsive patients, and 44% of the unresponsive patients post-resuscitation survived (Fig. 1). All of the survivors were discharged home, except 6 who were discharged to skilled nursing facilities. On long-term follow-up, which ranged from 7 months to 5.5 years, 4 more patients died. Survival was 64%, 61%, and 60% at 1, 6, and 15 months, respectively, for the whole group. The cumulative survival rate in the alert/minimally responsive group was 90% at 6.5 months from hospitalization, compared with 42% for the unresponsive group ($p < 0.0001$) (Fig. 2).

We used multivariate analysis to find predictors of mortality. Unresponsive patients were 47 times more likely to die when compared with alert patients. For every 1-min increase in time to ROSC, the odds of dying increased by 11%. For every 5-year increment in age, the odds of dying increased by 34%. Also, women were almost 6 times more likely to die compared with men (Table 2).

Full neurologic recovery, defined as being able to perform activities of daily living without assistance on assessment upon hospital discharge, was seen in 92% of survivors. Formal cognitive testing was not performed. Neurologic recovery, as well as survival, related to neurologic status post-resuscitation is documented in Figure 1. Predictors of neurologic deficit included longer time to ROSC, unresponsive post-resuscitation, and older age (Table 3).

Of the 59 patients who were unresponsive to pain and/or stimuli post-resuscitation, 44% survived to discharge, and full neurologic recovery was seen in 88% of

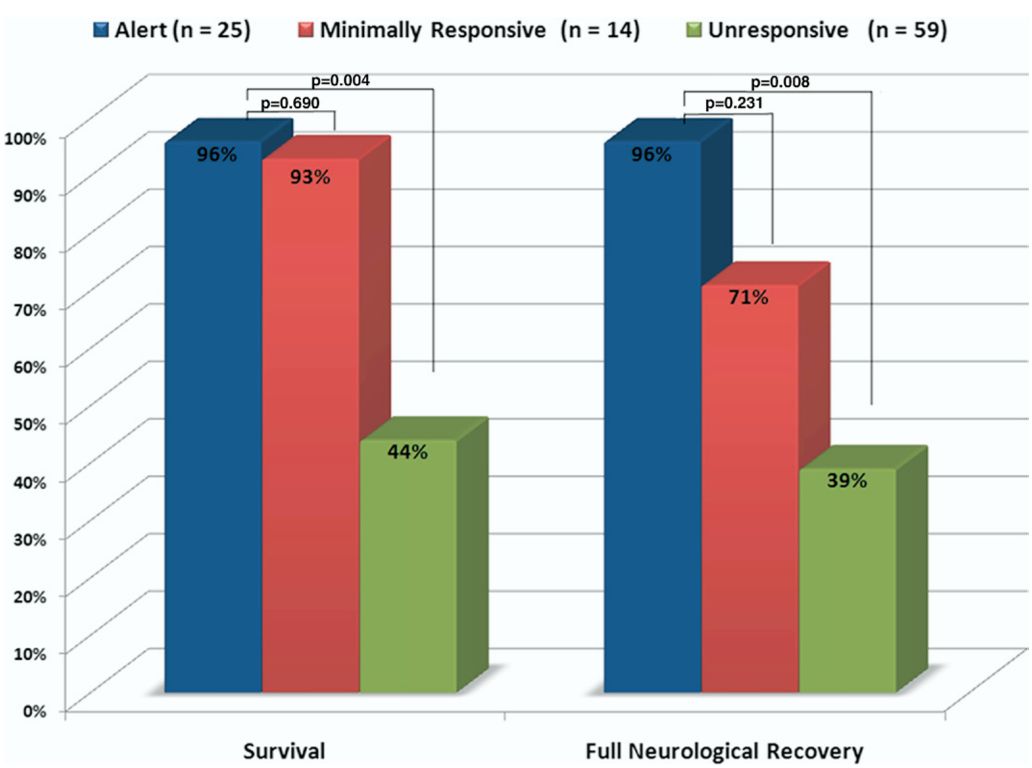

Figure 1 **Outcomes by Level of Consciousness Post-Resuscitation**

Patients who were alert or at least minimally responsive post-resuscitation had better survival and a better chance of full neurologic recovery than patients who remained unresponsive. Even in the subset of patients who were unresponsive, nearly one-half survived, and most had full neurologic recovery.

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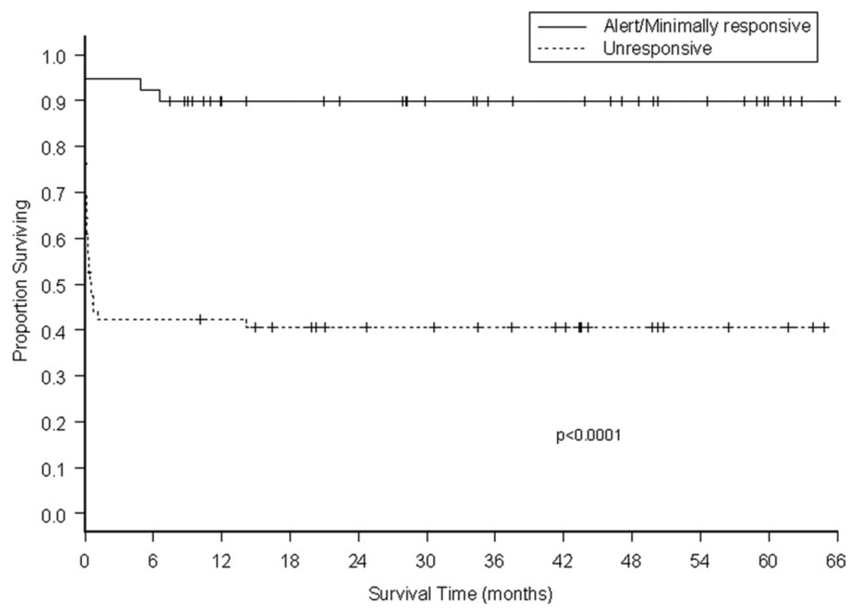

Figure 2 Kaplan-Meier Survival Curves for "Alert/Minimally Responsive" and "Unresponsive" Cardiac Arrest Patients

Tick marks indicate censored observations.

the survivors. Survival at 1, 6, and 15 months was 42%, 41%, and 41%, respectively. A quality-of-life assessment was not conducted. Multivariate analysis for predictors of mortality was performed in this group. Unwitnessed arrest, longer time to ROSC, and older age were associated with a higher risk of death (Table 4). Older age and longer time to ROSC were also predictors of poor neurologic recovery (Table 4).

Sixty-seven patients arrested in the field, whereas 31 arrested in the ED. Of those who arrested in the field, 85% (57 of 67) were witnessed, and 52% (35 of 67) of them were treated with immediate CPR. Three of the 67 patients initially arrested in the presence of emergency medical services personnel. Overall survival was 55% (37 of 67) for those who initially arrested in the field versus 84% (26 of 31) for those who arrested in the ED ($p = 0.006$). Full neurologic recovery was seen in 49% (33 of 67) of those who arrested in the field versus 81% (25 of 31) for those who arrested in the ED ($p = 0.0128$) (Fig. 3).

Revascularization was performed in 77 of the 98 patients at the discretion of the treating physician, and 21 patients were not revascularized (10 had angiographically normal coronaries/nonobstructive disease; 1 had a culprit lesion and died in the catheterization laboratory before PCI attempt; and 10 with multivessel disease without culprit lesions were inoperable, previously refused coronary artery bypass graft [CABG], and/or the treating physician decided against emergent CABG) (Table 5). Of the 77 revascularized patients, 64 underwent PCI and 13 had CABG. Of the 64 PCI patients, 62 had successful restoration of flow, 1 patient had Thrombolysis In Myocardial Infarction (TIMI) flow grade 0, and 1 had TIMI flow grade 1. In the unresponsive group, 40 of 59 patients were revascularized (33 had successful PCI performed and 7 underwent emergent

Table 2 Predictors of Death for the Entire Group (C Index = 0.92; n = 98)

Variable	Odds Ratio	95% CI	p Value
Neurologic response before catheterization			
Alert	1	—	—
Minimally responsive	2.05	0.061–68.11	0.690
Unresponsive	47.78	3.33–549.14	0.004
ROSC (for every 1-min increase)	1.11	1.04–1.19	0.002
Age (for every 5-yr increase)	1.34	1.08–1.67	0.009
Female	5.88	1.15–30.12	0.034

CI = confidence interval; ROSC = return of spontaneous circulation.

Table 3 Predictors of Neurologic Deficit for the Entire Group (C Index = 0.89; n = 98)

Variable	Odds Ratio	95% CI	p Value
Neurologic response before catheterization			
Alert	1	—	—
Minimally responsive	4.96	0.36–66.59	0.231
Unresponsive	18.86	2.16–164.37	0.008
ROSC (for every 1-min increase)	1.07	1.02–1.12	0.005
Age (for every 5-yr increase)	1.24	1.02–1.51	0.027

Abbreviations as in Table 2.

Table 4 Predictors of Death for the Unresponsive Group (C Index = 0.90; n = 59)

Variable	Odds Ratio	95% CI	p Value
Witnessed arrest	0.109	0.018–0.66	>0.016
ROSC (for every 1-min increase)	1.18	1.072–1.304	0.001
Age (for every 5-yr increase)	1.48	1.12–1.95	0.006
Predictors of neurologic deficit (C index = 0.87; n = 59)			
ROSC (for every 1-min increase)	1.15	1.056–1.25	0.001
Age (for every 5-yr increase)	1.39	1.076–1.794	0.012

Abbreviations as in Table 2.

Table 5 Angiographic Findings and Intervention in the Entire Group (n = 98)

Angiographic Findings	Revascularized	Nonrevascularized
Angiographically normal coronary arteries (n = 4)	0	4
Nonobstructive disease (n = 6)	0	6
Culprit lesion (n = 70)	69 (64 PCI, 5 CABG)	1
Multivessel disease without culprit lesion (n = 18)	8 (all CABG)	10
Total	77	21

CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

CABG) (Table 6). Of those who had PCI performed, 15 died in hospital, 2 had residual neurologic deficits, and 16 had full neurologic recovery. Of those who underwent emergent CABG, 2 died in hospital, 2 had residual neurologic deficits (1 subsequently died after discharge), and 3 had full neurologic recovery.

The effect of revascularization on survival in both total number of patients and the subgroup of unresponsive patients was examined. In-hospital mortality was lower for revascularized patients than nonrevascularized patients in the entire group (25% vs. 76%, $p < 0.0001$) and in the subgroup of unresponsive patients (42% vs. 84%, $p = 0.003$) (Table 6). Also, despite having ST-segment elevation on ECG, 20 patients had no critical culprit lesions identified during emergent angiography.

Discussion

The goal of this study was to identify predictors of survival and neurologic recovery in patients who experienced resuscitated cardiac arrest (both out of hospital and within the ED) who also have STEMI.

To facilitate emergent PCI, an expedited institutional protocol is used for all patients with STEMI, even in those resuscitated from cardiac arrest. The longer DTBT in our patient population may be due to these patients requiring more stabilization before catheterization.

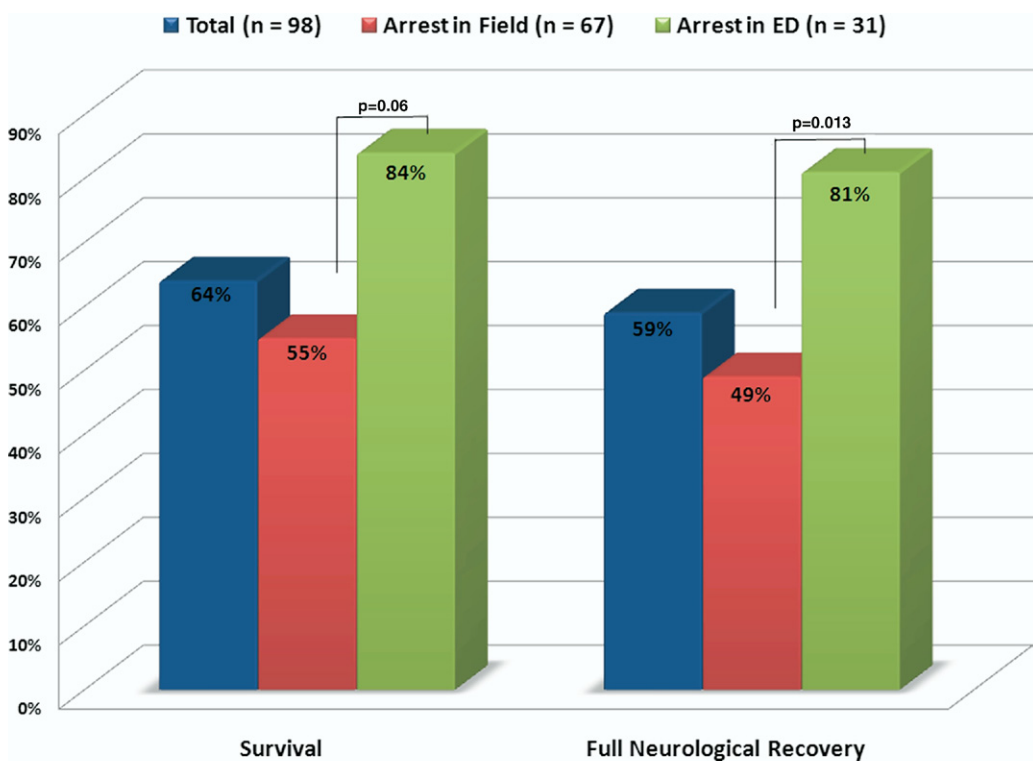

Figure 3 Outcomes by Location of Arrest

Patients who arrested in the emergency department (ED) had better survival and neurologic recovery than those who arrested in the field.

Table 6 Angiographic Findings in Unresponsive Patients (n = 59)

Angiographic Findings	Revascularized	Nonrevascularized
Angiographically normal coronary arteries (n = 3)	0	3
Nonobstructive disease (n = 5)	0	5
Culprit lesion (n = 36)	35 (33 PCI, 2 CABG)	1
Multivessel disease without culprit lesion (n = 15)	5 (all CABG)	10
Total	40	19

Abbreviations as in Table 5.

Sixty-four percent of patients survived to hospital discharge, and 92% of survivors had full neurologic recovery. This benefit was maintained long term: 60% of patients were alive post-discharge at 15 months. Shorter time to ROSC, younger age, neurologic status post-resuscitation (alert or minimally responsive), and male sex all predicted survival. Neurologic recovery was predicted by similar variables: shorter time to ROSC, neurologic status post-resuscitation, and younger age. Nearly one-half of the unresponsive patients survived, and most had full neurologic recovery. This is an important observation because not knowing the ultimate outcomes in these patients often causes the greatest uncertainty in the initial management strategy.

Patients who arrested in the ED were found to have significantly better survival rates and neurologic recovery than those who arrested outside of the hospital. Those who arrested in the ED had an understandably shorter ROSC (7.3 ± 10.7 min vs. 18.4 ± 14.9 min) and tended to have better neurologic function immediately after resuscitation (32% vs. 73% unresponsive). Shorter ROSC has been shown previously to improve outcome (3,7,9). Patients who arrested out of hospital, when analyzed separately, still did relatively well: 55% (37 of 67) of patients survived, and 89% (30 of 37) of the survivors had full neurologic recovery. Of those who arrested in the field, 85% (57 of 67) were witnessed, and 52% (35 of 67) of them were treated with immediate CPR. The high rate of CPR can be attributed to the large number of laypersons trained in CPR through the Public Access Defibrillation Trial and Delaware's First State-First Shock Program, designed to train bystanders in CPR and automated external defibrillator use (12,13).

Although this study was not randomized and not designed to examine the benefits of revascularization, unresponsive patients who were not revascularized because of an absence of a culprit lesion (either "multivessel disease without a culprit lesion" or "nonobstructive disease") were observed to have a poor prognosis. Nonrevascularized patients in this group were more likely to die than revascularized patients (84% vs. 42%, $p = 0.003$). This is most likely due to selection bias. The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial population, on the other hand, has some similarities to our group of patients. In that randomized trial, patients with cardiogenic shock, not cardiac arrest, derived benefit from revascularization (14).

There were 8 patients who, despite ST-segment elevation on ECG, had normal coronaries or had nonobstructive disease on angiography. This was not unique to our study (3). All of these patients died. Of the 10 patients with multivessel disease without culprit lesions who did not undergo revascularization, there was 70% mortality. We speculate that ST-segment elevation in these patients might be explained by a primary arrhythmic arrest with low flow in a narrowed artery, coronary vasospasm, or rupture of a nonobstructive plaque leading to thrombosis with subsequent spontaneous lysis of the thrombus. More investigation is needed to explain these findings.

Several studies similar to ours have been conducted with consistent findings (3–5,7,9,12,15,16). Other studies reported on a smaller number of patients, with the exception of Garot et al. (9). To our knowledge, our study is the largest U.S.-based study with the longest follow-up. Garot et al. (9) conducted a multicenter study in Paris, France, using a national registry, whereas ours was based on a single-center experience using patient-level data. Garot et al. (9) reported greater utilization of pre-hospital thrombolytics, hypothermia protocol, and mechanical ventilation. Of note, the emergency medical services system in Paris, France, includes a physician as part of the response team, unlike the U.S.

Nonetheless, our findings are similar to those of Garot et al. (9) with regard to the benefit of shorter time to arrival of first responder post-arrest, shorter ROSC time, prompt pre-hospital management, and immediate cardiac catheterization. They also found that the absence of shock on admission, no prior PCI, and no history of diabetes were independently associated with increased survival. We did not notice similar associations, possibly because of the smaller patient population.

Gorjup et al. (15) recently reported that "outcomes of patients with (acute) STEMI who regain consciousness after ROSC and undergo primary PCI is comparable to patients without cardiac arrest. This is in contrast with comatose survivors who, despite aggressive reperfusion treatment, had significantly worse outcomes." Knafelj et al. (16) found that a strategy of primary PCI and mild induced hypothermia in comatose survivors of ventricular fibrillation with STEMI is feasible and may improve survival with good neurologic recovery.

Quintero-Moran et al. (17) evaluated the outcomes of 63 patients undergoing primary PCI for STEMI who suffered cardiac arrest. They concluded that "combining immediate initiation of resuscitation maneuvers and primary PCI yields a very good clinical outcome in patients (both in-hospital and out-of-hospital) with acute myocardial infarction suffering from cardiac arrest." This correlated with our finding that shorter ROSC predicted survival.

Study limitations. Our study was a retrospective analysis and therefore shares the limitations of all retrospective analyses. Our sample size was relatively small despite being the largest in the U.S. to date. Also, our long-term follow-up was restricted to survival, and we did not have data on long-term neurologic status.

Conclusions

In our experience, when emergent angiography was performed in patients with cardiac arrest and STEMI and there was subsequent revascularization in the appropriate patients, 64% survived and 92% had full neurologic recovery. Predictors of survival were shorter ROSC, younger age, neurologic status post-resuscitation (alert or minimally responsive), and male sex. Most survivors had good neurologic recovery. Shorter ROSC, neurologic status post-resuscitation, and younger age were also predictors of neurologic recovery.

Patients who arrested in the ED fared quite well, but those who arrested in the field, when analyzed separately, fared better than expected. Even in the subset of patients who were unresponsive post-resuscitation, if emergent angiography was performed and there was subsequent revascularization, nearly one-half survived. Shorter time to ROSC, younger age, and a witnessed arrest were predictors of survival in this group. In addition, most had full neurologic recovery.

This study does not provide conclusive evidence regarding benefits of revascularization in this group of patients. Nonetheless, based on our observations, resuscitated patients with STEMI in the ED should be seriously considered for emergent angiography and revascularization, regardless of neurologic status. These patients should be treated with the same urgency as patients with acute STEMI without cardiac arrest.

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