SCAI Expert Consensus Statement on Out of Hospital Cardiac Arrest

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INTRODUCTION

Out of hospital cardiac arrest (OHCA) remains a significant public health problem with high mortality and morbidity. (1) The true magnitude of mortality and morbidity from OHCA is unknown due to the lack of mandatory reporting, unified national surveillance systems, difficulty in accounting for cases not attended by emergency medical services (EMS), variability in existing reporting systems and paucity of data regarding long term neurological and functional outcomes (Appendix 1). (1) Improving survival rates with good neurological outcomes among OHCA patients requires improved response times and quality of care in the “chain of survival” from early activation of EMS and resuscitation to advanced post admission care. (2) Given the high prevalence of coronary artery disease (CAD) as the cause for cardiac arrest in patients with a presenting rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), interventional cardiologists are often consulted to consider emergent coronary angiography (CAG) and possible percutaneous coronary intervention (PCI) in OHCA patients. While emergent CAG and PCI are indicated in selected OHCA patients when the post resuscitation electrocardiogram (ECG) shows ST-segment elevation myocardial infarction (STEMI), there are significant institutional and individual variations in performance and timing for those patients without STEMI on post resuscitation ECG. The role of the cardiac catheterization laboratory encompasses not only CAG and PCI but also hemodynamic assessment and mechanical circulatory support (MCS) device use in patients with concomitant cardiogenic shock (CS). The purpose of this document is to provide an evidence-based and patient-oriented recommendation for the management of these patients.
METHODS

This document has been developed according to SCAI Publications Committee policies for writing group composition, disclosure and management of relationships with industry (RWI), internal and external review, and organizational approval.

The writing group has been organized to ensure diversity of perspectives and demographics, multi-stakeholder representation, and appropriate balance of RWI. Relevant author disclosures are included in Supplemental Table 1. Before appointment, members of the writing group were asked to disclose all relevant financial relationships with industry (>\$25,000) from the 12 months prior to their nomination. A majority of the writing group disclosed no relevant financial relationships. Disclosures were periodically reviewed during document development and updated as needed. SCAI policy requires that writing group members with a current financial interest are recused from participating in discussions or voting on relevant recommendations. The work of the writing committee was supported exclusively by SCAI, a nonprofit medical specialty society, without commercial support. Writing group members contributed to this effort on a volunteer basis and did not receive payment from SCAI.

Literature searches were performed by group members designated to lead each section and initial section drafts were authored by the section leads. Recommendations were discussed by the full writing group on a series of teleconferences until all group members agreed on the text and qualifying remarks.

All recommendations are supported by a short summary of the evidence or specific rationale.

The draft manuscript was peer reviewed in [MONTH, YEAR] and the document was revised to address pertinent comments. The writing group unanimously approved the final version of the document. The SCAI Publications Committee and Executive Committee endorsed the document as official society guidance in [MONTH, YEAR].
SCAI consensus statements are primarily intended to help clinicians make decisions about treatment options. Clinicians also must consider the clinical presentation, setting, and preferences of individual patients to make judgements about optimal approaches.

**Invasive Coronary Angiography Strategies in Resuscitated OHCA Patients:**

Table 1 summarizes the study characteristics of large studies combining all OHCA patients that compared immediate or early coronary angiography with no or delayed coronary angiography. Table 2 summarizes recently published and ongoing randomized control trials (RCTs). The literature guiding the role and timing of CAG and PCI in resuscitated OHCA patients is predominantly limited to observational studies. (Appendix 2)

**Etiology of Death in Patients with OHCA in the Critical Care Unit:**

Irrespective of initial rhythm or ECG findings, the predominant cause of death in two-thirds of patients with OHCA is due to anoxic brain injury and another one third die due to a refractory post arrest shock and multi-organ failure. (3) The rate of survival to discharge with good neurologic function among OHCA patients is low with wide geographical variation estimated at 0.8 – 20%. (4) Anoxic brain injury and post-cardiac arrest shock share common risk factors that are related to the timing and quality of prehospital care. (5)

**Factors Associated with Unfavorable Neurological Outcome in OHCA patients:**

Among OHCA patients who are comatose after return of spontaneous circulation (ROSC), there is no single factor at the time of presentation to reliably prognosticate subsequent neurological outcome. While accurate prognostication is important to avoid pursuing futile treatments or inappropriately withdrawing treatment in patients with a chance of recovery, the quality of existing neurological
prognostication studies is insufficient to make any definitive recommendations for long term neurologic outcomes. Nevertheless, there are pre and intra arrest factors associated with unfavorable neurological outcomes (Table 3). (7) Kaji, 2014 #326

When deciding whether to offer invasive treatments, it is prudent to consider presence of comorbidities that portend a unfavorable short- and long-term prognosis, such as advanced age, severe dementia, chronic advanced respiratory failure, severe frailty or disability, end stage renal or liver disease, and advanced metastatic malignancy. (8)

**Risk stratification Tools:**

Risk stratification scores are often used in medicine for prognostication and decision making. (9) The Cardiac Arrest Hospital Prognosis score (CAHP), (10) CREST, and (11) C-GRAPH are risk stratification tools to assist in decision making. (12) (Table 4)

In addition to risk stratification tools, imaging tools are available to provide further information regarding clinical assessment and management. (13,14) (Table 5)

**DECISION MAKING BASED ON SITUATIONAL AWARENESS AND ASSESSMENT ALONG THE CONTINUUM OF CARE**

Given the heterogeneous nature of OHCA patients, fluidity in evolution of the clinical course, and uncertainty associated with neurological prognostication, we advocate a path of “Situational Awareness and Assessment” (15) taking into consideration all the clinical factors available to aid in clinical decision making along the continuum of care of these patients (Figure 1). (15) We advocate confirming all the pre-hospital and hospital clinical history and data, considering carefully patient’s comorbidities, patient’s and family wishes if known as well as all of the favorable and unfavorable prognostic factors, synthesizing the data to provide the best possible prediction regarding the etiology of the arrest and
anticipated neurological and hemodynamic outcomes to help guide the role and timing of invasive strategy in these patients (Figure 1).

We also support the use of terminology such as activation of cardiac cath Lab (CCL) rather than CAG as it encompasses other invasive procedures (CAG, PCI, Right Heart Cath, MCS, and others) that may need to be performed in this patient population. We recommend use of terminology – “Definite” or “Defer” activation of CCL along a decision making continuum at initial and subsequent encounters based on clinical history, presence of favorable / unfavorable resuscitation factors, initial rhythm, ECG and hemodynamic status (Figure 1). This terminology is subsequently used in all recommendations in this document (TABLE 6).

**OHCA Patients with Shockable Rhythm and STEMI on Post ROSC ECG:**

Among patients with an initial shockable rhythm and diagnostic ST-segment elevations on post ROSC ECG, the prevalence of acute thrombotic coronary occlusion or culprit lesion causing cardiac arrest is greater than 85%. (13) Given this observation, conscious survivors of OHCA at presentation with initial ECG showing STEMI should be treated with immediate CAG and primary PCI as is the current standard of care for STEMI patients. (16)

Among comatose OHCA patients with ROSC and STEMI, there are no RCTs to support favorable neurological outcomes or survival benefit of immediate CAG. In the targeted temperature management (TTM) trial, which evaluated 33°C versus 36°C after cardiac arrest, 41% of the 939 patients had acute STEMI on their initial ECG. In this study, lower time to ROSC was the highest predictor of survival with good neurological function. (17,18) In the International Cardiac Arrest (INTCAR) Registry, among 746 comatose post-arrest (79% OHCA) patients, 26.5 % presented with STEMI and 73.5% without STEMI on their initial ECG; 91% of STEMI patients had immediate CAG whereas 33% patients without STEMI had an immediate CAG. (19) The survival rate was 55.1% in the STEMI group versus 41.3% in the patients
without STEMI on their initial ECG. The decision to perform immediate CAG was based on operator preference rather than a predefined protocol targeting certain selected patients who might benefit with immediate CAG. Therefore, the ECG should not be the sole determinant when activating the CCL, and the ECG should be paired with the clinical presentation and the patient’s clinical findings when considering invasive assessment and potential therapies.

**OHCA Patients with Shockable Rhythm without STEMI on Post ROSC ECG:**

Among OHCA patients with an initial shockable rhythm without STEMI on post ROSC ECG, the prevalence of an acute thrombotic occlusion is approximately 3.4%–30%. (19,20) The prevalence of significant, stable or thrombotic, non-occlusive lesions on CAG ranges from 24–60%. (20,21) While ECG and biomarkers are used in patients with acute coronary syndrome without cardiac arrest, these lack specificity or sensitivity in predicting coronary ischemia as the cause of initial or recurrent cardiac arrest in these patients. (22) When ST elevation is not present, current noninvasive methods lack sensitivity to definitely assess ongoing coronary ischemia and tools to prognosticate neurological outcomes at presentation in comatose patients are inadequate as mentioned. As such, the decision of if and when to activate the CCL in these patients is challenging.

The existing literature on evaluating the benefit of CAG in these patients is predominantly from observational cohort studies (Table 1) with several limitations (Appendix 2). A meta-analysis of 23 observational studies showed that CAG performed within 24 hours was associated with improved survival (Risk Ratio: 1.52, 95% CI: 1.32 - 1.74, p <0.001) and better neurological outcomes (Risk ratio: 1.69, 95% CI: 1.40 - 2.04, p <0.001) compared to no or CAG performed more than 24 hours later. (23) The only published randomized trial, COACT, involving 538 patients showed no survival benefit at 90 days for immediate or early CAG in hemodynamically stable OHCA patients without STEMI on ECG compared to delayed CAG after neurological recovery. (24) Patients with cardiogenic shock
unresponsive to medical therapy, obvious or suspected non-coronary cause of arrest, and STEMI on the
ECG were excluded in this trial. TTM was initiated in more than 90% of patients and 87% of patients
received norepinephrine. Neurological etiologies were the cause of death in more than 70% of the
patients in both groups. In the delayed-angiography group, 14.4% of the patients underwent urgent
coronary angiography because of cardiogenic shock, recurrent ventricular arrhythmia, or recurrence of
ischemia. In 39.5% of these patients, an unstable lesion was detected, a percentage that was higher than
that in the immediate-angiography group (13.6%). PCI was performed in 22 of these patients (57.9%),
which is higher than the percentage of patients in the immediate-angiography group (33%), but the rate
of survival among these patients was not lower than that in the total cohort (71.1% and 65.4%,
respectively). (25)

OHCA Patients with Non – Shockable Rhythms:
While the prevalence of obstructive CAD in patients resuscitated from shockable rhythms including VT
or VF, ranges from 25-60%, (26-28) the prevalence of CAD in OHCA patients with initial non-shockable
rhythms, asystole or pulseless electrical activity (PEA), is not well defined. In OHCA patients presenting
with non-shockable rhythms, non-cardiac etiologies of OHCA often need to be considered. (29,30) The
overall survival and favorable prognosis is significantly higher with initial shockable rhythm compared to
a non- shockable rhythm. (19,31-40) (41)Primary PEA and asystole are more often due to non-coronary
etiologies especially in the elderly with multiple co morbidities. (42) It is also possible that some patients
with initial non-shockable rhythms may develop VF/ VT with administration of epinephrine during
resuscitation, and they should still be treated as OHCA with non-shockable rhythm. (43)
Patients with OHCA are at higher risk of bleeding when undergoing PCI due to injuries sustained as a result of loss of consciousness and often there is concern for intracranial bleeding. (44) These patients are also at higher risk of thrombotic complications because of potentially delayed bioavailability of oral antiplatelet agents either due to active vomiting or reduced absorption from the gut in the setting of low cardiac output state with concomitant cardiogenic shock. (45) The pro-inflammatory state resulting in endogenous changes in coagulation and anticoagulation cascades as part of post resuscitative state, multiorgan dysfunction and therapeutic hypothermia increases the risk of both bleeding and thrombotic complications in OHCA patients. (46)

**Vascular Access:**
Radial access is associated with reduced risk of bleeding complications compared with femoral access among patients undergoing PCI for ACS. (47) However, in a recent large RCT and a retrospective analysis, there was no difference in the primary outcome, mortality, among patients undergoing primary PCI between radial and femoral access. (48) (49). In the setting of OHCA, especially if there is concomitant shock, traditionally the femoral access site has been preferred – due to concerns of vasospasm, increasing procedural time to reperfusion and convenience of restricting the working field to groin area if hemodynamic support is required.

**Antiplatelet therapy:**
Among comatose survivors of OHCA undergoing PCI, post-resuscitative state and hypothermia may affect the absorption and metabolism of oral antiplatelets agents. (45) Some studies have shown an increased rate of stent thrombosis (ST) among post OHCA patients with hypothermia. (50) As demonstrated in patients with STEMI without cardiac arrest, the newer oral anti-platelet agents
(ticagrelor and prasugrel) in addition to aspirin may be associated with reduced risk of ST even among
comatose OHCA patients and are favored over clopidogrel. (51-54) In patients with a large thrombus
burden, bolus doses of glycoprotein IIb/IIIa inhibitors may be considered after carefully weighing against
the increased risk of bleeding. (55) Cangrelor – an intravenous P2 Y12 agent may be an option to use in
these patients as a bridge during delayed absorption of oral agents. (56)

**Anticoagulation therapy:**

Studies among patients with acute coronary syndromes have consistently showed increased risk of
acute ST with bivalirudin compared with unfractionated heparin. (57) OHCA patients undergoing PCI are
at high risk for thrombotic events and bleeding complications as described above and the risk of
bleeding should be weighed against thrombotic risk.

**POST RESUSCITATIVE STATE INTERDISCIPLINARY TEAM AND TARGETED TEMPERATURE**

**MANAGEMENT (TTM)**

Irrespective of whether a definite versus deferred CCL strategy is employed, post resuscitative support is
important to the patient’s overall outcome. Although studies have not specifically evaluated optimal
cardiac arrest team membership, studies evaluating OHCA care systems, hospital volumes, and receiving
hospital characteristics allow us to demonstrate that a multi-disciplinary approach may improve clinical
outcomes (Figure 3). (58-61)

Following the publication of 2 seminal trials (62,63) demonstrating improved survival with the delivery
of in-hospital mild hypothermia for patients with resuscitated VF or VT (Table 7), OHCA patients should
be assessed for TTM on arrival to the hospital. Pre hospital initiation of TTM has not demonstrated
improved clinical outcomes and in some situations it is associated with possible harm (table 8). (64-68)
SHOCK IN OHCA PATIENTS

Patients with OHCA and shock have substantially higher mortality rates and worse neurological outcomes. (69) Patients with shock have an onset of systemic hypoperfusion usually in response to ischemic cardiac injury. This hypoperfusion induces a cascade of proinflammatory signaling, vasomotor dysregulation, vasodilation, multisystem organ dysfunction, and death. (46) The early and late manifestations of shock in OHCA patients are related to a multitude of clinical factors; many of which may be unrelated to the underlying cardiac function. (70) Decisions surrounding extent of coronary revascularization are an important aspect of care among patients with shock. (71) In the randomized study - PCI Strategies in Patient with Acute Myocardial Infarction and Cardiogenic Shock (CULPRIT SHOCK) (72) - more than 50% of the patients had resuscitation prior to randomization, and more than 60% of the deaths were related to refractory cardiogenic shock. In patients who underwent PCI of the culprit lesion only, the composite risk of death and severe renal failure was significantly lower compared with those who underwent immediate multivessel PCI.

There are no large randomized trials to date evaluating the use of MCS devices among OCHA patients with shock. The role of MCS in patients with STEMI complicated by shock, excluding comatose patients with OHCA, is being evaluated in the DanGer Shock trial whereby 360 patients will be randomized to percutaneous transvalvular microaxial flow pump (Impella CP Abiomed, Danvers, Massachusetts) versus guideline therapy. (73) In the IMPRESS in Severe Shock (IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK) trial 48 patients, (92% with cardiac arrest prior to randomization) were randomly assigned to MCS (Impella CP Abiomed, Danvers, Massachusetts) versus IABP (Intra-Aortic Balloon Pump). Treatment with Impella CP did not reduce mortality compared to IABP at 30 days. (69) The use of MCS, specifically Impella, has rapidly been increasing among patients undergoing PCI with limited evidence of efficacy and possible increase in
adverse events. (74) Therefore, the role of MCS and extracorporeal membrane oxygenation in patients
with OHCA and shock, with a focus on patient selection criteria, needs to be evaluated in randomized
controlled trials, a topic which is beyond the scope of this document.

The role of extracorporeal life support (ECLS) for refractory OHCA is of interest and in single center at
sites with the necessary resources and regimented protocols have demonstrated benefit. (75) There are
ongoing randomized trials to determine if ECLS demonstrates benefit in carefully selected patients with
OHCA (Table 9). Whether this strategy can be employed outside of dedicated centers and is
generalizable has not been demonstrated. (76)

SCAI has proposed a simple classification system for rapid assessment of patients with cardiogenic
shock. (77) A recent article retrospectively analyzed hospital survivors to a single cardiac ICU over an 8
year period and associated the SCAI shock classification with post discharge mortality in patient with
acute coronary syndrome and heart failure but not cardiac arrest. (78) Institutions need to implement
appropriate pathways and transfer protocols to hospitals that have the adequate resources to provide
acute care for deteriorating patients (Figure 2). (79)

CURRENT BARRIERS AND FUTURE DIRECTIONS OF PUBLIC REPORTING

Public reporting of procedural outcomes for PCI and coronary artery bypass grafting is expected in
contemporary practice. (80) In the current public reporting formats, non-cardiac mortality (i.e.,
neurologic death) is indistinguishable from cardiac mortality and is therefore attributed as “PCI related
mortality”. This substantially impacts the observed clinical outcomes of both the physician and
institution performing PCI. Outcomes in high risk OHCA patients cannot be accurately accounted for by
current risk-adjustment models. (81-83). Also, it is uncertain if public reporting of outcomes leads to risk
averse behavior with fewer patients undergoing PCI or not. (84,85). A SCAI Position Statement on Public
Reporting has previously been published, recommending exclusion of OHCA patients from public
reporting of PCI outcomes and adjudication of high risk classification at local facility level as necessary. (80) In order to be able to identify OHCA as its own subset, the Chest Pain-MI Registry and the CathPCI Registry have recently undergone significant revisions (cvquality.acc.org/NCDR-Home/Data-Collection/What-Each-Registry-Collects). The data elements between these two registries have been harmonized for consistency. Cath PCI version 5 has recently added far more variables regarding cardiac arrest status (Appendix 3). The goal of collecting more comprehensive data on cardiac arrest is to develop accurate risk adjustment models for benchmarking and public reporting. Further efforts to standardize the data elements, metrics and definitions used in various OHCA registries will enhance collaboration to improve outcomes among these patients. (86)

CONCLUSION

Comatose patients with OHCA have a high mortality and morbidity. The management decisions in these patients are dynamic and interdependent, necessitating frequent clinical evaluations and multidisciplinary team-based approach along the entire continuum of care from pre hospital to post hospital care.
References:


77. Baran DA, Grines CL, Bailey S et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheter Cardiovasc Interv 2019;94:29-37.
EARLY ACCESS
HIGH-QUALITY CPR
RAPID DEFIBRILLATION
EARLY EMERGENCY MEDICAL SERVICES
ADVANCED HOSPITAL CARE

OHCA PATIENT
Situational Awareness Goal: Assessment of all clinical factors to aid decision

ROSC + awake
STEMI Suspected AMI Cardiogenic Shock
Definite Strategy Activate CCL

ROSC + comatose
Emergent Interventional Cardiology Evaluation
TTM assessment

Assess For Favorable Vs. Unfavorable Features Good Neurological Recovery

Favorable
- Low CAHP score
- Bystander CPR
- Time to ROSC < 30 min
- Shockable Rhythm
- Lactate < 4 mmol / L
- Arterial Ph > 7.2
- Age < 85 years
- No ESRD

Unfavorable
- High CAHP score
- No bystander CPR
- Time to ROSC > 30 min
- Non shockable Rhythm
- Lactate > 7 mmol / L
- Arterial Ph < 7.2
- Age > 85 years
- ESRD

Assess For Contraindications to ECLS
- Advanced Age / Multiple Comorbidities
- No-flow > 10 min
- Unwitnessed Arrest
- Initial Rhythm: Asystole / PEA
- Lactate from > 12 mmol / L
- Low ETCO2 (<10 mm Hg)
- Unfavorable Anatomy
- Collapse to ECLS > 60 minutes
- Ongoing CPR > 45 min
- Age ≥ 75 years
- ABG with paO2 < 50 mmHg

Consider initiating ECLS based on multi-disciplinary input

Ongoing CPR < 45 min Age < 75, consider ECLS

Definite Strategy: Activation of Cardiac Cath Lab on Initial Encounter. Includes performing all or any of the following as clinically necessary: 1. Coronary Angiogram 2. Percutaneous coronary intervention 3. Hemodynamic assessment with Right Heart Catheterization and use of Mechanical Circulatory Support Device as necessary. Transfer to ICU Post Cath Lab for continuing TTM

Definite / Defer Strategy
STEMI / Cardiogenic Shock
Definite Strategy
NSTEMI
Defer Strategy

Multiple Favorable
Multiple Unfavorable

STEMI / Cardiogenic Shock
Defer Strategy
NSTEMI
Definite / Defer Strategy

NSTEMI
Defer Strategy

OHCA: outside-hospital cardia arrest; CCL: cardiac cath lab; PEA: pulseless electrical activity; ESRD: end-stage renal disease; STEMI: ST segment elevated myocardial infarction; MCS: mechanical circulatory support; DNR: do not resuscitate; CAHP: cardiac arrest hospital prognosis; ROSC: return of spontaneous circulation; ECLS: extracorporeal life support; TTM: targeted temperature management; CPR: cardiopulmonary resuscitation; BLS: basic life support; ICU: intensive care unit; AMI: acute myocardial infarction
Figure 2: Proposed Levels Of Care Based on SCAI Cardiogenic Shock Classification Schema for Patients with Cardiac Arrest and Shock

**LEVEL I**
- CCL with capability to do PCI + Assess Hemodynamics + IABP, Right and Left Percutaneous MCS & ECMO
- CCU with Multidisciplinary Team

**LEVEL II**
- CCL with capability to do PCI + Assess Hemodynamics + IABP & Right and Left Percutaneous MCS
- CCU with Multidisciplinary Team

**LEVEL III**
- CCL with capability to do PCI + Assess Hemodynamics + IABP
- CCU with Multidisciplinary Team

**Stage A: At Risk**
- No signs or symptoms of shock, but at risk; Patients with AMI, and acute or acute on chronic heart failure

**Stage B: Beginning**
- Relative hypotension or tachycardia without hypotension

**Stage C: Classic**
- Hypoperfusion requires intervention Beyond volume resuscitation (Inotropes or mechanical support)

**Stage D: Deteriorating or Doom**
- Similar to C, but getting worse; Failure to respond to initial interventions

**Stage E: Extremis**
- Circulatory collapse, Frequently in refractory Cardiac Arrest with Ongoing CPR

Establish Appropriate Pathways & Transfer Protocols to Escalate Care As Necessary

Abbreviations: CCL - Cardiac Catheterization Laboratory; PCI – Percutaneous Coronary Intervention; IABP – Intra Aortic Balloon Pump; MCS – Mechanical Circulatory Support; ECMO – Extra Corporeal Membrane Oxygenation; CCU – Coronary Care Unit

*Modified from Baran DA et al (Ref 77) and Rab T et al (Ref 79)*
Figure 3. Out of Hospital Cardiac Arrest (OHCA) Care Team
<table>
<thead>
<tr>
<th>First Author, Year (Ref)</th>
<th>Design, Country of Recruitment</th>
<th>Total Patients</th>
<th>Patients with TTM(%)</th>
<th>Immediate / Early CAG Group</th>
<th>Delayed / No CAG Group</th>
<th>Favors early CAG</th>
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<tr>
<td>Nielsen N, 2009 (36)</td>
<td>Prospective, Observational Cohort Study, Multicenter, USA and Europe</td>
<td>986</td>
<td>986 (100)</td>
<td>479 0 0 479 (100) NA 299 (62) 303 (63) 278 (58) 507 207 (40) NA NA 253 (49) 3</td>
<td>YES HR – 1.27, 95% CI – 1.13 – 1.42</td>
<td>Unwitnessed arrest, non-shockable rhythm, delayed time to achieve ROSC were predictors of poor outcomes.</td>
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<tr>
<td>Callaway CW, 2014 (31)</td>
<td>Post analysis of Randomized T, Multicenter USA and Canada</td>
<td>3981</td>
<td>1566 (39)</td>
<td>765 0-24 591 (77) 356 (46) 705 (92) 495 (64) 413 (54) 321 (6) 1028 (32) 217 (6) NA NA 871 (27) 591 (18)</td>
<td>YES (OR:1.69 – 95% CI – 1.06 – 2.7)</td>
<td>Patients in Early CAG group were highly selected – 19% of all pts - had higher rate of VT/VF; Bystander CPR, and STEMI on EKG</td>
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<tr>
<td>Reynolds JC, 2014 (37)</td>
<td>Single Center Retrospective Cohort, UPMC, USA</td>
<td>1011</td>
<td>559 (55)</td>
<td>273 0 196 (72) 145 (53) 152 (56) NA 128 (47) 738 187 (25) 20 (3) 15 (21) NA 155 (21)</td>
<td>YES OR: 1.92, (95% CI – 1.2, 3.07)</td>
<td>Patient who got early CAG – Selective – 27% : Higher rates of VT/VF; STEMI; with less illness severity score. In more severe strata of illness, early CAG was not beneficial</td>
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<tr>
<td>Geri G, 2015 (33)</td>
<td>Prospective, Observational Cohort Study, France</td>
<td>1722</td>
<td>1222 (71)</td>
<td>1094 0-6 766 (70) 295 (27) 479 (44) 419 (38) NA 628 175 (28) 23 (4) NA 129 (21) NA</td>
<td>YES HR – 1.86, (95% CI – 1.57 – 2.21)</td>
<td>Patient with early CAG – higher rate of VT/VF, STEMI, witnessed arrest, bystander CPR and therapeutic hypothermia</td>
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<td>Kern KB, 2015 (19)</td>
<td>Retrospective and prospective cohort study, USA and Europe</td>
<td>754</td>
<td>738 (98)</td>
<td>439 0 328 (75) 192 (44) 209 (48) 272 (62) 250 (57) 315 109 (35) 6 (2) NA 63 (20) 49 (16)</td>
<td>YES HR – 1.65 (95% CI – 1.40 – 1.95)</td>
<td>Patients chosen for early CAG – higher rate of STEMI</td>
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<tr>
<td>Vyas A, 2015 (40)</td>
<td>Prospective, Multicenter, Observational Cohort</td>
<td>4029</td>
<td>2363 (59)</td>
<td>1953 0-24 1953 (100) 639 (33) 1253 (64) 1484 (76) 1147 (59) 207 6 2076 (100) 163 (8) NA 1234 (59) 821 (40)</td>
<td>YES OR – 1.52, 95%</td>
<td>All are shockable rhythms. Patients chosen for early CAG were younger, had</td>
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<td>Registry Data, USA</td>
<td>Dankiewicz J, 2015 (32)</td>
<td>Post hoc analysis of RCT, Europe and Australia</td>
<td>544</td>
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<td>729 (72)</td>
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<td>Jaeger D, 2018 (34)</td>
<td>Prospective, Multicenter Observational Cohort, Registry Data, France</td>
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<td>0 (Admission to cath lab)</td>
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</tbody>
</table>
| Staudacher II, 2018 (38) | Retrospective, Single Center Cohort Study, Denmark | 507 | 507 (100) | 291 | 0-3 | NA | 181 (62) | 208 (71) | 207 (71) | NA | 216 | NA | 39 (18) | 49 (23) | 137 (63) | NA | NO | HR – 0.69, 95% CI – 0.35 – 1.37 | Propensity matched analysis. Early CAG / PCI not associated with mortality benefit with or without ST elevation. Predictors of 30 day mortality – Older age, cardiogenic shock, elevated lactate and low hemoglobin at presentation. Significantly higher proportion of shock patients in early invasive group
Table 2. Recently Published/Ongoing Randomized Trials of Immediate vs. Delayed CAG in OHCA patients without STEMI on ECG at Presentation:

<table>
<thead>
<tr>
<th>Name of Study</th>
<th>Clinical Trials Identifier</th>
<th>Design, Country of Recruitment</th>
<th>Inclusion / Exclusion Criteria</th>
<th>Total Number of Patients</th>
<th>Primary Outcome</th>
<th>Groups</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>COACT, 2019 (24)</td>
<td>NTR 4973</td>
<td>Open Label, Multicenter, Netherlands</td>
<td>Inc: Comatose OHCA patients + Initial Shockable Rhythm + No STEMI of ECG Ex: Shock / obvious non cardiac cause</td>
<td>538</td>
<td>Survival at 90 days</td>
<td>Immediate: Upon presentation Delayed: After neurological recovery</td>
<td>No difference</td>
</tr>
<tr>
<td>ACCESS</td>
<td>NCT03119571</td>
<td>Open Label, Multicenter, United States</td>
<td>Inc: Comatose OHCA patients + Initial Shockable Rhythm + No STEMI on ECG Ex: STEMI</td>
<td>864</td>
<td>Survival to Hospital Discharge with good neurological outcome</td>
<td>Immediate: Admission to Cath Lab Delayed: Admission to ICU for further assessment</td>
<td>To be published</td>
</tr>
<tr>
<td>DISCO</td>
<td>NCT02309151</td>
<td>Open Label, Multicenter, Sweden</td>
<td>Inc: Witnessed OHCA with achieving ROSC &gt; 20 minutes Ex: STEMI / obvious non cardiac cause</td>
<td>1006</td>
<td>Survival at 30 days</td>
<td>Immediate: Within 120 minutes Not Immediate: No CAG or after 3 days</td>
<td>To be published</td>
</tr>
<tr>
<td>PEARL</td>
<td>NCT02387398</td>
<td>Open Label, Multicenter, USA</td>
<td>Inc: Comatose OHCA patients with No STEMI Ex: STEMI / obvious non cardiac etiology</td>
<td>99</td>
<td>Safety and Efficacy of early CAG</td>
<td>Interventional Early CAG : Within 120 minutes Control group: After 6 hours</td>
<td>To be published</td>
</tr>
<tr>
<td>EMERGE</td>
<td>NCT02876458</td>
<td>Open Label, Multicenter, France</td>
<td>Inc: Comatose OHCA patients Ex: STEMI on ECG/ obvious non cardiac etiology</td>
<td>970</td>
<td>Survival with no or minimal neurological sequelae at 180 days</td>
<td>Immediate: Upon presentation Delayed: 46 – 96 hours</td>
<td>To be published</td>
</tr>
<tr>
<td>TOMAHAWK</td>
<td>NCT02750462</td>
<td>Open Label, Multicenter, Germany</td>
<td>Inc: Comatose OHCA patients Ex: STEMI / Hemodynamic Instability</td>
<td>558</td>
<td>All cause mortality at 30 days</td>
<td>Immediate: Upon presentation Delayed: After 24 hours / neurological recovery</td>
<td>To be Published</td>
</tr>
<tr>
<td>COUPE</td>
<td>NCT 02641626</td>
<td>Open Label, Multicenter, Spain</td>
<td>Inc: Comatose OHCA patients Ex: STEMI / Hemodynamic Instability</td>
<td>166</td>
<td>Survival with good neurological outcome at 30 days</td>
<td>Urgent : Upon presentations Deferred: After neurological Recovery</td>
<td>To be published</td>
</tr>
</tbody>
</table>
Table 3. Factors associated with survival with neurological outcome in patients with out of hospital cardiac arrest

<table>
<thead>
<tr>
<th>Factors</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Each decade of life was significantly associated with a 21% decrease in the odds of a favorable neurological outcome</td>
</tr>
<tr>
<td>Witnessed arrest</td>
<td>In a meta-analysis of studies reporting the predictors of survival from OHCA, the survival to hospital discharge among patients with witnessed arrest was significantly higher at 13.5% compared to 6.4% in those with an unwitnessed arrest.</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>In the CARES registry (86) bystander CPR was initiated in 46.9% of all witnessed events and survival to discharge rate was significantly higher in these patients at 13.7% compared to 7.5% in those without bystander CPR.</td>
</tr>
<tr>
<td>Achievement of ROSC &lt; 25 minutes</td>
<td>Several studies report time to achieve ROSC as an important predictive variable; with a duration longer than thirty minutes to be associated with reduced rate of survival with good neurological status. (23) (58) A study of 227 patients with OHCA admitted to intensive care unit showed that mean time to achieve ROSC was significantly lower at 18.3±15.1 minutes for patients who had a CPC score of 1 or 2 at discharge compared to 48.6± 17.9 minutes for those with unfavorable neurological outcomes (CPC score of 3,4,5). (58) Even among those treated with TTM, a shorter time interval from collapse to ROSC was strongly associated with improved neurological outcomes.41</td>
</tr>
<tr>
<td>Shockable rhythm</td>
<td>In the 2017 CARES report, (86) patients with an initial VF / pVT had significantly higher rate of survival to discharge at 29.1% compared to 10.1% for patients with PEA and 2.4% for patients with asystole.</td>
</tr>
<tr>
<td>Lactate</td>
<td>There is strong correlation between elevated lactate level of greater than 7 mmol/l and a corresponding pH of less than 7.2 to be strongly associated with multiorgan failure, severe anoxic brain injury and increased mortality. (12)</td>
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</table>
Table 4. Out of Hospital Cardiac Arrest Risk Scores

<table>
<thead>
<tr>
<th>Study</th>
<th>Cohort</th>
<th>Variables</th>
<th>Outcomes</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrest Hospital Prognosis (CAHP) (10)</td>
<td>1410 patients 41% with post ROSC STEMI of ECG 69% male</td>
<td>Age as continuous variable Non shockable rhythm Time from collapse to BLS Time from BLS to ROSC Location of cardiac arrest Epinephrine dose Arterial pH</td>
<td>CAHP &lt; 150 86% had early invasive strategy 61% discharged alive from hospital with 95% with CPC score 1 or 2 CAHP 150-200 66% had early invasive strategy 10% discharged alive from hospital with 88% with CPC score 1 or 2 CAHP &gt; 200 47% had early invasive strategy 3% discharged alive from hospital with 86% with CPC score 1 or 2</td>
<td>C-statistic reached 0.93 (95% CI: 0.91 to 0.95) in the development cohort, and 0.91 (95% CI: 0.88 to 0.93) in the prospective validation cohort</td>
</tr>
<tr>
<td>CREST Model (11)</td>
<td>638 patients derivation 318 patients Validation No patients with STEMI 18.9% recognized identified as circulatory cause of death</td>
<td>History of coronary artery disease Non shockable rhythm Ejection fraction &lt; 30% at time of admission Shock at the time of admission Ischemic time &gt; 25 minutes</td>
<td>CREST score death due to shock 0 – 7.1% 1 – 9.5% 2 – 22.5% 3 – 32.4% 4 - 20% 5 – 50%</td>
<td>Area under the curve (AUC) 0.68 in the validation cohort</td>
</tr>
<tr>
<td>C-GRApH (12)</td>
<td>122 patients derivation 344 patients validation</td>
<td>History of coronary artery disease Glucose ≥ 200 mg/dL Non shockable rhythm Age &gt; 45 pH (arterial) ≤ 7.0</td>
<td>C-GRApH (0-1) 70% with CPC score of 1 or 2 C-GRApH (4-5) 98% with CPC score 3 to 5</td>
<td>AUC of 0.814 in the validation cohort with a c-statistics of 0.81</td>
</tr>
</tbody>
</table>

ROSC return of spontaneous circulation; STEMI ST segment elevation myocardial elevation; BLS basic life support; CPC cerebral performance categories; CI Confidence interval
Table 5. Imaging for Risk stratification of Patients with OHCA

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Evaluation</th>
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<tr>
<td>Computed topography of Head</td>
<td>Anoxic encephalopathy</td>
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<td></td>
<td>Intracranial bleeding</td>
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<tr>
<td></td>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>Post myocardial infarction complications</td>
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<tr>
<td></td>
<td>• Free wall rupture</td>
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<tr>
<td></td>
<td>• Ventricular septal defect</td>
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<tr>
<td></td>
<td>• Mitral valve papillary/chordae dysfunction/rupture</td>
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<tr>
<td></td>
<td>Pulmonary embolus</td>
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<tr>
<td></td>
<td>Pericardial tamponade/effusions</td>
</tr>
<tr>
<td></td>
<td>Valvular dysfunction</td>
</tr>
<tr>
<td></td>
<td>Regional wall motion abnormalities</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
</tbody>
</table>
Table 6. Consensus Statement on Out of Hospital Cardiac Arrest Recommendations

| Situational Awareness in Patients with OHCA | In all comatose OHCA patients, we recommend dynamic clinical decision making of “definite” or “defer” transport to CCL based on situational awareness and assessment involving all clinical factors along the entire continuum of care. |
| OHCA Patients with Non–Shockable Rhythms | In OHCA patients with initial non–shockable rhythm, we recommended deferring transport to CCL at initial encounter |
| OHCA Patients with Shockable Rhythm and STEMI on Post ROSC ECG | In selected comatose OHCA patients with ROSC exhibiting STEMI on ECG we recommend a definite invasive strategy. |
| OHCA Patients with Shockable Rhythm without STEMI on Post ROSC ECG | We recommend deferring invasive strategy at initial encounter in hemodynamically stable, comatose OHCA patients without STEMI on post ROSC ECG. |
| Access for Intervention | In OHCA patients undergoing PCI, we recommend choosing the access site as per the operator’s expertise and local standard catheterization lab protocols. For both routine femoral access and large bore access in case of hemodynamic support in patients with concomitant shock, we recommend the safe access site practices to reduce the risk of bleeding. |
| Antiplatelet therapy | We recommend ticagrelor or prasugrel as the preferred P2Y12 inhibitor in OHCA patients undergoing PCI. |
| Anticoagulation therapy | Among OHCA undergoing PCI we recommend the use of unfractionated heparin with monitoring as the peri-procedural anticoagulant given the availability of a reversal agent in cases of life threatening bleeding and reduced risk of acute stent thrombosis compared to bivalirudin. |
| Target temperature management (TTM) | We recommend against the use of prehospital TTM using cold intravenous crystalloids. We recommend initiating TTM inpatient as soon as possible. |
| Barriers and Public Reporting | SCAI advocates making OHCA exclusion based on exceptional risk from public reporting analysis of PCI outcomes. The principle to be followed is that “Public reporting of outcomes in high-risk patients, if done at all, should accurately reflect the performance of those operators and institutions.” Additionally, SCAI recommends continuing to track process measures and outcomes in all patients suffering OHCA, including early access to coronary angiography and use of PCI. |

**OHCA Out of hospital cardiac arrest; CCL Cardiac catheterization laboratory; STEMI ST-segment elevation myocardial infarction; ECG Electrocardiogram; ROSC Return of spontaneous circulation; PCI Percutaneous coronary intervention; SCAI Society of coronary angiography and intervention**
Table 7. Studies Showing Mild Therapeutic Hypothermia Improves Neurologic Outcomes in Comatose OHCA patients with Shockable rhythm

<table>
<thead>
<tr>
<th>First Author, Year (Ref)</th>
<th>Design, Country of Recruitment</th>
<th>Total Number of Patients</th>
<th>Inclusion / Exclusion Criteria</th>
<th>Target Temperature Protocol</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holzer M, 2002 (62)</td>
<td>Blinded, Randomized, Multicenter Trial in 5 European Countries (Austria, Italy, Belgium, Finland, Germany)</td>
<td>275</td>
<td>Hypothermia: 136 Normothermia: 137</td>
<td>Inc: &gt; 18 - &lt;75 years; Witnessed cardiac arrest, ventricular fibrillation or non-perfusing ventricular tachycardia as the initial cardiac rhythm, presumed cardiac origin of the arrest, estimated interval of 5-15 minutes from the patients collapse to first attempt at resuscitation, No more than 60 minutes from collapse to ROSC</td>
<td>Target Temperature of 32°C and 34°C was maintained for 24 hours followed by passive rewarming to a temperature above 36°C over a period of 8 hours</td>
</tr>
<tr>
<td>Bernard SA, 2002 (63)</td>
<td>Open labelled, Randomized, Multicenter Trial, Melbourne, Australia</td>
<td>77</td>
<td>Hypothermia: 43 Normothermia: 34</td>
<td>Inc: Ventricular fibrillation, Persistent coma after ROSC Ex: &lt;18 years for men; &lt; 50 years for women (because of possibility of pregnancy), cardiogenic shock, possible causes of shock other than cardiac arrest</td>
<td>Basic cooling initiated in ambulance. Core temperature of 33°C was maintained for at least 12 hours after arrival to hospital. Beginning at 18 hours, active rewarming was done for next 6 hours.</td>
</tr>
</tbody>
</table>
Table 8: Prehospital Cooling

<table>
<thead>
<tr>
<th>Trial Reference</th>
<th>Number of Patients</th>
<th>Type of Cooling</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernard SA (64)</td>
<td>234 patients</td>
<td>Rapid infusion of 2 L of ice-cold lactated Ringer's solution</td>
<td>Mean core temperature decreased by 0.8 °C No difference in outcomes (47.5% pre hospital cooled, 52.6% in hospital cooled risk ratio 0.90, 95% confidence interval 0.70 to 1.17, P=0.43) Median volume 1900 mL</td>
</tr>
<tr>
<td>Castren M (66)</td>
<td>200 patients</td>
<td>Intra-arrest cooling with transnasal evaporative cooling pre hospital</td>
<td>There were no significant differences in rates of return of spontaneous circulation between the groups (38% pre hospital cooling versus 43% in hospital subjects, P=0.48), in overall survival of those admitted alive (44% versus 31%, respectively, P=0.26)</td>
</tr>
<tr>
<td>Bernard, SA (65)</td>
<td>163 patients</td>
<td>Two liters ice-cold Hartmann's solution 40 mL/Kg Goal fluid &lt; 8°C</td>
<td>Decreased mean core temperature compared to control (1.4°C pre hospital cooling versus 0.2°C in hospital cooling p&lt;.001) No difference in outcomes (12% pre hospital cooled, 9% in hospital cooled p=0.5). Median Volume received 1500 mL</td>
</tr>
<tr>
<td>Kim, F (67)</td>
<td>1359 patients</td>
<td>2 L of 4°C normal saline following ROSC</td>
<td>Decreased mean core temperature both groups (1.2°C patients with VF and 1.3 °C in patients without VF) Survival to hospital discharge was similar among the intervention and control groups among patients with VF (62.7% [95% CI, 57.0%-68.0%] vs 64.3% [95% CI, 58.6%-69.5%], respectively; P = .69) Increased rates of rearrest and pulmonary edema Patient with VF 49% received 2 L Patient without VF 44% received 2 L</td>
</tr>
<tr>
<td>Nordberg P (68)</td>
<td>677 patients</td>
<td>Intra-arrest cooling with transnasal evaporative cooling pre hospital</td>
<td>In the intervention group, 60 of 337 patients (17.8%) were alive at 90 days vs 52 of 334 (15.6%) in the control group (difference, 2.2% [95% CI, −3.4% to 7.9%]; RR, 1.14 [95% CI, 0.81-1.57]; P = .44).</td>
</tr>
</tbody>
</table>
Table 9. Extracorporeal Life Support Studies in Cardiac arrest

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Exclusion</th>
<th>Location</th>
</tr>
</thead>
</table>
| A Comparative Study Between a Pre-hospital and an In-hospital Circulatory Support Strategy (ECMO) in Refractory Cardiac Arrest (APACAR2) (APACAR2) NCT02527031 | 210 Patients  
  - Refractory cardiac arrest (defined by the failure of professionals to resuscitate at the 20th minute of cardiac arrest with a minimum of 3 Automatic External Defibrillator (AED) or equivalent analyze  
  - And Beginning of external cardiac massage within the first 5 minutes after cardiac arrest (no flow < 5 min.) with shockable rhythm or the presence of signs of life during resuscitation (any rhythm): spontaneous movement, absence of mydriasis and/or pupillary response, spontaneous breathing movements  
  - And Medical cause of the cardiac arrest  
  - And End-Tidal CO2 (ETCO2) above 10 mm Hg at the time of inclusion  
  - And Absence of major co-morbidity. And Extracorporeal Membrane Oxygenation (ECMO) team available and on-site before the 40th minute |  
  - Children under 18 years of age  
    - Adults over 65 years of age  
    - Period of more than 5 minutes without cardiac massage after collapsing  
    - Known co-morbidity that compromises the prognosis for short or medium-term survival  
    - Cardiac arrest during transportation times | Survival with good neurological outcome (CPC 1 or 2) at 6 months  
Paris, France |
| Early Initiation of Extracorporeal Life Support in Refractory OHCA (INCEPTION) NCT03101787 | 110 Patients | 1. ≥18 - ≤70 years  
2. Witnessed OHCA  
3. Initial rhythm of VF/VT or AED administered  
4. Bystander BLS  
5. No ROSC | 1. ROSC  
2. Terminal heart failure (NYHA III or IV)  
3. Severe pulmonary disease (COPD GIII of GIV)  
4. Oncological disease  
5. Pregnancy  
6. Bilateral femoral bypass surgery  
7. Pre-arrest CPC-score of 3 or 4  
8. Advanced directive  
9. Multitrauma (ISS >15)  
10. Start cannulation > 60 min after arrest | 30-day survival rate with favorable neurological status | Maastricht University Medical Center |

| ECPR for Refractory Out-Of-Hospital Cardiac Arrest (EROCA) NCT03065647 | 30 Patients | • OHCA of presumed non-traumatic etiology requiring CPR  
• Predicted arrival time at ECPR-capable hospital within timeframe specified | • Sustained return of spontaneous circulation (ROSC)  
• Advanced directive indicating do not attempt resuscitation (DNAR) or do not intubate (DNI) | 1. ED arrival interval [Time Frame: Measured within one hour cardiac arrest onset]  
   Proportion of patients with emergency department (ED) arrival less than or equal to Time Frame | University of Michigan |
<table>
<thead>
<tr>
<th>Hyperinvasive Approach in Cardiac Arrest NCT01511666</th>
<th>170 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>minimum of 18 and maximum of 65 years</td>
<td>minimum of 5 minutes of ACLS performed by emergency medical service team without sustained ROSC</td>
</tr>
<tr>
<td>witnessed out-of-hospital cardiac arrest of presumed cardiac cause</td>
<td>unconsciousness (Glasgow Coma Score &lt; 8)</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>ECMO team and bed-capacity in cardiac center available.</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>witnessed collapse</td>
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<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>pregnancy</td>
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<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>sustained ROSC within 5 minutes of ACLS performed by EMS team</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>conscious patient</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>known bleeding diathesis or suspected or confirmed acute or recent intracranial bleeding</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>suspected or confirmed acute stroke</td>
</tr>
<tr>
<td>OHCA of presumed non-cardiac cause</td>
<td>Composite endpoint of survival with good neurological outcome (CPC 1-2) 6 months</td>
</tr>
</tbody>
</table>

2. ECPR initiation interval

| Time Frame: Measured within 2 hours of cardiac arrest onset |

Proportion of ECPR eligible patients with ECPR flow initiated less than or equal to 30 minutes from ED arrival.

Charles University, Czech Republic
- known severe chronic organ dysfunction or other limitations in therapy
- "do not resuscitate" order or other circumstances making 180 day survival unlikely
- known pre-arrest cerebral performance category CPC ≥ 3.
Supplemental Table 1. Author RWI Disclosures

<table>
<thead>
<tr>
<th>Group Member</th>
<th>Date</th>
<th>Consultant</th>
<th>Speaker’s Bureau</th>
<th>Ownership/Stock/Shareholder</th>
<th>Grant or Research Support</th>
<th>Institutional or Organizational Relationship</th>
<th>Expert Witness</th>
<th>Advisory Board</th>
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<tr>
<td>Amir Lotfi, MD, FSCAI (Chair)</td>
<td>10/15/2018</td>
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<tr>
<td>Lloyd W. Klein, MD, MSCAI (Co-chair)</td>
<td>10/12/2018</td>
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<td>Ravi S. Hira, MD, FSCAI</td>
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<td>Jaya Mallidi, MD, MHS</td>
<td>10/13/2018</td>
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<td>Roxana Mehran, MD, MScAI</td>
<td>10/22/2018</td>
<td>Abbott, Boston Scientific, Cardiovascular Systems Inc., Medscape, Siemens, Medical Solutions, Spectranetics, Roivant Sciences Inc., Volcano Corporation, Abiomed, The Medicines Company (Spouse)</td>
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<td>Claret Medical, Elixir Medical (equity &lt;1%)</td>
<td>AstraZeneca, Bayer, Beth Israel Deaconess, BMS, CSL Behring, Eli Lilly/DSI, Medtronic, Novartis Pharmaceuticals, OrbusNeich</td>
<td>Abbott, Boston Scientific, Cardiovascular Systems Inc., Medscape, Siemens, Medical Solutions, Spectranetics, Roivant Sciences Inc., Volcano Corporation</td>
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<td>Janssen (Executive Committee), Osprey Medical (Executive Committee)</td>
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<tr>
<td>John C. Messenger, MD, FSCAI</td>
<td>10/13/2018</td>
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<td>Abiomed, Medtronic</td>
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<tr>
<td>Duane S. Pinto, MD, MPH, FSCAI</td>
<td>1/10/2020</td>
<td>Abiomed, Abbott, Boston Scientific, Medtronic, NuPulseCV, Teleflex</td>
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<td>Michael R. Mooney, MD, FSCAI</td>
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<td>Syed Tanveer Rab, MD, FSCAI</td>
<td>4/11/2019</td>
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<td>Demetri Yannopoulos, MD</td>
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<td>Sean van Diepen, MD, FRCPC, FAHA</td>
<td>10/12/2018</td>
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## Appendix 1. Definitions

<table>
<thead>
<tr>
<th>Topic</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>OHCA</strong></td>
<td>Cessation of cardiac mechanical activity associated with loss of signs of systemic circulation occurring outside of a hospital setting that rapidly translates into sudden cardiac death without successful resuscitation</td>
</tr>
<tr>
<td><strong>Incidence of OHCA</strong></td>
<td>Based on extrapolation to the total population of US in 2014/15, the estimated annual incidence of EMS assessed OHCA among adults is 347 322 (140.7 per 100 000 population).</td>
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<tr>
<td><strong>Incidence of shockable rhythm</strong></td>
<td>Initial shockable rhythm is estimated to be – 39 003 (15.8 per 100 000 population)</td>
</tr>
<tr>
<td><strong>Etiology of OHCA</strong></td>
<td>It is presumed coronary etiology is estimated to be between 32-80%</td>
</tr>
<tr>
<td><strong>Survival of patients with OHCA</strong></td>
<td>Cardiac Arrest Registry to Enhance Survival (CARES) 2016 report, among all EMS treated patients, 9.6% of patients survived to discharge The survival rate is 29.5% with a shockable rhythm Geographic variance in rate of survival</td>
</tr>
<tr>
<td><strong>Mode of death in patients with OHCA</strong></td>
<td>Two thirds death are related to neurological injury</td>
</tr>
</tbody>
</table>
Appendix 2. Limitations of this existing literature

<table>
<thead>
<tr>
<th>Bias</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type</td>
<td>With the exception one study the remaining studies are observational studies. Positive publication bias (87)</td>
</tr>
<tr>
<td>Selection bias</td>
<td>All observational studies are inherently prone to selection bias – patients likely to have a favorable outcome are chosen for early invasive strategy. When meta-analysis of biased observational studies is conducted, the effect size of the associated benefit of early invasive strategy in OHCA patients is spuriously magnified.(88)</td>
</tr>
<tr>
<td>Unmeasured confounders</td>
<td>The decision to do CAG on a comatose OHCA patient is influenced a multitude of factors. Some of these are measurable however intangible factors cannot be measured and adjusted for in studies. These unmeasured variables cause residual confounding and bias even in the most rigorously conducted observational studies.</td>
</tr>
<tr>
<td>Heterogeneity and selection in use of other treatments influencing outcomes</td>
<td>Early CAG facilitates natural selection of patients for a higher intensity of care, rigorous invasive hemodynamic monitoring, rapid titration of vasoactive drips, use of mechanical circulatory support devices and consideration of alternate diagnosis such as pulmonary embolism that influence treatment decisions and outcomes, there by exaggerating the true or direct potential benefit of CAG in this patient population. (38,89)</td>
</tr>
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Appendix 3. CathPCI version 5 Cardiac Arrest Data

<table>
<thead>
<tr>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Hospital Cardiac Arrest</td>
</tr>
<tr>
<td>• If Yes, Arrest Witnessed?</td>
</tr>
<tr>
<td>• If Yes, Arrest after Arrival of EMS?</td>
</tr>
<tr>
<td>• If Yes, First Cardiac Arrest Rhythm?</td>
</tr>
<tr>
<td>Cardiac Arrest Location</td>
</tr>
<tr>
<td>• Cardiac Arrest at Transferring Facility?</td>
</tr>
<tr>
<td>• Cardiac Arrest at this facility?</td>
</tr>
<tr>
<td>Hypothermia Protocol Initiated</td>
</tr>
<tr>
<td>• If Yes, Timing of Hypothermia</td>
</tr>
<tr>
<td>Level of Consciousness</td>
</tr>
<tr>
<td>• At start of PCI s/p cardiac arrest</td>
</tr>
<tr>
<td>• If deceased, highest level of consciousness s/p cardiac arrest</td>
</tr>
<tr>
<td>Discharge</td>
</tr>
<tr>
<td>• Hospice care at time of discharge?</td>
</tr>
<tr>
<td>If deceased, cause of death?</td>
</tr>
<tr>
<td>• Includes all causes including neurological</td>
</tr>
<tr>
<td>• Comfort measure only?</td>
</tr>
</tbody>
</table>