

## EDITORIAL COMMENT

# Are We There Yet?

## Should All Comatose Cardiac Arrest Survivors Go to the Cath Lab?\*



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Major progress in the treatment of coronary artery disease has been made over the past several decades. Yet in 2014, coronary heart disease (CHD) remains the leading cause of death worldwide. The first manifestation of CHD in at least 50% of patients is sudden cardiac death (SCD); it most often occurs unexpectedly, within 6 h of symptom onset and usually outside of the hospital setting. In the United States, SCD is estimated to occur in 300,000 to 350,000 patients annually (1). Approximately 80% of all SCDs are due to CHD, and this incidence has not decreased over the past several decades despite the decrease in age-adjusted CHD mortality in the United States. Although progress has been made in treating survivors of SCD, the outcomes in this population remain poor. A recent meta-analysis of global studies of out-of-hospital cardiac arrest (OHCA) demonstrated worldwide differences in survival to discharge, but rates remain very low at only 2.2 to 10.7% (2).

### KNOWLEDGE GAPS IN SCD

No adequate risk prediction models for SCD exist. Traditional risk factors for atherosclerosis, such as those in the Framingham Risk Index, provide insight into populations, leading to primary prevention strategies that have affected mortality. They are less helpful for individual SCD risk prediction, likely due to very low event rates. Risk prediction improves in

patients with established disease, but only modestly (3). Electrophysiological, anatomic, autonomic, and genetic markers have been proposed to improve individual risk prediction, but none have yet proved clinically useful.

Differences between the sexes remain poorly understood. Among patients with signs and symptoms of ischemic heart disease, women more often than men have nonobstructive coronary artery disease (4). Differences also exist in the pathology of women with SCD. Fewer women with SCD demonstrate CHD as the underlying etiology of their event. Among those with obstructive CHD, younger women more often have plaque erosion versus plaque rupture. Plaque rupture is the more common pathology found in older women with SCD, as it is in men. Curiously, smoking is more often associated with plaque erosion in younger women and plaque rupture in men (5). Dissimilarities may also exist in the hormone levels of patients with SCD, possibly influencing their risk profile, but mechanistic explanations are lacking (6). Even a woman's proximity to roadways has been linked to an increased risk of SCD, a possible surrogate for air pollution and roadway noise (7).

### RESUSCITATION FROM CARDIAC ARREST

At the time of SCD, survival to hospital discharge is improved with bystander cardiopulmonary resuscitation, the presence of ventricular tachycardia or fibrillation, if the arrest is witnessed, or by the return of spontaneous circulation (ROSC) (8). Newer approaches such as cardiocerebral resuscitation and "Take Heart America" have led to improvements in survival (9,10). Some accepted techniques for resuscitation, however, have come under scrutiny. An observational study comparing advanced life support

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with basic life support in Medicare beneficiaries with OHCA suggested both survival to hospital discharge (13.1% vs. 9.2%; 3.9 percentage point difference [95% confidence interval: 2.3 to 5.7]) and neurological outcomes (8.0% vs. 5.4%; 2.6 percentage point difference [95% confidence interval: 1.2 to 4.0]) were better with basic life support versus advanced life support, respectively (11). In another study, of 1,134 OHCA patients who achieved ROSC, pre-hospital use of epinephrine was associated with worse survival in a dose-dependent fashion (12). These data reinforce the high mortality of OHCA patients and the ongoing need for further research into improvements in the care of SCD patients.

### POST-RESUSCITATION TREATMENT

The optimal treatment of OHCA survivors is not fully defined (Table 1). Two main goals of post-resuscitation care are the preservation of neurological function and limiting cardiac failure. Therapeutic hypothermia (TH) has emerged as a viable strategy to improve neurological outcomes. After randomized clinical trials in 2002, the International Liaison Committee for Resuscitation and the American Heart Association endorsed TH, cooling to a core temperature of 33°C to 36°C, for all comatose OHCA survivors (13). Perhaps due to logistical issues, health care systems have been slow to adopt its use.

Coronary artery disease is the other target. Investigators have identified a high prevalence of both CHD and occluded coronary arteries in comatose OHCA survivors (14). Without randomized trials, available evidence suggests that post-cardiac arrest patients with ST-segment elevation have better survival-to-discharge and neurological outcomes if triaged to coronary angiography with percutaneous coronary intervention as appropriate (15). Less clear is how to treat patients who have achieved ROSC and remain comatose, but no ST-segment elevation is seen on their electrocardiogram.

In one of the largest studies to date, Kern et al. (16), in this issue of *JACC: Cardiovascular Interventions*,

followed 746 comatose post-cardiac arrest patients enrolled in the International Cardiac Arrest Registry Cardiology Database. Remarkably, 98% of these patients were treated with TH. Survival to hospital discharge was greatest among patients with ST-segment elevation, presumably a result of immediate angiography with percutaneous coronary intervention as indicated. Fewer patients without ST-segment elevation underwent immediate angiography (45.1% vs. 96.9%;  $p < 0.0001$ ), but survival to hospital discharge was no different than in the ST-segment elevation cohort (57.9% vs. 54.7%;  $p = 0.60$ ). Survival was poor in both groups without immediate coronary angiography (20.3% vs. 33.3%;  $p = 0.61$ ). Favorable neurological outcomes were seen in most survivors, but among those without ST-segment elevation, the use of coronary angiography predicted better functional outcomes.

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### LIMITATIONS/CONTRIBUTIONS

One of the more challenging triage decisions for the interventional cardiologist is when to take comatose post-cardiac arrest patients with ROSC to the catheterization laboratory. That decision is easier when ST-segment elevation is present. The data from Kern et al. (16), although favorable for the group without ST-segment elevation, should be interpreted cautiously. The patient population was heterogeneous, with only 79% OHCA patients. Were the other 21% in-hospital cardiac arrest patients whose event was related to surgery, trauma, or another cause? The underlying etiology of these events is likely different, and including them makes generalization to the OHCA population difficult.

The stated aim of the study was to “determine whether immediate coronary angiography after resuscitation was associated with improved survival in those with and without STEMI.” The use of immediate coronary angiography differed significantly by enrolling center and by the patient’s clinical presentation. This analysis initially dichotomized patients into those who did and did not have an STEMI, only then dissecting further to see the effect of immediate angiography. Physicians might have been more informed by a strategy directly comparing patients undergoing immediate coronary angiography with those who did not, regardless of the electrocardiographic findings.

The limitations of registry data are highlighted by the higher survival rate of patients who underwent delayed coronary angiography, as shown in their

	Therapeutic Hypothermia	Immediate Angiography
ST-segment elevation		
Comatose	Recommended	Recommended
Noncomatose	Recommended	Recommended
No ST-segment elevation		
Comatose	Recommended	Unclear
Noncomatose	Recommended	Unclear

Table 2 (16), compared with those undergoing immediate coronary angiography. Although this likely represents selection bias, it emphasizes the need for a randomized comparison. Finally, the majority of patients in the current study were men. Whether the data from Kern et al. (16) also apply to women would be useful information.

Kern et al. (16) add to a growing body of evidence suggesting that, in the absence of an identifiable noncardiac cause, patients remaining comatose despite ROSC after cardiac arrest should be considered

for immediate coronary angiography regardless of the presence of ST-segment elevation. The DISCO (Direct or Subacute Coronary Angiography for Out-of-hospital Cardiac Arrest) trial is currently enrolling and should help to clarify this further (NCT02309151).

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