

THE PRESENT AND FUTURE

COUNCIL PERSPECTIVES

Cardiac Arrest

A Treatment Algorithm for Emergent Invasive Cardiac Procedures in the Resuscitated Comatose Patient



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ABSTRACT

Patients who are comatose after cardiac arrest continue to be a challenge, with high mortality. Although there is an American College of Cardiology Foundation/American Heart Association Class I recommendation for performing immediate angiography and percutaneous coronary intervention (when indicated) in patients with ST-segment elevation myocardial infarction, no guidelines exist for patients without ST-segment elevation. Early introduction of mild therapeutic hypothermia is an established treatment goal. However, there are no established guidelines for risk stratification of patients for cardiac catheterization and possible percutaneous coronary intervention, particularly in patients who have unfavorable clinical features in whom procedures may be futile and affect public reporting of mortality. An algorithm is presented to improve the risk stratification of these severely ill patients with an emphasis on consultation and evaluation of patients prior to activation of the cardiac catheterization laboratory. (J Am Coll Cardiol 2015;66:62-73)
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Over the past 30 years, significant advances have been made in resuscitation therapy for cardiac arrest victims, with improved survival and neurological outcomes (1,2). The vast majority of adult cardiac arrests are associated with obstructive coronary artery disease (3). Emergent coronary revascularization in appropriate patients, coupled with therapeutic hypothermia (TH) and hemodynamic support, has continued to improve outcomes (4,5). Therefore, the standard practice in many centers is to emergently activate the cardiac

catheterization laboratory (CCL) in patients presenting with cardiac arrest, the majority being out-of-hospital cardiac arrests (OHCAs). This is particularly true in cardiac arrest patients with ST-segment elevation myocardial infarction (STEMI). Although the 2013 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines for the management of STEMI (6) have a Class I recommendation for performing immediate angiography and percutaneous coronary intervention (PCI) in comatose patients with STEMI after OHCA when indicated,

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there are no guidelines for comatose cardiac arrest patients without ST-segment elevation on electrocardiogram (STE).

In patients with OHCA, 64% will be comatose, and the neurological status on presentation has a dramatic effect on subsequent mortality and mortality (7). Mortality in post-cardiac arrest patients with STEMI who are awake and undergo successful PCI is only 5%, but it increases to 50% if patients are comatose (7).

Although PCI can offer important benefits to resuscitated patients who remain comatose, current quality metrics and public reporting programs have not recognized the expected high mortality rate in this population and may de incentivize appropriate care. Whereas door-to-balloon time (D2B) in OHCA patients is excluded from core measures, hospital and operator mortality are key performance metrics and are not excluded. In addition, insurance programs offer hospitals quality improvement programs with significant financial reward if the adjusted mortality rate after PCI is <1%. Therefore, public reporting of adverse outcomes in this high-risk population without adequate risk adjustment, coupled with financial incentives for hospitals with low PCI mortality, has created a significant misalignment of goals. There is concern in the interventional community that this may lead to risk-averse behavior, resulting in suboptimal care by not providing early cardiac catheterization to appropriate patients.

RISK STRATIFICATION

Early risk stratification of patients with OHCA in the emergency room and the recommendations for early angiography vary considerably amongst providers and institutions. Many regional STEMI systems include automatic activation of the CCL for all STEMI and OHCA patients. The role of first responders, emergency room doctors, and noncardiologists focuses on the process, rather than the appropriateness of the activation. Although many patients have improved outcomes with an early invasive approach, some patient subsets may not derive a benefit and may experience excess risk.

A strategy to reliably identify patients who benefit from early angiography and those who benefit from compassionate supportive care is clearly needed. An algorithm may assist front line clinicians in identifying appropriate cardiac arrest patients for emergent cardiac catheterization. Recently, our European colleagues published a comprehensive review delineating their approach to OHCA patients (8). Although our approach addresses the care of OHCA patients in

the United States, we hope that continued universal dialogue and research will accelerate improved outcomes in this critically ill population. We propose an algorithm to best risk stratify cardiac arrest patients who are comatose on presentation for emergent CCL activation for coronary angiography and possible intervention (**Central Illustration**).

EXPLANATION OF THE ALGORITHM

The principal purpose of this algorithm is to provide an easily implementable aid in identifying appropriate care for all comatose survivors of cardiac arrest and to identify patients who are unlikely to receive substantial benefit from an early invasive approach.

CARDIAC ARREST, RETURN OF SPONTANEOUS CIRCULATION, AND THE COMATOSE PATIENT.

This algorithm focuses on patients who have experienced OHCA and have achieved return of spontaneous circulation (ROSC), but remain comatose. Although an initial shockable rhythm, such as ventricular tachycardia (VT) or ventricular fibrillation (VF), improves the likelihood of ROSC (6,9-11) and of a favorable outcome (12), non-shockable rhythms may also be caused by coronary artery occlusion (12).

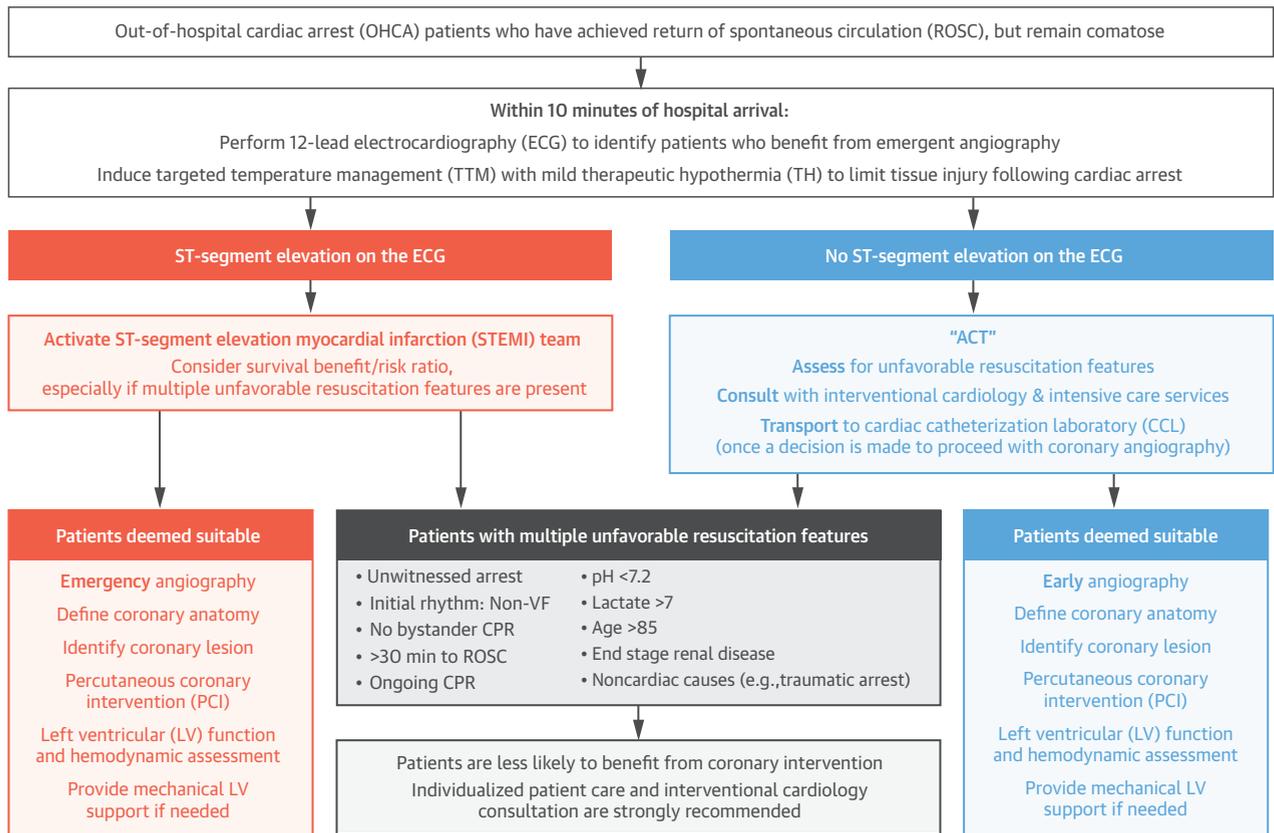
Successfully resuscitated comatose patients represent a heterogeneous population with a baseline survival rate of only 25%. With hypothermia and PCI, survival improves to 60%, with favorable neurological outcomes achieved in 86% of survivors (3,4,10,12-15) (Table 1). However, the presence of certain unfavorable features reduces the likelihood of a good outcome.

TARGETED TEMPERATURE MANAGEMENT WITH MILD TH AND CORONARY ANGIOGRAPHY POST-CARDIAC ARREST.

Early initiation of targeted temperature management (TTM) is critical and should neither delay nor interfere with an early invasive approach. TTM is the active control of systemic body temperature to limit tissue injury after ischemia-reperfusion conditions occurring from cardiac arrest. The use of mild TH has been demonstrated to improve survival and neurological outcomes when combined with PCI in patients with OHCA who remain comatose on presentation (11,12,16-28). One nonrandomized report found an associated 20% increase in mortality rate with every hour of delay in initiating cooling (12). In 2002, 2 randomized clinical trials found that lowering body temperature to 32°C to 34°C for 12 to 24 h in those still comatose after being resuscitated from VF OHCA improved survival and neurological

ABBREVIATIONS AND ACRONYMS

- ACCF** = American College of Cardiology Foundation
- AHA** = American Heart Association
- CCL** = cardiac catheterization laboratory
- ECG** = electrocardiogram
- OHCA** = out-of-hospital cardiac arrest
- PCI** = percutaneous coronary intervention
- ROSC** = return of spontaneous circulation
- STE** = ST-segment elevation on electrocardiogram
- STEMI** = ST-segment elevation myocardial infarction
- TH** = therapeutic hypothermia
- TTM** = targeted temperature management

CENTRAL ILLUSTRATION Algorithm for Risk Stratification of Comatose Cardiac Arrest Patients

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ACT = assessment, consultation, transport; CCL = cardiac catheterization laboratory; CPR = cardiopulmonary resuscitation; ECG = electrocardiography; LV = left ventricular; OHCA = out-of-hospital cardiac arrest; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation; STEMI = ST-segment elevation myocardial infarction; TH = therapeutic hypothermia; TTM = targeted temperature management; VF = ventricular fibrillation.

function of survivors (16,26). Recently, 2 other randomized clinical trials of TTM in post-resuscitated patients have found equally impressive survival rates, whether cooled to 33°C versus 36°C (24) or whether initiated in the field or after arrival at the hospital (29). During the decade after the original reports of TTM efficacy in post-cardiac arrest patients, clinical cohort studies signaled that the combination of early coronary angiography and TTM might produce the best outcomes in the resuscitated, but unconscious, critically ill population. There are now a total of 28 cohort studies of post-arrest STEMI patients who were comatose upon hospital arrival and therefore received TTM and coronary angiography. A summary of these data shows a survival to hospital discharge rate of 60%, with 86% of such survivors being neurologically intact (3,10-12,14,17,22,27,28,30-37) (Table 1).

The International Liaison Committee on Resuscitation included the following statement in their 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations, “Therapeutic hypothermia is recommended in combination with primary PCI, and should be started as early as possible, preferably before initiation of PCI” (38,39), and the AHA 2010 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care states, “angiography and/or PCI need not preclude or delay other therapeutic strategies including therapeutic hypothermia” (39). Within the last few years, both the European Society of Cardiology 2012 (40) and the ACCF/AHA 2013 (6) STEMI guidelines included a Class I recommendation for the use of TTM for STEMI patients who are resuscitated from cardiac arrest but remain comatose on arrival at the

hospital (14,37). There are numerous choices for cooling post-arrest patients, including simple ice packs, intravenous cold saline (1 to 2 l), surface temperature-regulating devices, intranasal spray devices, and intravascular catheter-based systems. Although some are more convenient, none have been shown superior to the others for patient outcomes (41,42).

The application of TTM, particularly the maintenance of hypothermia, in those undergoing coronary angiography and PCI, has raised concerns about possible increased bleeding, particularly from vascular access sites, and the potential to increase stent thrombosis. Excess bleeding, seen in earlier studies of extreme hypothermia (<28°C) has not been seen with the TTM recommended in cardiac arrest (32°C to 36°C) (34,43). In the largest report to date, the Resuscitation Outcomes Consortium reported a severe bleeding incidence of 2.7% (106 of 3,981) among all OHCA survivors admitted to the hospital, with similar rates among those receiving TTM (2.7%; 42 of 1,566), those receiving early coronary angiography (3.8%; 29 of 765), and those receiving reperfusion therapy (3.1%; 22 of 705).

There have been 3 reports of increased early stent thrombosis in patients treated post-arrest with PCI while simultaneously being cooled (44,45). All were relatively small series, with a total of 15 of 110 (13.6%) patients having an acute or subacute stent thrombosis. Possible mechanisms include increased platelet activation, poor absorption of antiplatelet agents, multiorgan failure with altered metabolism of antiplatelet/antithrombotic agents, and procoagulant effects. A fourth report found no increase in stent thrombosis among the post-cardiac arrest population receiving both PCI and TTM (2 of 77 = 2.6% vs. 30 of 1,377 = 2.2% in their nonarrested STEMI patients) (46). The observed increase in stent thrombosis did not adversely affect long-term outcomes (47,48).

12-LEAD ELECTROCARDIOGRAM. A 12-lead electrocardiogram (ECG) should be performed within 10 min of arrival to identify patients who benefit from emergent angiography. This should be undertaken simultaneously with initiation of TH.

STEMI on the ECG. This defines the Class I recommendation for emergent catheterization laboratory activation in the ACCF/AHA guidelines (6). There is substantial evidence demonstrating efficacy of early angiography and PCI in OHCA patients with STEMI (3,4,13,14,49-51). Nonetheless, if multiple unfavorable resuscitation features are present, the benefit/futility ratio of proceeding to the catheterization laboratory should be carefully considered.

No STEMI on the ECG. The presence of an identifiable culprit vessel is found in 33% of patients without

TABLE 1 28 Clinical Reports of Combining TTM and Early Coronary Angiography in Resuscitated, But Comatose Patients With STEMI on the ECG

First Author, Date (Ref. #)	Survivors to DC (n = 2,687/4,510 [60%])	Good Neuro Among Survivors (n = 2,090/2,426 [86%])
Hovdenes et al., 2007 (17)	41/50	34/41
Richling et al., 2007 (33)	24/46	22/24
Knafelj et al., 2007 (18)	30/40	22/30
Wolfrum et al., 2008 (22)	12/16	11/12
Peels et al., 2008 (104)	22/44	NA
Schefold et al., 2009 (34)	NA	19/31
Reynolds et al., 2009 (14)	52/96	NA
Nielsen et al., 2009 (35)	303/479	278/303
Batista et al., 2010 (27)	8/20	6/8
Dumas et al., 2010 (3)	171/435	160/171
Koeth et al., 2010 (105)	114/143	NA
Stub et al., 2011 (28)	52/81	46/52
Laish-Farkash et al., 2011 (36)	69/110	59/69
Tømte et al., 2011 (37)	140/252	132/140
Radsel et al., 2011 (31)	154/212	128/154
Mooney et al., 2011 (12)	78/140	72/78
Cronier et al., 2011 (11)	60/111	54/60
Gräsner et al., 2011 (90)	143/183	118/143
Bro-Jeppesen et al., 2012 (30)	211/360	207/219
Zanuttini et al., 2012 (10)	29/48	NA
Liu et al., 2012 (106)	36/81	NA
Nanjayya et al., 2012 (59)	18/35	14/18
Strote et al., 2012 (58)	44/61	34/44
Waldo et al., 2013 (107)	57/84	NA
Velders et al., 2013 (32)	187/222	168/183
Callaway et al., 2014 (43)	495/765	413/495
Thomas et al., 2014 (108)	168/348	115/168
Sideris et al., 2014 (88)	97/300	80/97

Values are n/N.
 DC = discharge; ECG = electrocardiogram; neuro = neurological function; TTM = targeted temperature management.

STEMI. Approximately 70% of these culprit vessels are occluded (52). Hence, emergent cardiac catheterization to define a possible ischemic culprit and to perform revascularization if indicated should be considered in these patients. There is great clinical variability in the management of these patients and a lack of consensus about the best approach to risk stratification and the role of early revascularization (3,10-12,14,25,28,30,37,43,53-61).

The acronym *ACT* implies *assessment* for unfavorable resuscitation features, a multidisciplinary team *consultation*, including the interventional cardiologist, and urgent *transport* to the CCL, once a decision is made to proceed with coronary angiography.

UNFAVORABLE RESUSCITATION FEATURES. The presence of unfavorable resuscitation features that adversely affect the procedural risk/survival benefit of PCI must be considered prior to reaching a decision

to proceed with coronary angiography, especially when multiple unfavorable features are present.

Patients with unfavorable resuscitation features are less likely to benefit from coronary intervention. In these cases, individualized care and interventional cardiology consultation are strongly recommended. Multidisciplinary team members should include physicians from the emergency department, critical care unit, neurology, cardiology, and interventional cardiology. All of the following features are relative, and are not absolute predictors of poor outcomes:

1. **Unwitnessed arrest.** Extended time without systemic circulation prior to the resuscitation effort is associated with a decreased ROSC rate (62) and decreased survival-to-discharge rate (63-66). When successful ROSC and survival are achieved after unwitnessed arrest, the rate of favorable neurological outcome is less than in those with witnessed arrest (65).
2. **Initial rhythm non-VF.** Although the presence of an initial shockable rhythm, such as VT or VF, improves the likelihood of ROSC (6,9-11) and of a favorable outcome (12) after PCI to an acute culprit artery stenosis, severe coronary artery stenosis may also be present among patients with non-shockable rhythms (12). Nonshockable rhythms are associated with worse short- and long-term outcomes (62-64,67). Patients with an initial nonshockable rhythm that transforms into a shockable rhythm fare worse than those presenting with an initial shockable rhythm (68).
3. **No bystander cardiopulmonary resuscitation.** Recent studies have confirmed that the lack of bystander cardiopulmonary resuscitation (CPR) is associated with poor long-term outcomes (62-64). A recent meta-analysis reported that bystanders witnessed 53% of cardiac arrests, but only 32% of cardiac arrests received CPR. Survival was 16.1% in those who received bystander CPR versus 3.9% in those who did not (2).
4. **Longer than 30 min to ROSC.** Early data from in-hospital cardiac arrest patients found that when the resuscitation efforts exceeded 30 min, the survival to discharge was markedly decreased (69). More recent data from OHCA has demonstrated similar results (12). Kamatsu et al. (70) found the mean time to ROSC for those with favorable (Cerebral Performance Category 1 or 2) neurological function post-arrest to be 18 ± 15 min compared with 47 ± 18 min for those with unfavorable (Cerebral Performance Category 3, 4, or 5) neurological function (70). Multiple logistic regression analysis showed a significant relationship with the time interval from receipt of the emergency call (911) to ROSC. A longer time to ROSC correlated with poor neurological outcome (odds ratio [OR]: 0.86; 95% confidence interval [CI]: 0.81 to 0.92; $p < 0.001$) (70).
5. **Ongoing CPR.** Whereas short CPR duration (e.g., <16 min) correlates with a favorable prognosis, continuous or ongoing CPR for >30 min, especially in the presence of unwitnessed arrest, has been shown to significantly reduce the chance of survival. Additionally, studies have shown that the duration of CPR is an independent predictor of poorer functional status after OHCA (71).
6. **and 7. Evidence of unresponsive hypoperfusion and microcirculatory failure (pH and lactate levels).** Cardiac arrest leads to systemic hypoperfusion with a low flow state and microcirculatory failure resulting in tissue ischemia, anaerobic metabolism, and the development of lactic acidosis (72). Normal lactate levels are <1 mmol/l and correspond to a pH of 7.40. A lactate level of 7 mmol/l corresponds to a pH of 7.2 (72) and suggests a very poor prognosis post-resuscitation. Lactic acidosis is independently associated with a 3-fold increase in mortality (72) secondary to multiorgan failure, including severe anoxic brain injury with poor neurological outcome (73).
 - In the PROCAT (Parisian Region Out of hospital Cardiac Arrest) study with 435 cardiac arrest patients, there were 264 nonsurvivors, of whom 112 had a lactate level >7 mmol/l (3,32). In post-cardiac arrest patients, a pH <7.2 reflects severe acidemia, with increased risk of left ventricular dysfunction (74,75) and poor neurological recovery, whereas those with a pH >7.2 had a >3-fold chance of neurological recovery (76,77).
 - Severe lactic acidosis is present when the lactate level is >18 mmol/l, corresponding to a pH of 7.0 (72). In the CHEER (Refractory Cardiac Arrest Treated With Mechanical CPR, Hypothermia, ECMO and Early Reperfusion) trial, 14 of the 26 enrolled patients with cardiac arrest did not survive, and their deaths were associated with a pH of 6.8 (78).
8. **Age >85 years.** Although age alone is not an exclusion criterion, it is a poor prognostic indicator and should be carefully assessed (including physiological age vs. true age) before an emergent cardiac catheterization is undertaken. Although controversial, age needs to be considered, as studies suggest a worse outcome with advanced age, particularly in octogenarians (3,11,49,77,79). Of 179 post-cardiac arrest patients >75 years of age treated with TH/TTM and PCI, only 33% survived

to discharge and only 28% attained good functional recovery (77). In a large registry of patients >85 years of age, 60% failed to achieve ROSC and the mortality rate was 90% (80). A recent abstract from a Danish registry reported a successful resuscitation rate of only 25% in octogenarians (mean age 85 years) after cardiac arrest, compared with 40% among younger patients. Those octogenarians who were successfully resuscitated had a 30-day survival of 19% (compared with 45% for younger patients). However, most who survived in both groups (75% and 85%, respectively) had good functional status (81). These studies illustrate the substantial effect of age on survival, but did not address the specific effect of an early invasive approach. Given the potential challenges of delineating futility among high-risk patients, we recommend careful assessment of those >85 years of age, prior to emergent activation of CCL.

9. End-stage renal disease on hemodialysis.

Compared with the general population, patients with end-stage renal disease on dialysis are at increased risk for sudden cardiac arrest. Myocardial ischemia secondary to coronary artery disease is the primary cause of cardiac arrest. In addition to the usual triggers of cardiac arrest, hemodialysis patients may have electrolyte derangements resulting from fluid shifts or changes in pH, leading to the arrest. Survival rates for dialysis patients with cardiac arrest are dismal, with <15% of dialysis patients alive at 1 year (82-84). Of 729 patients who experienced cardiac arrest while in the hemodialysis unit, 310 (42.5%) were alive at 24 h, with only 80 survivors (11%) at 6 months (83). There were 110 cardiac arrests at outpatient dialysis centers in Seattle, Washington, between 1990 and 2004. Only 51 patients (46%) were alive at 24 h, 26 (24%) survived to hospital discharge, and only 16 (15%) were alive at 1 year (84). Recent reviews report mortality in excess of 60% in the first 48 h, with a 1-year mortality of 87% (85-87).

10. Noncardiac causes. Patients with cardiac arrest due to drugs, drowning, choking, acute stroke, respiratory failure, terminal cancer, and trauma are typically not appropriate candidates for emergent cardiac catheterization. Although many of these patients may have a reasonable prognosis, it is unlikely to be enhanced by early angiography.

OTHER COMORBIDITIES OR CONTRAINDICATIONS TO AGGRESSIVE TREATMENT. The effect on post-arrest outcomes of other comorbidities, such as advanced dementia, chronic ventilator dependence, respiratory failure, severe frailty and disability, and

other multisystem illnesses are not well characterized within the published data. However, these conditions are likely to result in a poor outcome post-resuscitation and need to be taken into consideration. Moreover, many patients with these conditions have care plans and do not wish aggressive treatment, including resuscitation. If it becomes apparent during the evaluation that a patient did not want to be resuscitated, an invasive approach should not be undertaken (77).

IMMEDIATE CORONARY ANGIOGRAPHY IN PATIENTS WITHOUT STE ON ECG

The majority of patients resuscitated from cardiac arrest do not have STE on post-arrest ECG (3,12,30,56,88,89). Although there is strong evidence to support immediate coronary angiography and PCI in patients with resuscitated cardiac arrest and STEMI, data supporting immediate coronary angiography in patients without STE is less clear.

Approximately one-fourth of patients without STE have an acute occlusion (25,31,52,55,58) and nearly 60% have significant obstructive lesions (3,14,30,31,55,56) (Table 2). Clinical and electrocardiographic characteristics are poor predictors of the presence of an acutely occluded vessel. In 1 report (53) of 84 patients with cardiac arrest referred for coronary angiography, the presence of chest pain preceding the arrest and the presence of STE on ECG were the only independent predictors of an acute occlusion (OR: 4.0; 95% CI: 1.3 to 10.1; $p = 0.016$; and OR: 4.3; 95% CI: 1.6 to 2.0; $p = 0.004$, respectively). However, the positive and negative predictive values associated with the presence of 1 of these 2 factors were only 0.63 and 0.74, respectively. If both variables were present, the positive and negative predictive values were 0.87 and 0.61, respectively. More importantly, 11% of patients with an acute coronary occlusion did not have STE. These data suggest that coronary angiography remains the “gold standard” for the identification of a culprit artery that may benefit from early revascularization.

Observational studies have demonstrated that patients resuscitated from cardiac arrest and referred for early coronary angiography and/or PCI have better outcomes, as compared with patients who are conservatively treated post-arrest (3,10-12,14,25,28,32,37,43,53-55,58,90) (Table 3). In all but 1 of these reports, the examined population included patients with and without STE, which limits the ability to assess the prognostic effect of early angiography specifically in those patients without STE on ECG. The study by Hollenbeck et al. (25) is the

TABLE 2 Angiographic Findings in Patients With Cardiac Arrest and No ST-Segment Elevation on ECG

First Author, Year (Ref. #)	Acute Occlusion	Culprit Lesion*	Significant CAD†
Merchant et al., 2008 (55)	6/17 (35)	–	10/17 (55)
Reynolds et al., 2009 (14)	–	–	31/54 (57)
Anyfantakis et al., 2009 (56)	–	–	27/44 (61)
Radsel et al., 2011 (31)	4/54 (7)	13/54 (24)	32/54 (59)
Bro-Jeppesen et al., 2012 (30)	–	–	43/82 (52)
Dumas et al., 2010 (3)	–	–	176/301 (58)
Hollenbeck et al., 2014 (25)	44/163 (27)	–	–
Kern et al., 2015 (52)	23	33	–
Total (%)	23	29	58

Values are n/N (%) or %. *Defined as acute occlusion or irregular plaque morphology with or without thrombus. †Defined according to the definition used in each study.

CAD = coronary artery disease; ECG = electrocardiogram.

only report to examine the effect of an early invasive strategy on neurological outcome and in-hospital survival in a group of patients resuscitated from cardiac arrest who did not have STE (25) on ECG. In this study of 269 comatose patients after cardiac arrest due to VF or VT, 122 patients (45%) underwent “early” cardiac catheterization (defined as a procedure performed immediately after hospital admission or during hypothermia treatment). As compared with late or no catheterization, early cardiac catheterization was associated with a lower adjusted OR for in-hospital mortality (OR: 0.35; 95% CI: 0.18 to 0.70; $p = 0.003$). Furthermore, long-term survival and a favorable neurological outcome on follow-up were significantly higher in the group of patients referred for early catheterization (60.0% vs. 40.4%, $p = 0.005$; and 60.0% vs. 39.7%, $p = 0.004$, respectively).

The data summarized in Table 3 support early coronary angiography in patients after cardiac arrest, irrespective of the presence or absence of STE. Although these results imply improved outcomes among patients referred for cardiac catheterization, they should be interpreted with caution due to the observational nature of the studies. Observational reports are frequently confounded and seldom adequately control for all factors affecting physicians’ decisions regarding management. Randomized controlled trials of early coronary angiography versus no or late coronary angiography in patients without STE after cardiac arrest are needed. Until then, we recommend proceeding with coronary angiography in appropriate patients. The principal goal of angiography is to define the coronary anatomy and identify culprit lesions that require urgent PCI. Coronary anomalies would also be noted. If angiography is considered, it should be done early after hospital

presentation. In the study by Hollenbeck et al. (25), early angiography was defined as a procedure within the first 24 h. We favor a quicker time to angiography, ideally as soon as possible after the initial triage and assessment for unfavorable features (as outlined in our algorithm), with an emphasis on emergent consultation by a multidisciplinary team. Patients unlikely to benefit from coronary angiography and possible PCI should be identified early and should not proceed to the catheterization laboratory. In patients referred for angiography, the decision to proceed with PCI should be on the basis of the angiographic findings, coupled with the hemodynamic and electrical status of the patient.

THE CHALLENGES OF PUBLIC REPORTING

Although several states have been publicly reporting PCI outcomes for years, the passage of the Patient Protection and Affordable Care Act in 2010 increased the focus on public reporting and quality improvement. The National Quality Forum recently endorsed risk-adjusted total in-hospital PCI mortality and 30-day all-cause risk-standardized PCI mortality with STEMI and/or cardiogenic shock for public reporting (91).

Although paved with noble intentions, public reporting of mortality can have unintended consequences, possibly promoting risk-averse behaviors that negatively affect the patients who potentially have the most to gain from the procedure (92). Patients with OHCA and ROSC have an approximately 10-fold higher mortality rate than non-cardiac arrest patients with STEMI (5). Furthermore, most of the mortality in this population is due to neurological complications or multiorgan failure, despite receiving appropriate care. Moreover, current risk modeling does not adequately adjust for these extremes of risk, and high volumes of cardiac arrest patients can adversely affect individual and institutional outcomes. This is particularly important in the context of lower-volume centers, where patients who are appropriately treated for OHCA can have an outsized effect on mortality rates. Public reporting inadvertently places clinicians in the difficult situation of having to choose between what may be in their patient’s interest and what may be best for their own quality metrics or for their hospital’s reported outcomes.

Importantly, there is little evidence that public reporting of mortality improves outcomes in PCI, especially for patients with OHCA. In fact, several studies evaluating the effect of public reporting on PCI mortality in New York, Massachusetts, and Pennsylvania suggest that risk-averse behaviors

TABLE 3 Outcomes of Patients With Cardiac Arrest Referred for Coronary Angiography

First Author, Year (Ref. #)	Early CAG Group (Includes Patients With and Without STE, Unless Otherwise Indicated)				No/Late CAG Group			Comments
	No STE	Early CAG	PCI (% of CAG)	Survival/Good Outcome (% of CAG)	No/Late CAG	PCI	Survival/Good Outcome	
Spaulding et al., 1997 (53)	49 (58)	84 (99)	37 (44)	32 (38)	1 (1)	–	0 (0)	All patients were intended to receive CAG; adjusted odds for survival with successful PCI: 5.2; 95% CI: 1.1-24.5; p = 0.04.
Werling et al., 2006 (54)	NA	24 (28)	13 (54)	16 (67)	61 (72)	–	11 (18)	The majority of CAG patients had STEMI; adjusted analysis not performed; unadjusted OR for survival with CAG: 9.1; 95% CI: 3.6-21.5; p < 0.0001.
Merchant et al., 2008 (55)	17 (57)*	30 (27)	18 (60)	24 (80)	80 (73)	–	43 (54)	Adjusted odds for survival overall with CAG: 3.8; 95% CI: 1.35-10.90; p < 0.05; in patients without STE OR: 3.01; 95% CI: 0.84-10.8; p = 0.091.
Reynolds et al., 2009 (14)	189 (78)	96 (40)	48 (50)	52 (54)	145 (60)	–	36 (25)	Propensity-adjusted logistic regression OR for good neurological outcome with CAG: 2.16; 95% CI: 1.12-4.19; p < 0.02.
Anyfantakis et al., 2009 (56)	49 (68)	72 (100)	25 (35)	35 (49)	–	–	–	All patients studied got CAG; by multivariate analysis, attempted PCI was not an independent predictor of improved survival.
Dumas et al., 2010 (3)	301 (69)	435 (100)	202 (46)	171 (39)	–	–	–	All patients studied got CAG; successful PCI was an independent predictor of survival, adjusted OR: 2.06; 95% CI: 1.16-3.66; p = 0.013.
Nanjayya et al., 2011 (59)	NA	35 (50)	21 (60)	18 (51)	35 (50)	1 (2)	12 (34)	Adjusted odds for survival with good neurological outcome with CAG: 1.32; 95% CI: 0.26-7.37; p = 0.78.
Mooney et al., 2011 (12)	72 (51)	101 (72)	56 (55)	63 (62)	39 (29)	–	15 (38)	It is not indicated whether the use of CAG was included in the multivariate analysis of factors related to survival.
Aurore et al., 2011 (61)	367 (82)	133 (30)	71 (53)	30 (23)	312 (70)	–	30 (9.6)	p values for comparisons not provided.
Tømte et al., 2011 (37)	NA	145 (83)	80 (55)	76 (52)	29 (17)	–	9 (31)	Adjusted odds for good outcome with emergency CAG: 11.21; 95% CI: 2.96-42.49; p < 0.001.
Stub et al., 2011 (28)	46 (37)	82 (66)	41 (50)	–	43 (34)	–	–	Also included conscious patients; unadjusted OR for survival with CAG: 7.6; 95% CI: 3.2-17.5; p = 0.01. Adjusted analysis not performed.
Strote et al., 2012 (58)	158 (66)	61 (25)	38 (62)	44 (72)	179 (75)	13 (30)†	87 (49)	Assessed survival by terciles of likelihood of getting CAG. In highest tercile group, survival was higher with early CAG (73% vs. 33%; p = 0.001).
Zanuttini et al., 2012 (10)	61 (66)	48 (52)	25 (52)	29 (60)	45 (48)	6 (33)†	21 (47)	Adjusted odds for survival overall with successful PCI: 2.32; 95% CI: 1.23-4.38; p = 0.009.
Cronier et al., 2011 (11)	61 (55)	91 (82)	46 (51)	NA	–	–	–	Only patients without hemodynamic instability got CAG; adjusted OR for death with PCI: 0.30; 95% CI: 0.11-0.79; p = 0.01.
Bro-Jeppesen et al., 2012 (30)	244 (68)	82 (34)*	24 (29)*	54 (66)*	162 (66)*	–	83 (53)*	Adjusted HR for mortality in with emergency CAG in group without STE: 0.69; 95% CI: 0.4-1.2; p = 0.18.
Søholm et al., 2013 (60)	1,020 (84)	128 (13)*	NA	NA	892 (87)*	NA	NA	Univariate OR for 30-day mortality with early CAG: 0.35; 95% CI: 0.18-0.70; p = 0.003; early CAG was not an independent predictor of mortality.
Hollenbeck et al., 2014 (25)	269 (100)	122 (45)	40 (33)	80 (66)	147 (55)	16 (11)†	71 (49)	Adjusted OR for mortality with CAG: 0.35; 95% CI: 0.18-0.70; p = 0.003.
Callaway et al., 2014 (43)	3,408 (86)	765 (19)	705 (92)	495 (65)	3,216 (81)	–	871 (27)	Adjusted OR for survival with early CAG: 1.69; 95% CI: 1.06-2.70

Values are n (%). *Among those without STE. †Among those getting CAG.
 CAG = coronary angiography; CI = confidence interval; HR = hazard ratio; NA = not available; OR = odds ratio; PCI = percutaneous coronary intervention; STE = ST-segment elevation; STEMI = ST-segment elevation myocardial infarction.

related to public reporting may actually negatively affect patient outcomes. The 3 public reporting states rank 42nd, 48th, and 50th for utilization of PCI for acute myocardial infarction, a guideline-supported

indication (93). Furthermore, the adjusted mortality for patients presenting with STEMI is 35% higher in states with public reporting compared with those without public reporting. This is, in part, related to

lower utilization of angiography and PCI in patients with STEMI (61.8% vs. 68%; OR: 0.73; 95% CI: 0.59 to 0.89; $p = 0.002$), including patients with either cardiogenic shock or cardiac arrest (41.5% vs. 46.7%; OR: 0.79; 95% CI: 0.64 to 0.98; $p = 0.03$) compared with states that do not publicly report mortality outcomes. This lower utilization of revascularization and higher mortality for cardiac arrest patients in states with public reporting was echoed in an analysis of 84,121 patients from the National Inpatient Sample database (94). Interestingly, in Massachusetts, the rates of PCI were similar to those in other non-reporting states prior to public reporting, but began to diverge after public reporting was implemented, strongly implicating public reporting in the decline in optimal care. Finally, being identified as a “negative outlier” in risk-adjusted mortality in Massachusetts has been associated with a significant decline in predicted mortality in subsequent years, suggesting that risk-averse behaviors led to the exclusion of critically ill patients (95).

Given these limitations in public reporting of PCI mortality, especially in patients at extreme risk, such as OHCA patients, we endorse the recommendations set forth in the scientific statement from the AHA:

“OHCA cases should be tracked but not publicly reported or used for overall PCI performance ranking, which would allow accountability for their management but would not penalize high-volume cardiac resuscitation centers (CRCs) for following the 2010 AHA Guidelines for CPR and ECC. Until an adequate risk adjustment model is created to account for the numerous out-of-hospital and in-hospital variables that impact survival more than the performance of PCI, we believe that categorizing OHCA STEMI-PCI cases separately from other STEMI-PCI cases should occur. These patients should not be included in public reporting” (5).

ETHICAL ISSUES

Ethical challenges are unavoidable in the care of acutely ill patients resuscitated from OHCA. Although these challenges cannot be eliminated, there are ways to maximize ethical decision-making regarding angiography/PCI in this context.

First, there is an ethical imperative for rigorous research to inform decisions, particularly given heterogeneous practice patterns and varied standards of care. Randomized trials for treatment of cardiac arrest and other critical illnesses are at times controversial, largely due to ethical challenges regarding informed

consent (96,97). However, regulations exist to facilitate these trials under an exception from informed consent (98,99). These regulations balance the need for research with important protections for patients and communities, and trials conducted under these regulations have resulted in significant insights and improvements in cardiac arrest care (1,24).

Second, decision-making in treatment of OHCA requires confronting issues of futility. The proposed algorithm highlights factors that may help to define when angiography/PCI is most likely futile. For example, a combination of comorbidities, advanced age, and prolonged ischemia (as indicated by severe lactic acidosis or long resuscitative efforts) may signify a high enough chance of multiorgan failure or anoxic brain injury that the incremental benefit of restoring coronary perfusion is truly minimal. However, these predictors are imperfect, and it is unknown how many unfavorable resuscitation features result in futility. Moreover, there are no established thresholds for what chance of a favorable outcome warrants aggressive treatment. If an intervention improves expected survival with good neurological status from 10% to 20%, many physicians or patients would likely not consider it futile, although the prognosis remains dismal. In contrast, an improvement from 1% to 2% represents the same relative benefit, but is likely futile.

Determinations of futility problematically involve quantitative and qualitative assessments with marked heterogeneity among providers. Most importantly, they require judging the value of different outcomes (100-103). In cardiac arrest, these judgments must be made without discussing the issues directly with the patient. Three key ethical implications must be emphasized in the context of futility in OHCA: 1) first, the unavoidable need for clinical judgment; 2) the need for better data and prognostic tools; and 3) the need for transparent discussion at the practice and policy levels about what characterizes appropriate or futile care. These discussions should substantially inform policies regarding reporting practices and quality metrics.

Finally, post-arrest care must involve assessing the patient's likely preferences. A key component of pausing to individualize care is an attempt to contact family or other proxy decision-makers to assess whether aggressive treatment is consistent with the patient's values or preferences. If pre-existing advance directives or do not resuscitate orders are revealed, they should be respected. Perhaps most importantly, direct and honest communication with proxy decision-makers is essential to preserving transparency and trust, and maximizing compatibility of decisions with patients' values and goals.

CONCLUSIONS

1. We propose an easily implementable algorithm to identify resuscitated comatose patients after cardiac arrest who are appropriate candidates for emergent coronary angiography.
2. Urgent consultation and evaluation by a multidisciplinary team, including the interventional cardiologist, should occur before the patient is transferred to the CCL.
3. Early initiation of TTM is strongly recommended.
4. We emphasize our viewpoint and explicitly recommend without reservation that PCI outcomes

in cardiac arrest patients not be included in public reporting. A national platform for tracking outcomes of cardiac arrest patients undergoing PCI is needed and should distinguish patients with and without ST-segment elevation.

5. Randomized controlled trials of early PCI in post-cardiac arrest patients without ST-segment elevation are needed.

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REFERENCES

1. Hallstrom AP, Ornato JP, Weisfeldt M, et al., for the Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004;351:637-46.
2. Sasson C, Rogers MA, Dahl J, et al. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes* 2010;3:63-81.
3. Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac Arrest) registry. *Circ Cardiovasc Interv* 2010;3:200-7.
4. Bendz B, Eritsland J, Nakstad AR, et al. Long-term prognosis after out-of-hospital cardiac arrest and primary percutaneous coronary intervention. *Resuscitation* 2004;63:49-53.
5. Peberdy MA, Donnino MW, Callaway CW, et al., for the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Impact of percutaneous coronary intervention performance reporting on cardiac resuscitation centers: a scientific statement from the American Heart Association. *Circulation* 2013;128:762-73.
6. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;61:e78-140.
7. Gorjup V, Radsel P, Kocjancic ST, et al. Acute ST-elevation myocardial infarction after successful cardiopulmonary resuscitation. *Resuscitation* 2007;72:379-85.
8. Noc M, Fajadet J, Lassen JF, et al. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European Association for Percutaneous Cardiovascular Interventions (EAPCI)/Stent for Life (SFL) groups. *EuroIntervention* 2014;10:31-7.
9. Field JM, Hazinski MF, Sayre MR, et al. Part 1: executive summary: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122 Suppl 3:S640-56.
10. Zanuttini D, Armellini I, Nucifora G, et al. Impact of emergency coronary angiography on in-hospital outcome of unconscious survivors after out-of-hospital cardiac arrest. *Am J Cardiol* 2012;110:1723-8.
11. Cronier P, Vignon P, Bouferrache K, et al. Impact of routine percutaneous coronary intervention after out-of-hospital cardiac arrest due to ventricular fibrillation. *Critical Care* 2011;15:R122.
12. Mooney MR, Unger BT, Boland LL, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest: evaluation of a regional system to increase access to cooling. *Circulation* 2011;124:206-14.
13. Garot P, Lefevre T, Eltchaninoff H, et al. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. *Circulation* 2007;115:1354-62.
14. Reynolds JC, Callaway CW, El Khoudary SR, et al. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. *J Intensive Care Med* 2009;24:179-86.
15. Kern KB. Optimal treatment of patients surviving out-of-hospital cardiac arrest. *J Am Coll Cardiol Intv* 2012;5:597-605.
16. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002;346:557-63.
17. Hovdenes J, Laake JH, Aaberge L, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest: experiences with patients treated with percutaneous coronary intervention and cardiogenic shock. *Acta Anaesthesiol Scand* 2007;51:137-42.
18. Knafelj R, Radsel P, Ploj T, et al. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation* 2007;74:227-34.
19. Noc M, Radsel P. Urgent invasive coronary strategy in patients with sudden cardiac arrest. *Curr Opin Crit Care* 2008;14:287-91.
20. Rossetti AO, Oddo M, Logroscino G, et al. Prognostication after cardiac arrest and hypothermia: a prospective study. *Ann Neurol* 2010;67:301-7.
21. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2007;73:29-39.
22. Wolfrum S, Pierau C, Radke PW, et al. Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention. *Crit Care Med* 2008;36:1780-6.
23. Zimmermann S, Flachskampf FA, Schneider R, et al. Mild therapeutic hypothermia after out-of-hospital cardiac arrest complicating ST-elevation myocardial infarction: long-term results in clinical practice. *Clin Cardiol* 2013;36:414-21.
24. Nielsen N, Wetterslev J, Cronberg T, et al., for the TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med* 2013;369:2197-206.
25. Hollenbeck RD, McPherson JA, Mooney MR, et al. Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. *Resuscitation* 2014;85:88-95.
26. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002;346:549-56.
27. Batista LM, Lima FO, Januzzi JL Jr., et al. Feasibility and safety of combined percutaneous coronary intervention and therapeutic hypothermia following cardiac arrest. *Resuscitation* 2010;81:398-403.
28. Stub D, Hengel C, Chan W, et al. Usefulness of cooling and coronary catheterization to improve survival in out-of-hospital cardiac arrest. *Am J Cardiol* 2011;107:522-7.
29. Kim F, Nichol G, Maynard C, et al. Effect of prehospital induction of mild hypothermia on

- survival and neurological status among adults with cardiac arrest: a randomized clinical trial. *JAMA* 2014;311:45-52.
- 30.** Bro-Jeppesen J, Kjaergaard J, Wanscher M, et al. Emergency coronary angiography in comatose cardiac arrest patients: do real-life experiences support the guidelines? *Eur Heart J Acute Cardiovasc Care* 2012;1:291-301.
- 31.** Radsel P, Knafelj R, Kocjancic S, et al. Angiographic characteristics of coronary disease and postresuscitation electrocardiograms in patients with aborted cardiac arrest outside a hospital. *Am J Cardiol* 2011;108:634-8.
- 32.** Velders MA, van Boven N, Boden H, et al. Association between angiographic culprit lesion and out-of-hospital cardiac arrest in ST-elevation myocardial infarction patients. *Resuscitation* 2013;84:1530-5.
- 33.** Richling N, Herkner H, Holzer M, et al. Thrombolytic therapy vs primary percutaneous intervention after ventricular fibrillation cardiac arrest due to acute ST-segment elevation myocardial infarction and its effect on outcome. *Am J Emergency Med* 2007;25:545-50.
- 34.** Scheffold JC, Storm C, Joerres A, et al. Mild therapeutic hypothermia after cardiac arrest and the risk of bleeding in patients with acute myocardial infarction. *Int J Cardiol* 2009;132:387-91.
- 35.** Nielsen N, Hovdenes J, Nilsson F, et al., for the Hypothermia Network. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand* 2009;53:926-34.
- 36.** Laish-Farkash A, Matetzky S, Oieru D, et al. Usefulness of mild therapeutic hypothermia for hospitalized comatose patients having out-of-hospital cardiac arrest. *Am J Cardiol* 2011;108:173-8.
- 37.** Tømte Ø, Andersen GØ, Jacobsen D, et al. Strong and weak aspects of an established post-resuscitation treatment protocol—a five-year observational study. *Resuscitation* 2011;82:1186-93.
- 38.** O'Connor RE, Bossaert L, Arntz H-R, et al., for the Acute Coronary Syndrome Chapter Collaborators. Part 9: Acute Coronary Syndromes: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2010;122 16 Suppl 2:S422-65.
- 39.** O'Connor RE, Brady W, Brooks SC, et al. Part 10: Acute coronary syndromes: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010;122 16 Suppl 2:S787-817.
- 40.** Authors/Task Force Members, Steg PG, James SK, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33:2569-619.
- 41.** Heard KJ, Peberdy MA, Sayre MR, et al. A randomized controlled trial comparing the Arctic Sun to standard cooling for induction of hypothermia after cardiac arrest. *Resuscitation* 2010;81:9-14.
- 42.** Castrén M, Nordberg P, Svensson L, et al. Intra-arrest transnasal evaporative cooling: a randomized, prehospital, multicenter study (PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness). *Circulation* 2010;122:729-36.
- 43.** Callaway CW, Schmicker RH, Brown SP, et al., for the ROC Investigators. Early coronary angiography and induced hypothermia are associated with survival and functional recovery after out-of-hospital cardiac arrest. *Resuscitation* 2014;85:657-63.
- 44.** Joffre J, Varenne O, Bougouin W, et al. Stent thrombosis: An increased adverse event after angioplasty following resuscitated cardiac arrest. *Resuscitation* 2014;85:769-73.
- 45.** Ibrahim K, Christoph M, Schmeinck S, et al. High rates of prasugrel and ticagrelor non-responder in patients treated with therapeutic hypothermia after cardiac arrest. *Resuscitation* 2014;85:649-56.
- 46.** Rosillo SO, Lopez-de-Sa E, Iniesta AM, et al. Is therapeutic hypothermia a risk factor for stent thrombosis? *J Am Coll Cardiol* 2014;63:939-40.
- 47.** Kern KB, Boyella RR, Patel RM, et al. Stent thrombosis after aggressive post resuscitation care: the beginning or the end? *Resuscitation* 2014;85:711-3.
- 48.** Stone GW. VELOCITY: a prospective, randomized trial of peritoneal hypothermia in patients with acute ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. Paper presented at: *Transcatheter Therapeutics* 2014; September 15, 2014; Washington, DC.
- 49.** Hosmane VR, Mustafa NG, Reddy VK, et al. Survival and neurologic recovery in patients with ST-segment elevation myocardial infarction resuscitated from cardiac arrest. *J Am Coll Cardiol* 2009;53:409-15.
- 50.** Pleskot M, Babu A, Hazukova R, et al. Out-of-hospital cardiac arrests in patients with acute ST elevation myocardial infarctions in the East Bohemian region over the period 2002-2004. *Cardiology* 2008;109:41-51.
- 51.** Valente S, Lazerri C, Saletti E, et al. Primary percutaneous coronary intervention in comatose survivors of cardiac arrest with ST-elevation acute myocardial infarction: a single-center experience in Florence. *J Cardiovasc Med (Hagerstown)* 2008; 9:1083-7.
- 52.** Kern KB, Patel N, Mooney MR, et al. Outcomes of comatose cardiac arrest survivors with and without STEMI: importance of coronary angiography. *J Am Coll Cardiol Intv* 2015;8:1031-9.
- 53.** Spaulding CM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med* 1997; 336:1629-33.
- 54.** Werling M, Thorén AB, Axelsson C, et al. Treatment and outcome in post-resuscitation care after out-of-hospital cardiac arrest when a modern therapeutic approach was introduced. *Resuscitation* 2007;73:40-5.
- 55.** Merchant RM, Abella BS, Khan M, et al. Cardiac catheterization is underutilized after in-hospital cardiac arrest. *Resuscitation* 2008;79:398-403.
- 56.** Anyfantakis ZA, Baron G, Aubry P, et al. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. *Am Heart J* 2009;157:312-8.
- 57.** Garcia S, Mahoney B, Frascione R, et al. Early access to cardiac catheterization laboratory for patients resuscitated from cardiac arrest due to a shockable rhythm: The Minnesota Resuscitation Consortium Twin Cities unified protocol (abstr). *J Am Coll Cardiol* 2014;63 Suppl 12:A339.
- 58.** Strote JA, Maynard C, Olsufka M, et al. Comparison of role of early (less than six hours) to later (more than six hours) or no cardiac catheterization after resuscitation from out-of-hospital cardiac arrest. *Am J Cardiol* 2012;109:451-4.
- 59.** Nanjajya VB, Nayyar V. Immediate coronary angiogram in comatose survivors of out-of-hospital cardiac arrest—an Australian study. *Resuscitation* 2012;83:699-704.
- 60.** Sørensen H, Wachtell K, Nielsen SL, et al. Tertiary centres have improved survival compared to other hospitals in the Copenhagen area after out-of-hospital cardiac arrest. *Resuscitation* 2013;84:162-7.
- 61.** Aurore A, Jabre P, Liot P, et al. Predictive factors for positive coronary angiography in out-of-hospital cardiac arrest patients. *Eur J Emerg Med* 2011;18:73-6.
- 62.** Idris AH, Guffey D, Auferdeide TP, et al., for the Resuscitation Outcomes Consortium (ROC) Investigators. The relationship between chest compression rate and outcome from cardiac arrest. *Circulation* 2012;125:3004-12.
- 63.** Rea TD, Cook AJ, Stiell IG, et al., for the Resuscitation Outcomes Consortium Investigators. Predicting survival after out-of-hospital cardiac arrest: role of the Utstein data elements. *Ann Emerg Med* 2010;55:249-57.
- 64.** Bobrow BJ, Spaite DW, Berg RA, et al. Chest compression-only CPR by lay rescuers and survival from out-of-hospital cardiac arrest. *JAMA* 2010; 304:1447-54.
- 65.** Spaite DW, Bobrow BJ, Stolz U, et al., for the Arizona Cardiac Receiving Center Consortium. Regionalization of postarrest care for out-of-hospital cardiac arrest: association with survival and neurologic outcome. *Ann Emerg Med* 2014;64:496-506.
- 66.** Abrams HC, McNally B, Ong M, et al. A composite model of survival from out-of-hospital cardiac arrest using the Cardiac Arrest Registry to Enhance Survival (CARES). *Resuscitation* 2013;84:1093-8.
- 67.** Reynolds JC, Rittenberger JC, Toma C, et al., for the Post Cardiac Arrest Service. Risk-adjusted outcome prediction with initial post-cardiac arrest illness severity: implications for cardiac arrest survivors being considered for early invasive strategy. *Resuscitation* 2014;85:1232-9.
- 68.** Meaney PA, Nadakami VM, Kern KB, et al. Electrocardiographic rhythms and outcomes from in-hospital cardiac arrests. *Crit Care Med* 2010;38:101-8.
- 69.** Bedell SE, Delbanco TL, Cook EF, et al. Survival after cardiopulmonary resuscitation in the hospital. *N Engl J Med* 1983;309:569-76.

70. Kamatsu T, Kinoshita K, Sakurai A, et al. Shorter time until return of spontaneous circulation is the only independent factor for a good neurological outcome in patients with post-cardiac arrest syndrome. *Emerg Med J* 2014;31:549-55.
71. Reynolds JC, Frisch A, Rittenberger JC, et al. Duration of resuscitation efforts and functional outcome after out-of-hospital cardiac arrest: when should we change to novel therapies? *Circulation* 2013;128:2488-94.
72. Kraut JA, Madias NE. Lactic acidosis. *N Engl J Med* 2014;371:2309-19.
73. Kliegel A, Losert H, Sterz F, et al. Serial lactate determinations for prediction of outcome after cardiac arrest. *Medicine (Baltimore)* 2004;83:274-9.
74. Mitchell JH, Wildenthal K, Johnson RL Jr. The effects of acid-base disturbances on cardiovascular and pulmonary function. *Kidney Int* 1972;1:375-89.
75. Wildenthal K, Mierziak DS, Myers RW, et al. Effects of lactic acidosis on left ventricular performance. *Am J Physiol* 1968;214:1352-9.
76. Ganga HV, Kallur K, Patel NB, et al. The impact of severe acidemia on neurologic outcome of cardiac arrest survivors undergoing therapeutic hypothermia. *Resuscitation* 2013;84:1723-7.
77. Seder DB, Patel N, McPherson J, et al., for the International Cardiac Arrest Registry (INTCAR)-Cardiology Research Group. Geriatric experience following cardiac arrest at six interventional cardiology centers in the United States 2006-2011: interplay of age, do-not-resuscitate order, and outcomes. *Crit Care Med* 2014;42:289-95.
78. Stub D, Bernard S, Pellegrino V, et al. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial). *Resuscitation* 2014;86:88-94.
79. Mager A, Kornowski R, Murninkas D, et al. Outcome of emergency percutaneous coronary intervention for acute ST-elevation myocardial infarction complicated by cardiac arrest. *Coron Artery Dis* 2008;19:615-8.
80. Larkin GL, Copes WS, Nathanson BH, et al. Pre-resuscitation factors associated with mortality in 49,130 cases of in-hospital cardiac arrest: a report from the National Registry for Cardiopulmonary Resuscitation. *Resuscitation* 2010;81:302-11.
81. Soholm H. No Age Limit on Resuscitation. Paper presented at: ESC 2014; August 31, 2014; Barcelona, Spain.
82. Herzog CA. Cardiac arrest in dialysis patients: approaches to alter an abysmal outcome. *Kidney Int Suppl* 2003;63:S197-200.
83. Pun PH, Lehrich RW, Smith SR, et al. Predictors of survival after cardiac arrest in outpatient hemodialysis clinics. *Clin J Am Soc Nephrol* 2007;2:491-500.
84. Davis TR, Young B, Eisenberg MS, et al. Outcome of cardiac arrests attended by emergency medical services staff at community outpatient dialysis centers. *Kidney Int* 2008;73:933-9.
85. Shamseddin MK, Parfrey PS. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. *Nat Rev Nephrol* 2011;7:145-54.
86. Saravanan P, Davidson NC. Risk assessment for sudden cardiac death in dialysis patients. *Circ Arrhythm Electrophysiol* 2010;3:553-9.
87. Surana SP, Pun PH, Keithi-Reddy SR, et al. Sudden cardiac arrest in ESRD patients. *Clin Nephrol* 2014;81:121-31.
88. Sideris G, Voicu S, Yannopoulos D, et al. Favourable 5-year postdischarge survival of comatose patients resuscitated from out-of-hospital cardiac arrest, managed with immediate coronary angiogram on admission. *Eur Heart J Acute Cardiovasc Care* 2014;3:183-91.
89. Möllmann H, Szardien S, Liebetrau C, et al. Clinical outcome of patients treated with an early invasive strategy after out-of-hospital cardiac arrest. *J Int Med Res* 2011;39:2169-77.
90. Gräsner JT, Meybohm P, Caliebe A, et al., for the German Resuscitation Registry Study Group. Postresuscitation care with mild therapeutic hypothermia and coronary intervention after out-of-hospital cardiopulmonary resuscitation: a prospective registry analysis. *Crit Care* 2011;15:R61.
91. Dehmer GJ, Drozda JP Jr., Brindis RG, et al. Public reporting of clinical quality data: an update for cardiovascular specialists. *J Am Coll Cardiol* 2014;63:1239-45.
92. McMullan PW Jr., White CJ. Doing what's right for the resuscitated. *Cath Cardiovasc Interv* 2010;76:161-3.
93. Joynt KE, Blumenthal DM, Orav EJ, et al. Association of public reporting for percutaneous coronary intervention with utilization and outcomes among Medicare beneficiaries with acute myocardial infarction. *JAMA* 2012;308:1460-8.
94. Waldo SW, McCabe JM, O'Brien C, et al. Association between public reporting of outcomes with procedural management and mortality for patients with acute myocardial infarction. *J Am Coll Cardiol* 2015;65:1119-26.
95. McCabe JM, Joynt KE, Welt FG, et al. Impact of public reporting and outlier status identification on percutaneous coronary intervention case selection in Massachusetts. *J Am Coll Cardiol Intv* 2013;6:625-30.
96. Biros MH. Struggling with the rule: the exception from informed consent in resuscitation research. *Acad Emerg Med* 2007;14:344-5.
97. Ostrom CM. Harborview to test drug on the unconscious without consent. *The Seattle Times*. July 9, 2014.
98. Granger CB, Becker LB. Randomized clinical trial progress to inform care for out-of-hospital cardiac arrest. *JAMA* 2014;311:31-2.
99. Office of Good Clinical Practice (OGCP) in the Office of the Commissioner (OC), Food and Drug Administration (FDA), in consultation with FDA's Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), and the Center for Drug Evaluation and Research (CDER). Guidance for Institutional Review Boards, Clinical Investigators and Sponsors: exception from informed consent requirements for emergency research. US Food and Drug Administration publication, 2013. Available at: <http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm249673.pdf>. Accessed May 8, 2015.
100. Alpers A, Lo B. Futility: not just a medical issue. *Law Med Health Care* 1992;20:327-9.
101. Curtis JR, Park DR, Krone MR, et al. Use of the medical futility rationale in do-not-attempt-resuscitation orders. *JAMA* 1995;273:124-8.
102. Swetz KM, Burkle CM, Berge KH, et al. Ten common questions (and their answers) on medical futility. *Mayo Clinic Proc* 2014;89:943-59.
103. Schneiderman LJ, Jecker NS, Jonsen AR. Medical futility: its meaning and ethical implications. *Ann Intern Med* 1990;112:949-54.
104. Peels HO, Jessurum GAJ, Van Der Horst ICC, et al. Outcome in transferred and nontransferred patients after primary percutaneous coronary intervention for ischaemic out-of-hospital cardiac arrest. *Catheter Cardiovasc Interv* 2008;71:147-51.
105. Koeth O, Zahn R, Bauer T, et al. Primary percutaneous coronary intervention and thrombolysis improve survival in patients with ST-elevation myocardial infarction and pre-hospital resuscitation. *Resuscitation* 2010;81:1505-8.
106. Liu HW, Pan W, Wang F, et al. Impact of emergency percutaneous coronary intervention on outcomes of ST-segment elevation myocardial infarction patients complicated by out-of-hospital cardiac arrest. *Chin Med J* 2012;125:405-9.
107. Waldo SW, Armstrong EJ, Kulkarni A, et al. Comparison of clinical characteristics and outcomes of cardiac arrest survivors having versus not having coronary angiography. *Am J Cardiol* 2013;111:1253-8.
108. Thomas JL, Bosson N, Kaji AH, et al. Treatment and outcomes of ST segment elevation myocardial infarction and out-of-hospital cardiac arrest in a regionalized system of care based on presence or absence of initial shockable cardiac arrest rhythm. *Am J Cardiol* 2014;114:968-71.

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