Journal of the Society for Cardiovascular Angiography & Interventions 2 (2023) 100536

JSCAI

The official journal of the Society for Cardiovascular Angiography & Interventions

Comprehensive Review

# Coronary Angiography in Patients With Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation on Electrocardiograms: A Comprehensive Review

Sachin Kumar, MD [a], Bahaa Abdelghaffar, MD [a], Meghana Iyer, BS [b], Ghaith Shamaileh, BS [c], Raunak Nair, MD [a], Weili Zheng, MD [a], Beni Verma, MD [a], Venu Menon, MD [a], Samir R. Kapadia, MD [a], Grant W. Reed, MD, MSc [a,*]

[a] *Section of Interventional Cardiology, Department of Cardiovascular Medicine, Heart, Vascular & Thoracic Institute, Cleveland Clinic, Cleveland, Ohio;* [b] *Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio;* [c] *Tulane University School of Medicine, New Orleans, Louisiana*

## ABSTRACT

Out-of-hospital cardiac arrest (OHCA) is among the most common causes of death in the United States. Early coronary angiography (CAG) and percutaneous coronary intervention (PCI) have been associated with improved long-term outcomes in patients with ST-segment elevation (STE) on prearrest or postarrest electrocardiograms. However, data on the utility of catheterization and PCI for improving outcomes after OHCA in patients without STE on electrocardiograms are heterogeneous, with variable results. Although older data have suggested that there is a benefit, recent randomized controlled trials have demonstrated that performing early CAG in patients with OHCA without STE on electrocardiograms may not improve outcomes. In recognition that neurologic devastation and multiorgan failure are common in these patients, physicians face the challenge of selecting appropriate patients for cardiac catheterization and PCI. This review aims to summarize the current data on this topic, with the goal to guide decision making regarding the timing and appropriateness of CAG in patients with OHCA without STE on electrocardiograms, utilizing an evidence-based approach to streamline the patient selection process.

## Introduction

Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death worldwide.[1] It has been estimated that ~395,000 adults experience OHCA in the United States annually, with a survival rate of 6% to 10%, leading to >350,000 deaths per year.[2,3] Despite continuous advancements in resuscitation science and postarrest management, the overall prognosis remains very poor. Even among patients who achieve return of spontaneous circulation (ROSC) and are admitted to a hospital, mortality remains very high, with the rate of survival to discharge with good neurologic function ranging from 0.8% to 20%, with wide geographic variation.[4] Coronary artery disease (CAD) is discovered in up to 70% of patients with OHCA after ROSC.[5] Hence, it has been suggested that immediate coronary angiography (CAG) and percutaneous coronary intervention (PCI) should be considered in all patients after OHCA. Current guidelines strongly recommend emergency CAG for all successfully resuscitated patients with OHCA with ST-segment elevation (STE) on prearrest or postarrest electrocardiograms (ECGs)[6-9] and an estimated reasonable neurologic prognosis. However, the potential benefit of immediate CAG in patients without STE on post-ROSC ECGs is less certain, because the studies on this topic are heterogeneous in their design and results. As a consequence, forming a recommendation on if and when to perform CAG for such patients is challenging; yet, this area remains of utmost importance given the complex decision making and heavy resource utilization that these patients often demand.

Accordingly, the current review aims to provide a concise summary of the existing evidence of the role of CAG in patients with OHCA without STE on pre- or post-ROSC ECGs. Existing observational studies, randomized controlled trials (RCTs), and meta-analyses as of July 2022 have been summarized and reviewed. An evidence-based, conceptual framework for the management of patients with OHCA has been presented.

*Abbreviations:* ACE, Assess, Consult & Expect; CAD, coronary artery disease; CAG, coronary angiography; CI, confidence interval; ECG, electrocardiogram; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; STE, ST-segment elevation.

*Keywords:* out-of-hospital cardiac arrest; shockable rhythm; ST-segment elevation; coronary angiography; percutaneous coronary intervention; cardiac cath lab.

* Corresponding author: reedg2@ccf.org (G.W. Reed).

https://doi.org/10.1016/j.jscai.2022.100536
Received 24 July 2022; Received in revised form 29 September 2022; Accepted 24 October 2022
Available online 25 November 2022

## Rationale for performing CAG in patients with OHCA

Cardiac catheterization has long been considered an essential diagnostic test for all patients following cardiac arrest to rule out acute coronary syndrome (ACS) as an antecedent cause. This thought process changed with the recognition that although CAD is often discovered as an incidental finding, it is not the cause of cardiac arrest in the majority of patients with OHCA without a shockable rhythm (ventricular tachycardia or ventricular fibrillation) and those without STE on pre- or post-ROSC ECGs. Patients with OHCA with an initial shockable rhythm and STE on post-ROSC ECGs have a prevalence of >85% for acute coronary occlusion, and 70% to 95% demonstrate significant CAD (defined as at least 1 stenosis of >70%) using diagnostic angiography (Figure 1).[10-12] Similarly, for patients with OHCA with a shockable rhythm who are not able to achieve ROSC because of refractory ventricular tachycardia or fibrillation, the prevalence of significant CAD is 80% to 85% and that of acute coronary lesions is 60% to 65%.[13-15] Conversely, among patients with OHCA with an initial shockable rhythm without STE on ECGs, the prevalence of acute coronary occlusion is much lower, at 5% to 30%, whereas that of significant CAD is 25% to 60%.[12,16-18] Unlike the prevalence of CAD in patients with a shockable rhythm, the prevalence of CAD in patients with an unshockable rhythm is not well defined[19,20]; based on limited data, it has been estimated that in patients without STE on post-ROSC ECGs, the prevalence of significant CAD is ~50% and that of a culprit lesion is ~7%.[21]

Among patients who achieve ROSC and are discovered to have coronary artery stenoses of >50%, the diagnosis of type 1 myocardial infarction (MI) can be challenging. Many survivors of OHCA have elevated levels of cardiac troponin; however, this may be due to type 2 MI in the setting of hypoperfusion secondary to shock, even in cases secondary to a noncardiac etiology. The features that predict acute coronary occlusion as the etiology of OHCA are the presence of cardiovascular risk factors at baseline, chest pain preceding the arrest, an initial shockable rhythm, and STE on postresuscitation ECGs.[22,23]

## Potential downsides of early CAG

Although CAG may allow one to identify and treat ongoing cardiac ischemia, performing it emergently in patients following OHCA may pose logistic challenges and expose the patient to further risk. Early CAG requires patient mobilization often during a time of hemodynamic instability, results in exposure to contrast agents, and carries procedural risks, including bleeding, stroke, and other complications.[24,25] Prioritizing CAG as the primary focus may delay other critical and potentially life-saving interventions and slow the identification of the possible etiology when a coronary lesion is not the event trigger.[26]

## Current trends

The offering and timing of CAG in patients with OHCA varies significantly among institutions. In a study from the International Cardiac Arrest Registry, which represents 44 centers in the United States and Europe, 66% of patients with OHCA with a shockable rhythm and no STE on post-ROSC ECGs underwent CAG, with PCI performed in 37.7% of those who underwent CAG.[27] According to a meta-analysis by Verma et al,[28] 85 CAG and 24 PCI procedures are conducted per 100 patients with OHCA without STE on post-ROSC ECGs. Most of the existing observational studies found that an early CAG strategy is employed in 35% to 65% of patients with OHCA without STE on post-ROSC ECGs.[29-33]

The studies evaluating the benefit of early CAG in such patients with OHCA are mixed. Although many of the early observational studies have suggested a possible benefit, more recent high-quality cohort studies and RCTs have indicated that the benefit of early CAG in all comers is unlikely and that a selective approach to CAG in appropriate patients is warranted.

## Review of the existing data

### *Observational data*

Several observational studies evaluating the optimal timing of CAG in patients with OHCA without STE on post-ROSC ECGs are summarized in Table 1.[34-42] These are difficult to interpret given their conflicting outcomes, different patient populations, heterogeneous designs, potential biases, and confounding results.

### *RCTs*

Guideline recommendations to date have mainly been derived from observational studies and expert consensus. Fortunately, in the last few years, there has been rigorous growth in the level of evidence because

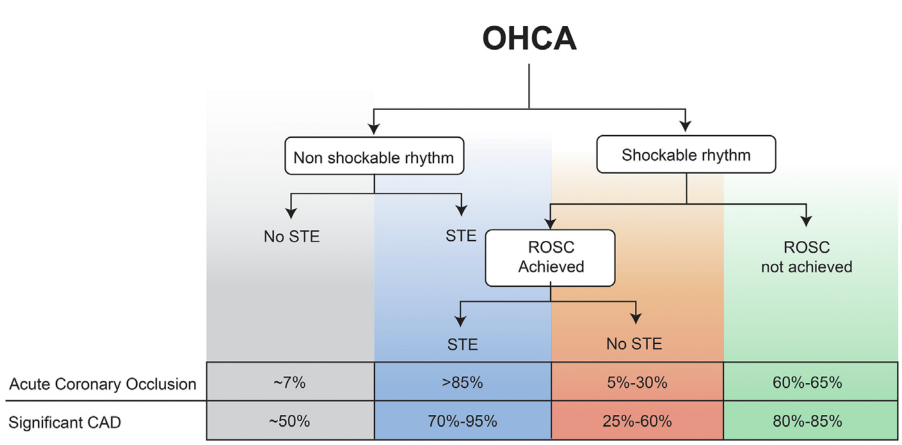



**Figure 1.**
**Prevalence of acute coronary occlusion and significant coronary artery disease in successfully resuscitated patients with out-of-hospital cardiac arrest.** Significant coronary artery disease defined as >70% stenosis in at least 1 major epicardial coronary vessel. ACS, acute coronary syndrome; CAD, coronary artery disease; OHCA, out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation; STE, ST-segment elevation.

**Table 1.** Summary of key observational studies evaluating the role of coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on electrocardiogram[a]

| Reference, year | Design | No. of patients | Definition of early CAG | Definition of nonearly CAG | Primary end point | Favors early angiography |
|---|---|---|---|---|---|---|
| Bro-Jeppesen et al,[34] 2012 | Nonrandomized, prospective | 244 | Within 12 h of cardiac arrest | After 12 h of cardiac arrest, within 30 d | 30-d and 1-y survival rates | No |
| Hollenbeck et al,[29] 2014 | Retrospective cohort | 269 | Either immediately upon hospital admission or during hypothermia treatment | After completing hypothermia protocol and assessment for neurologic recovery (at least 24 h after admission) | Survival to hospital discharge | Yes |
| Reynolds et al,[35] 2014 | Retrospective cohort | 191 | Occurring directly from the ED, ICU, or referring facility | Late or none | Good outcome, defined as discharge to home or acute rehabilitation facility | Yes |
| Vyas et al,[36] 2015 | Nonrandomized prospective registry | 4029 | Within 1 d of cardiac arrest | After 24 h of cardiac arrest | Survival to discharge | Yes |
| Kleissner et al,[30] 2015 | Nonrandomized prospective registry | 99 | <2 h from hospital admission | Decision to perform delayed CAG or to not perform CAG at all was made only after completion of hypothermia protocol and reassessment of neurologic status | In-hospital and 6-mo mortality as well as neurologic performance | No |
| Dankiewicz et al,[31] 2015 | Post hoc analysis of RCT | 544 | Performed on admission to OR in <6 h of cardiac arrest | >6 h of cardiac arrest or not | Mortality at the end of the trial | No |
| Kern et al,[12] 2015 | Retrospective and prospective cohort study | 548 | Within 2 h of arrival at a PCI-capable hospital | >2 h of arrival at a PCI-capable hospital | Survival to hospital discharge | Yes |
| Geri et al,[37] 2015 | Prospective cohort | 1404 | <6 h after collapse | No patient underwent delayed CAG | 30-d and 10-y survival rates | Yes |
| Garcia et al,[11] 2016 | Nonrandomized prospective registry | 203 | <6 h of arrival at the ED | >6 h of arrival at the ED | Survival to hospital discharge with favorable neurologic outcomes | Yes |
| Staudacher et al,[38] 2018 | Retrospective cohort | 287 | ≤3 h | >3 h after hospital admission | All-cause mortality at 30 d | No |
| Elfwén et al,[32] 2018 | Nonrandomized prospective registry | 799 | <24 h | >24 h but within 4 wk (during same hospitalization) | Survival at 30 d, 1 y, and 3 y | Yes |
| Jentzer et al,[39] 2018 | Prospective registry | 599 | <24 h of ROSC | >24 h of ROSC | Survival to hospital discharge | Yes |
| Kim et al,[33] 2019 | Retrospective registry | 227 | Immediate: ≤2 h after ROSC or presentation to the ED | Early: 2-24 h after ROSC or presentation to the ED | Good neurologic outcomes at 1 mo, defined as a CPC score of 1-2 | No |
| Song et al,[40] 2021 | Prospective observational cohort study | 678 | ≤24 h | >24 h or not performed | Good neurologic outcome at 6 mo, with a CPC score of 1-2 | Yes |
| Vedamurthy et al,[41] 2021 | Retrospective cohort | 158 | Within 24 h of presentation to the ER | >24 h after presenting to the ER or not | In-hospital mortality rates and final inpatient CPC | When risk adjusted and divided on the basis of CAHP score: No |
| Lim et al,[42] 2021 | Prospective registry | 976 | Within 1 d of ROSC | After 1 d of ROSC | 30-d survival and neurologic outcome | Yes |

CAG, coronary angiography; CAHP, cardiac arrest hospital prognosis; CPC, cerebral performance category; ED, emergency department; ER, emergency room; ICU, intensive care unit; OR, operating room; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; ROSC, return of spontaneous circulation.

[a] Major observational studies evaluating the role of early versus nonearly coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on an electrocardiogram performed after return of spontaneous circulation.

of newly published RCTs in this area. Most of the RCTs focused on short-term outcomes, which is appropriate because mortality primarily occurs during the first 2 to 3 months after an arrest, and if patients survive with a good neurologic status, long-term outcomes are generally favorable.[43,44] Table 2[45-49] depicts a summary of published and ongoing RCTs, summarizing the highest-quality evidence in this area.

Given the importance of these RCTs in clinical decision making, the important highlights are summarized below:

- The Coronary Angiography after Cardiac Arrest (COACT) trial was the first RCT investigating the difference in outcomes between immediate and delayed CAG in patients with OHCA with an initial shockable rhythm and without STE on ECGs. The trial randomized 552 patients to undergo immediate CAG, defined as CAG performed within 2 hours after randomization, versus delayed CAG, defined as CAG after neurologic recovery. COACT found no difference in survival at 90 days, regardless of whether the patients underwent early versus delayed CAG. At 90 days, 64.5% of patients from the immediate CAG group and 67.2% from the delayed CAG group were alive (odds ratio for death, 0.89; 95% CI, 0.62-1.27; $P =$ .51). Further, despite the early CAG group receiving therapeutic hypothermia earlier, there was no difference in the Cerebral Performance Category (CPC) score between the 2 groups at 90 days. To test the hypothesis of whether immediate PCI improves outcomes, a prespecified, exploratory analysis was used to measure the differences in survival; MI; revascularization; implantable cardiac defibrillator shock; quality of life; hospitalization for heart failure; and the composite of death, MI, and revascularization after 1 year. No significant differences were observed for any of the mentioned outcomes,[43] regardless of whether the early versus delayed CAG

**Table 2.** Summary of key randomized controlled trials evaluating the role of coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on electrocardiogram[a]

| Reference, year, study title | Clinical trial identifier, location | No. of patients | Definition of early CAG | Definition of nonearly CAG | Primary end point | Key results on the primary end point | Favors early angiography |
|---|---|---|---|---|---|---|---|
| Lemkes et al,[16] 2019 COACT | NTR4973, Netherlands | 552 | <2 h after randomization | After neurologic recovery | Survival at 90 d | OR, 0.89; 95% CI, 0.62-1.27; $P = .51$ | No |
| Desch et al,[45] 2021 TOMAHAWK | NCT02750462, Germany | 530 | As soon as possible after hospital admission | >24 h after cardiac arrest or not at all | Death due to any cause at 30 d | HR, 1.28; 95% CI, 1.00-1.63; $P = .06$ | No |
| Kern et al,[46] 2020 PEARL | NCT02387398, USA, Slovenia, and Australia | 99 | <120 min of admission | >6 h from admission or not at all | Safety and efficacy of early CAG | 55.1% vs 46.0%; $P = .64$ | No |
| Hauw-Berlemount et al,[47] 2022 EMERGE | NCT02876458, France | 279 | Transferred directly to the catheterization laboratory | Admitted to the intensive care unit, and CAG planned 48-96 h after admission | 180-d survival rate, with no or minimal neurologic sequelae; CPC score of 1 or 2 | HR, 0.87; 95% CI, 0.65-1.15; $P = .324$ | No |
| COUPE | NCT02641626, Spain | 166 | As soon as possible after randomization | After extubation if the patient has a good neurologic prognosis | Composite of in-hospital survival and 6-mo survival free of severe dependence (CPC score of 1 or 2) | Yet to be published | |
| DISCO | NCT02309151, Sweden | 1006[b] | <120 min from randomization | Should preferably not be performed until 3 d after the cardiac arrest | 30-d survival | Yet to be published | |
| Lavi S, Cardiac Catheterization in Cardiac Arrest | NCT02587494, Canada | 75[b] | Within 12 h of ROSC | After completion of mild therapeutic hypothermia or apyrexia for >24 h after ROSC | Composite of death and poor neurologic outcomes (CPC score of 1 or 2) at 30 d | Yet to be published | |
| ARREST | NCT03872960, United Kingdom | 804 | To be treated same as ST-segment elevation after ROSC. Patient to be transferred to the cath lab. | Triage for cath lab to be delayed until at least 72 hours after arrest | 30-d all cause mortality | Yet to be published | |

ARREST, A Randomised Trial of Expedited Transfer to a Cardiac Arrest Centre for Non-ST Elevation Out-of-hospital Cardiac Arrest; CAG, coronary angiography; CI, confidence interval; COACT, Coronary Angiography After Cardiac Arrest; COUPE, Coronariography in Out of Hospital Cardiac Arrest; CPC, cerebral performance category; DISCO, Direct or Subacute Coronary Angiography in Out-of-hospital Cardiac Arrest; EMERGE, Emergency vs Delayed Coronary Angiogram in Survivors of Out-of-Hospital Cardiac Arrest; HR, hazard ratio; OHCA, out-of-hospital cardiac arrest, OR, odds ratio; PEARL, Randomized Pilot Clinical Trial of Early Coronary Angiography vs No Early Coronary Angiography for Postcardiac Arrest Patients Without ST-Segment Elevation; ROSC, return of spontaneous circulation; TOMAHAWK, Immediate Unselected Coronary Angiography vs Delayed Triage in Survivors of Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation.

[a] Randomized controlled trials evaluating the role of early versus nonearly coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on an electrocardiogram performed after return of spontaneous circulation. [b] Estimated enrollment.

strategy was used. It is to be noted that the COACT trial only included patients with a shockable rhythm, which constituted only 60% of patients with OHCA without STE.

- The Immediate Unselected Coronary Angiography vs Delayed Triage in Survivors of Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation (TOMAHAWK) trial[45] is a recently published multicenter, international RCT on this topic. Unlike COACT, TOMAHAWK included patients with OHCA and no STE on ECGs, with either a shockable or nonshockable rhythm. Similar to COACT, TOMAHAWK compared the mortality and neurologic deficit at 30 days in patients randomized to a strategy of either immediate or delayed CAG. The trial analyzed 530 randomized patients who had been successfully resuscitated after OHCA to undergo CAG as soon as possible after hospital admission or delayed CAG, with transfer to the intensive care unit with the intention to proceed to CAG only after a minimum delay of at least 24 hours, except in limited prespecified situations such as development of cardiogenic shock. The prevalence of CAD in the immediate CAG group was 60.7%, and the prevalence of CAD in the delayed CAG group was 72.1%. A coronary culprit lesion was found to be the causative trigger event in 40% of the participants. At 30 days, 54% of patients in the immediate CAG group and 46% in the delayed CAG group died (hazard ratio, 1.28; 95% CI, 1.00-1.63; $P = .06$). Interestingly, the composite outcome of death and severe neurologic deficit followed similar trends and occurred more frequently in the immediate CAG group than in the delayed CAG group, with a relative risk of 1.16 (95% CI, 1.00-1.34). The authors postulated that this could have been due to delays in the diagnosis of other noncoronary underlying triggers for OHCA in the immediate CAG group. With these results, the TOMAHAWK trial supported the findings of the COACT trial and found that immediate CAG had no benefit over delayed or selective CAG.
- The Emergency vs Delayed Coronary Angiogram in Survivors of Out-of-Hospital Cardiac Arrest (EMERGE) trial[47] is the most recently published multicenter RCT. Unlike the previous trials, it investigated a longer-term outcome, 180-day survival rate with a CPC score of ≤2 for emergent versus delayed CAG in patients with OHCA without STE on post-ROSC ECGs. A total of 279 patients who experienced OHCA, with ROSC, with no obvious noncardiac cause of cardiac arrest and no STE on post-ROSC ECGs were randomized to undergo either emergency angiography, with direct transfer to the catheterization laboratory, or delayed CAG, with admission to the intensive care unit and CAG planned within 48 to 96 hours after admission. Of 141 patients randomized into the emergency CAG group, 126 (89.4%) patients underwent CAG. Of 138 patients in the delayed CAG group, 74 (53.6%) patients underwent CAG. It is important to note that the main reason for not performing CAG in the delayed

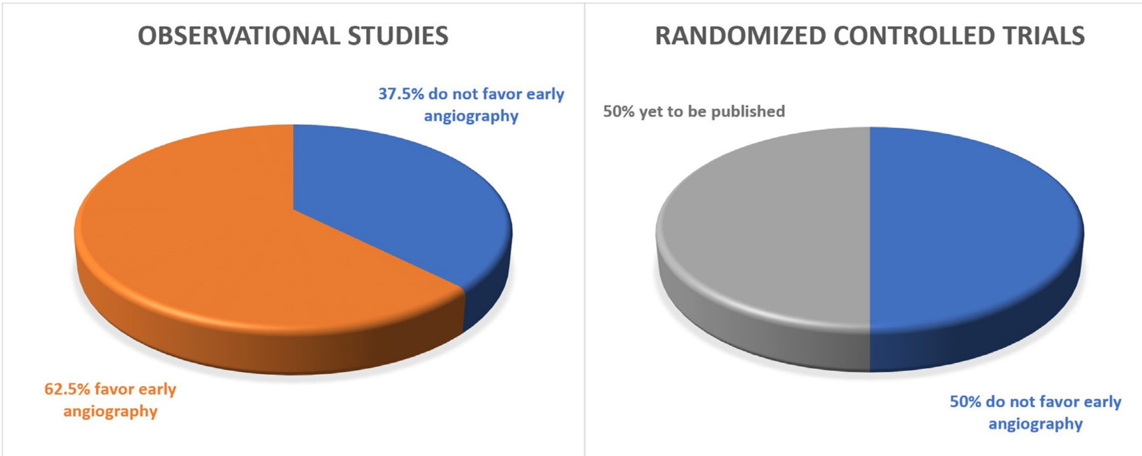



**Figure 2.**
**High-level evidence for the timing of coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on an electrocardiogram.** As depicted, no randomized controlled trial published to date has shown that immediate coronary angiography is superior to delayed coronary angiography.

group was early death. No significant CAD was found in 45.2% of the patients who underwent emergency CAG and 55.4% of the patients who underwent delayed CAG. PCI was performed in 38 (30.2%) patients in the emergency CAG group compared with 17 (23%) patients in the delayed CAG group. No difference was found in the 180-day survival rate among patients with a CPC score of ≤2 in the emergency CAG group (34.1%) versus that among patients with a CPC score of ≤2 in the delayed CAG group (30.7%), with a hazard ratio of 0.87 (95% CI, 0.65-1.15; $P = .32$). Furthermore, there was no difference in the overall survival at 180 days between the emergency CAG (36.2%) and delayed CAG groups (33.3%), with a hazard ratio of 0.86 (95% CI, 0.64-1.15; $P = .31$). Although the EMERGE trial was underpowered, similar to COACT and TOMAHAWK, it did not support the early CAG strategy.

- The Randomized Pilot Clinical Trial of Early Coronary Angiography vs No Early Coronary Angiography for Postcardiac Arrest Patients Without ST-Segment Elevation (PEARL) trial pilot (n = 99) trial also randomized patients with OHCA with a shockable or nonshockable rhythm without STE on post-ROSC ECGs to undergo either early angiography, ie, ≤120 minutes from arrival at a PCI-capable facility, or nonearly CAG. Although the study was terminated prematurely, it showed similar results of no benefit with early CAG.[46]
- The direct or subacute coronary angiography in out-of-hospital cardiac arrest (DISCO) pilot study (n = 79) trial found that performing immediate CAG in patients with OHCA without STE on ECGs is feasible and safe.[49] A secondary analysis of the DISCO pilot trial found no difference in the left ventricular ejection fraction at 24 hours, peak troponin T levels, lactate clearance, and N-terminal pro-b-type natriuretic peptide at 72 hours between the immediate and deferred CAG groups.[50] The outcomes of immediate versus deferred CAG groups are yet to be published in the DISCO trial.

Several possible factors contributed to the differences between the results of the RCTs and those of early observational studies (Figure 2). First, the definition of early CAG in most of the observational studies varied significantly, ranging from 0 to 24 hours. Second, in most observational studies, the decision to undergo early versus delayed or no CAG was based on clinical presentation and clinicians' judgments; younger patients with fewer comorbidities and those who were expected to have better neurologic and overall outcomes were likely to undergo early CAG compared with the rest, which raises the possibility of a selection bias. Third, many of the early observational studies included patients with OHCA with and without STE as a single cohort, when, in fact, they are very different patient populations,[51-54] and this limits the external validity of these studies to apply to patients with OHCA without STE.[12,34,52,55-58] RCTs eliminate these biases and are inherently more statistically sound and valid than observational studies by virtue of their design.

*Meta-analyses*

To evaluate the evidence in totality, Table 3[28,51,59-63] presents the key findings of the meta-analyses published in the last 5 years. It is apparent that older meta-analyses had concluded the early CAG approach to be superior to the delayed CAG approach; however, these studies mostly included observational data and acknowledged the "low quality" or "very low quality" of available evidence because of the inherent nature of these observational studies. The more recent meta-analyses included the RCTs summarized in Table 2[45-49] and, as a result, indicated no benefit of early CAG over delayed CAG. Another reason for the discrepancy could have been that the older meta-analyses included studies that grouped patients with OHCA with and without STE as a single cohort, as mentioned above. Because the benefit of immediate CAG is well established for patients with OHCA with STE, this jeopardizes the external validity of their results to patients with OHCA without STE.

The meta-analysis by Barbarawi et al[60] was the first to find no difference in mortality between early and delayed CAG groups. The patients were divided into 3 treatment groups: immediate, delayed, and no CAG. Eleven studies were included, and it was concluded that there is no difference in mortality between the early and delayed groups. In a more clinically relevant analysis, Verma et al[28] minimized the selection bias that may have affected their predecessors by including patients not offered angiography in the delayed CAG group. Because the clinical question for physicians is often whether to offer early or delayed angiography (if at all), this study design most reflects the dilemma that clinicians face at the time of patient care. Verma et al[28] included 11 studies, and a random-effects analysis showed no difference in 30-day mortality (relative risk, 0.86; 95% CI, 0.71-1.04; $P = .12$), neurologic status (relative risk, 1.08; 95% CI, 0.94-1.24; $P = .28$), and the rate of PCI (relative risk, 1.22; 95% CI, 0.94-1.59; $P = .13$) between the 2 groups. Additionally, factors such as the presence of type 2 diabetes mellitus, chronic renal failure, previous PCI, and elevated lactate levels predicted mortality more than the decision of whether to undergo the CAG procedure itself. A sensitivity analysis showed no small study or publication bias. Furthermore, Subahi et al[61] performed a similar meta-analysis, which included 3 RCTs, and found no significant difference in mortality between immediate and delayed CAG or noninvasive groups (hazard ratio, 1.0; 95% CI, 0.7-1.4).

**Table 3.** Summary of key meta-analyses evaluating the role of coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on electrocardiogram[a]

| Reference, year | Included studies | Primary outcome | Secondary outcome | Key results on the primary end point | Favors early angiography |
|---|---|---|---|---|---|
| Khan et al,[59] 2017 | 8 studies: 7 observational and 1 RCT | Short- (at discharge) and long-term (at 6-14 mo of follow-up) mortality | Good neurologic outcome (CPC score of 1 or 2) at discharge and follow-up | Short-term: OR, 0.46; 95% CI, 0.36-0.56; $P < .001$ Long-term: OR, 0.59; 95% CI, 0.44-0.74; $P < .001$ | Yes |
| Welsford et al,[51] 2018 | 23 studies: 22 observational and 1 post hoc analysis of RCT | Survival and good neurologic outcome: Short-term (discharge OR, 30 d) Intermediate-term (3-11 mo) Long-term (1-5 y) | | Survival short-term: RR, 1.52; 95% CI, 1.32-1.74; $P <.00001$ Survival long-term: RR, 1.56; 95% CI, 1.14-2.14; $P = .006$ | Yes |
| Barbarawi et al,[60] 2019 | 11 studies: 8 observational, 1 post hoc analysis, and 2 RCTs | Long-term mortality | Short-term mortality CPC score of 1-2 at the longest follow-up period | Immediate vs no CAG: OR, 0.21; 95% CI, 0.05-0.82 Delayed vs no CAG: OR, 0.11; 95% CI, 0.03-0.43 | No |
| Subahi et al,[61] 2020 | 3 RCTs | All-cause mortality | NA | HR, 1.0; 95% CI, 0.7-1.4 | No |
| Yang et al,[62] 2020 | 10 studies: 8 observational and 2 RCTs | Survival: At hospital discharge (OR, 1.78; 95% CI, 1.51-2.11; $P < .0001$) Middle-to-long-term follow-up (6-14 mo) (OR, 1.21; 95% CI, 0.93-1.57; $P = .15$) Neurologic outcomes, with a CPC score of 1 to 2: At discharge (OR, 1.66; 95% CI, 1.37-2.02; $P < .00001$) Middle-term follow-up (1-3 mo) (OR, 0.74; 95% CI, 0.59-0.97) | | | Yes |
| Verma et al,[28] 2020 | 11 studies: 7 observational, 1 post hoc analysis, and3 RCTs | 30-d mortality | Neurologic status and the rate of PCI following cardiac arrest | RR, 0.86; 95% CI, 0.71-1.04; $P = .12$ | No |
| Abusnina et al,[63] 2022 | 6 RCTs | Mortality at 30 d | Neurologic status with a CPC score ≤2 Rate of PCI following CAG | RR, 1.06; 95% CI, 0.94-1.20; $P = .32$ | No |

CAG, coronary angiography, CPC, cerebral performance category; HR, hazard ratio; NA, not applicable; OR, odds ratio; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; RR, risk ratio.

[a] Summary of key meta-analyses evaluating the role of early versus nonearly coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation on an electrocardiogram performed after return of spontaneous circulation.

Hauw-Berlemont et al[47] performed a meta-analysis of the 4 major RCTs, the COACT, PEARL, TOMAHAWK, and EMERGE trials. A combined analysis of 1446 patients was included along with the results of the EMERGE trial, and it showed no benefit of an early CAG approach compared with a nonearly CAG approach (risk ratio, 1.04; 95% CI, 0.92-1.18) in patients with OHCA without STE on post-ROSC ECGs.

## Current guidelines

A concise summary of the current guidelines on this topic is provided in Table 4.[6,8,9] It is important to note that these guidelines were authored prior to the publication of the COACT, TOMAHAWK, and EMERGE trials as well as subsequent meta-analyses and, thus, are heavily weighted toward the observational studies mentioned in Table 1.[34-42]

- The 2020 International Liaison Committee on Resuscitation Consensus of Science, American Heart Association, guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care[64] recommend that CAG be performed emergently for all patients with a suspected cardiac cause of OHCA and STE on ECGs. It also suggests that emergency CAG is reasonable in select comatose patients, such as those who are electrically or hemodynamically unstable and have a suspected cardiac cause of arrest even without STE on ECGs.

**Table 4.** Summary of guidelines on the role of coronary angiography in patients with out-of-hospital cardiac arrest[a]

| Guideline | Postresuscitation ECG with ST-segment elevation | Postresuscitation ECG without ST-segment elevation |
|---|---|---|
| 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation[8] | IB recommendation: primary PCI strategy recommended | IIa C: urgent angiography (and PCI if indicated) should be considered for patients with high suspicion |
| 2019 SCAI expert consensus statement on out-of-hospital cardiac arrest[6] | For select comatose patients with OHCA: definite invasive strategy | Defer invasive strategy at initial encounter in hemodynamically stable comatose patients |
| 2020 ILCOR Consensus on Science: American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[9] | COR 1 (LOE B-NR): CAG should be performed emergently for all patients with a suspected cardiac cause of arrest | COR 2a (LOE B-NR): Emergency CAG is reasonable in select (such as electrically or hemodynamically unstable) comatose patients with a suspected cardiac cause of arrest |

CAG, coronary angiography; COR, classification of recommendation; ECG, electrocardiogram; ESC, European Society of Cardiology; IB, Class I recommendation with level of evidence B; IIa C, Class IIa recommendation with level of evidence C; ILCOR, International Liaison Committee on Resuscitation; LOE, level of evidence; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions.

[a] Summary of current guideline-based recommendations on the management of successfully resuscitated patients with out-of-hospital cardiac arrest.

- The 2019 Society for Cardiovascular Angiography & Interventions expert consensus document[6] recommends deferring cardiac catheterization for patients with OHCA and a nonshockable rhythm. For patients with OHCA and a shockable rhythm, the consensus recommends an invasive strategy only in select patients who are found to have STE on post-ROSC ECGs. This selection is defined by the absence of unfavorable factors determining the likelihood of neurologic recovery, such as high Cardiac Arrest Hospital Prognosis scores, no bystander CPR, time to ROSC >30 minutes, lactate level >7 mmol/L, arterial pH <7.2, age >85 years, and the presence of end-stage renal disease. For patients with the absence of STE on post-ROSC ECGs, the consensus recommends deferring CAG in hemodynamically stable patients and transferring them to the intensive care unit for targeted temperature management, postresuscitative care, clinical reassessment, and the assessment of neurologic recovery.
- The 2017 European Society of Cardiology guidelines for the management of acute MI in patients presenting with STE[8] recommends urgent CAG (within 2 hours) in survivors of OHCA with STE on ECGs, including unresponsive survivors. In the absence of STE on post-ROSC ECGs, urgent CAG is recommended for patients with a high suspicion of ongoing myocardial ischemia (such as the presence of chest pain before the arrest, a history of established CAD, and abnormal or uncertain ECG results). The European Society of Cardiology guidelines also strongly recommend considering unfavorable factors for the likelihood of neurologic recovery in the decision making process—such as unwitnessed cardiac arrest; late arrival of a prehospital team, without lay basic life support for >10 minutes; the presence of an initial nonshockable rhythm; or >20 minutes of advanced life support, without ROSC—as arguments against an invasive strategy.

We favor the guidelines for the management of patients with OHCA outlined by the American Heart Association and Society for Cardiovascular Angiography & Interventions over those proposed by the European Society of Cardiology. These guidelines are newer and based on more recent data, and they recommend performing CAG only in a subset of patients with OHCA without STE on ECG. They emphasize the assessment of the likelihood of a cardiac cause to be the etiology of arrest and the presence of unfavorable factors that predict a poor prognosis.

## Patient selection for early CAG

Data from recent RCTs and meta-analyses advise against the practice of routinely performing CAG in all patients with OHCA. These data indicate that CAG may be futile in patients without myocardial ischemia as the cause of arrest, which may lead to delay in the management of underlying medical issues and subsequent harm. The benefit of CAG is associated with providing PCI, and, therefore, it is crucial to identify patients without STE who are likely to have ACS and favorable resuscitation features and those who would benefit from early CAG or PCI. Various studies have attempted to create models to identify such patients.

In 2015, the American College of Cardiology Interventional Council proposed 10 unfavorable resuscitation features for triaging comatose survivors of OHCA for emergency cardiac activation in the catheterization laboratory. These include the following: unwitnessed arrest, initial rhythm nonventricular fibrillation, no bystander CPR, >30 minutes from collapse to ROSC (time to ROSC), ongoing CPR, pH < 7.2, lactate level > 7 mmol/L, age > 85 years, end-stage renal disease, and noncardiac etiology.[65] Nonshockable rhythm has been associated with poor survival and neurologic recovery.[8,66] It has been suggested that the presence of multiple unfavorable features can predict a poor outcome in a patient questioning the utility of advanced cardiac interventions. An algorithm to identify patients in whom further treatment may not add meaningful value was proposed to help inform physicians' decisions on whether to proceed with invasive management. However, there were several limitations of such recommendations. First, there was no ranking of such "unfavorable factors" in terms of their importance. Second, there was no set number of these factors that would render the decision to proceed with an intervention futile. Third, these factors and algorithm were not evaluated in a large patient cohort up until 2021. To address this, Harhash et al[67] validated these 10 factors and showed that the presence of ≥3 of these factors predict a survival rate of <40% in successfully resuscitated patients with OHCA. Further, the absence ≥6 of the unfavorable features predicted survival, thus making a reasonable case for such patients to not undergo an invasive procedure or have it at a later time, once their status improves. Age >85 years, >30 minutes of time to ROSC, and initial nonshockable rhythm were found to be the 3 most powerful predictors of adverse outcomes. It was also found that the presence of these 3 factors predicted a 95% possibility of a ≤10% rate of survival to discharge. Although the study included patients with and without STE, no difference was seen in the number of unfavorable features associated with a very poor outcome while stratifying the patients based on the presence or absence of STE.

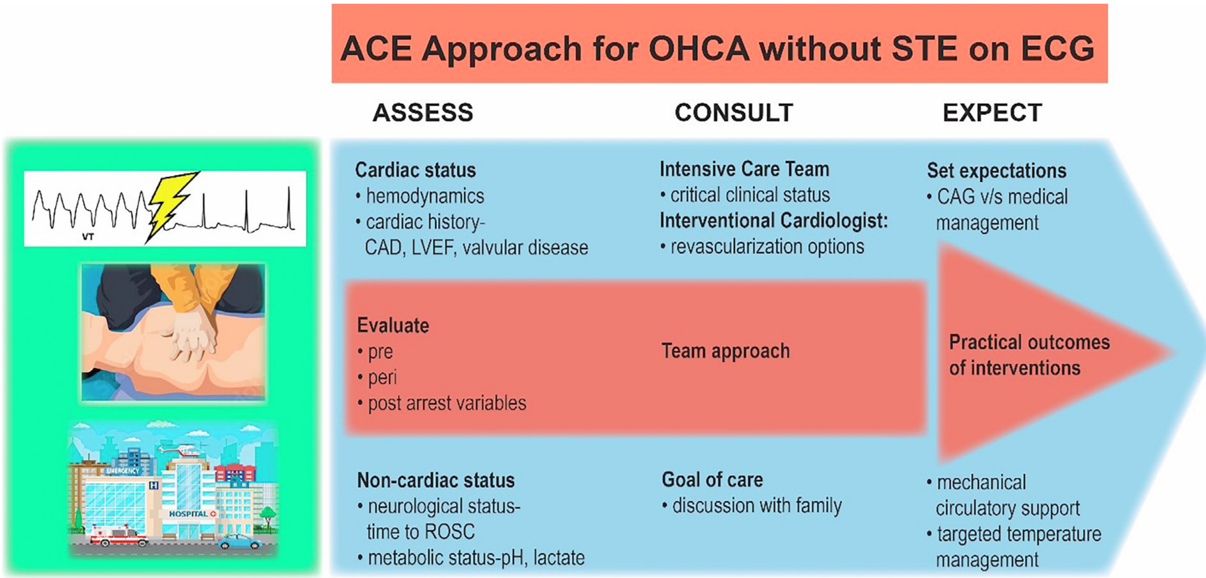
Bascom et al[68] retrospectively analyzed 638 patients in the International Cardiac Arrest Registry to quantify the risk of death due to a circulatory etiology in patients with OHCA without STE on post-ROSC ECGs. A point was assigned for each associated factor in the model, yielding a CREST score (C, history of CAD; R, nonshockable rhythm; E, initial ejection fraction < 30%; S, circulatory shock at the time of presentation; and T, total ischemic time > 25 minutes) of 0 to 5, which was reasonably predictive of in-hospital circulatory death, with an area under the curve of 0.68. However, the CREST model did not include neurologic status, which is a very important predictor of mortality in patients with OHCA.

Interestingly, Baldi et al[69] retrospectively studied 370 patients to analyze the impact of time from achieving ROSC to obtaining ECG on the diagnostic accuracy of ECG for STEMI. It was found that false-positive STE was up to 3 times greater in ECGs that were performed within 7 minutes of achieving ROSC. The study suggested waiting for 8 minutes after ROSC to capture ECG to reduce false-positive STE and increase true-negative STE on post-ROSC ECGs.

## The "Assess, Consult & Expect" approach

Given the complexity of managing patients with OCHA without STE on ECGs, the authors of this review developed a simple framework to guide patients' care. The "Assess, Consult & Expect" (ACE) approach is outlined in the Central Illustration. With the ACE approach, the goal is to "ACE" the management of patients with OHCA.

Using the ACE approach, the provider should first assess the patient's overall condition, cardiac and noncardiac status. A careful assessment of the unfavorable resuscitation features should be performed, including an assessment of the patient's neurologic status, arterial pH, and lactate level. History should be gathered regarding existing comorbidities such as advanced cancer, dementia, functional status, and quality of life at baseline. With this background, the provider can then consult with colleagues, such as critical care intensivists and interventional cardiologists. The patient's surrogate decision maker should be approached and presented with a tentative prognosis, and the goals of care should be discussed. Defining expectations—in terms of realistic results expected from PCI, mechanical circulatory support devices, and other interventions—is critically important.[27] The team should appropriately discuss what to "expect" from interventions such as CAG, PCI, and mechanical circulatory support devices (such as intra-aortic balloon pump, Impella, and extracorporeal membrane oxygenation) and weigh them against the associated risks of changing the overall patient outcome. The implementation of this 3-step approach can help reduce variability and promote consistency while selecting patients for CAG from a cohort of patients with OHCA without STE.




**Central Illustration.**

**"Assess, Consult & Expect" (ACE) approach for patients with out-of-hospital cardiac arrest without ST-segment elevation on electrocardiograms.** The ACE approach may serve as a conceptual framework for the management of patients with out-of-hospital cardiac arrest (OHCA) and no ST-segment elevation (STE) on electrocardiograms. CAD, coronary artery disease; CAG, coronary angiography; ECG, electrocardiogram; LVEF, left ventricle ejection fraction; ROSC, return of spontaneous circulation.

The ACE approach provides a stepwise holistic approach specifically for patients with OHCA and no evidence of STE on ECGs. It is different from prior algorithms in several ways.[6,65,70] First, in addition to considering unfavorable resuscitation-related factors, the ACE approach takes into consideration cardiac and noncardiac history to predict the likelihood of a cardiac etiology behind OHCA. Second, the ACE approach advocates for a multidisciplinary team, which involves an interventional cardiologist, intensivist, and, most importantly, the family, with the discussion of the goals of care and reaching a shared medical decision. Third, the ACE approach involves setting appropriate expectations and consideration of realistic outcomes with the use of different modalities and interventions such as temperature management, CAG, and mechanical circulatory support.

The clinical dilemma of the use of the CAG strategy in patients with OHCA without STE has been well answered by recent evidence, resulting in a paradigm shift in the management of these patients. Accordingly, we anticipate and recommend an upgrade of the current guidelines with regard to CAG and PCI for such patients as we await results from current trials that are underway. Whether a particular subgroup would benefit from an early CAG and PCI strategy is yet to be discovered. We recommend future studies to be directed toward better identifying such subgroups, improving neurologic prognostication of comatose patients, and recognizing interventions that improve outcomes in these patients. Until then, it is imperative for multidisciplinary teams to make decisions using relevant clinical data to provide individualized care.

## Conclusions

Patients who experience OHCA without a shockable rhythm and without STE on post-ROSC ECGs are among the most challenging patients encountered by critical care and interventional cardiologists. With limited options, early CAG and PCI have long been embraced as interventions associated with improved outcomes. However, the results of recent RCTs and meta-analyses contradict these assumptions and indicate that the strategy of routine early CAG is not beneficial and, in fact, has similar short- and long-term outcomes as of the delayed or selective CAG strategy.

The challenge ahead of the critical care team of the next decade is to identify patients with OHCA without STE on ECGs who will benefit from CAG at all. The approach should integrate the likelihood of an acute coronary lesion to be the cause of OHCA as well as the patient's on-presentation neurologic, cardiac, and systemic statuses and should involve a multidisciplinary team to work closely to determine which interventions are most likely to benefit the patient.

## Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## References

1. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. *Circulation*. 2020;141(9):e139–e596.
2. Graham R, McCoy MA, Schultz AM, eds. *Strategies to Improve Cardiac Arrest Survival: A Time to Act*. National Academies Press; 2015.
3. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *Circulation*. 2017;135(10):e146–e603.
4. Girotra S, van Diepen S, Nallamothu BK, et al. Regional variation in out-of-hospital cardiac arrest survival in the United States. *Circulation*. 2016;133(22):2159–2168.
5. 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(23):1629–1633.
6. Lotfi A, Klein LW, Hira RS, et al. SCAI expert consensus statement on out of hospital cardiac arrest. *Catheter Cardiovasc Interv*. 2020;96(4):844–861.
7. Neumar RW, Shuster M, Callaway CW, et al. Part 1: executive summary: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(18_suppl 2):S315–S367.
8. Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39(2):119–177.
9. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary

resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(16): S366–S468 (suppl 2).

10. Kim YJ, Min SY, Lee DH, et al. The role of post-resuscitation electrocardiogram in patients with ST-segment changes in the immediate post-cardiac arrest period. *JACC Cardiovasc Interv*. 2017;10(5):451–459.
11. Garcia S, Drexel T, Bekwelem W, et al. Early access to the cardiac catheterization laboratory for patients resuscitated from cardiac arrest due to a shockable rhythm: the Minnesota Resuscitation Consortium Twin Cities Unified Protocol. *J Am Heart Assoc*. 2016;5(1):e002670.
12. Kern KB, Lotun K, Patel N, et al. Outcomes of comatose cardiac arrest survivors with and without ST-segment elevation myocardial infarction: importance of coronary angiography. *JACC Cardiovasc Interv*. 2015;8(8):1031–1040.
13. Yannopoulos D, Bartos JA, Raveendran G, et al. Coronary artery disease in patients with out-of-hospital refractory ventricular fibrillation cardiac arrest. *J Am Coll Cardiol*. 2017;70(9):1109–1117.
14. Lamhaut L, Tea V, Raphalen JH, et al. Coronary lesions in refractory out of hospital cardiac arrest (OHCA) treated by extra corporeal pulmonary resuscitation (ECPR). *Resuscitation*. 2018;126:154–159.
15. Yannopoulos D, Bartos JA, Aufderheide TP, et al. The evolving role of the cardiac catheterization laboratory in the management of patients with out-of-hospital cardiac arrest: a scientific statement from the American Heart Association. *Circulation*. 2019;139(12):e530–e552.
16. Lemkes JS, Janssens GN, van der Hoeven NW, et al. Coronary angiography after cardiac arrest without ST-segment elevation. *N Engl J Med*. 2019;380(15): 1397–1407.
17. 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(3):200–207.
18. Radsel P, Knafelj R, Kocjancic S, Noc M. Angiographic characteristics of coronary disease and postresuscitation electrocardiograms in patients with aborted cardiac arrest outside a hospital. *Am J Cardiol*. 2011;108(5):634–638.
19. Silfvast T. Cause of death in unsuccessful prehospital resuscitation. *J Intern Med*. 1991;229(4):331–335.
20. Virkkunen I, Paasio L, Ryynänen S, et al. Pulseless electrical activity and unsuccessful out-of-hospital resuscitation: what is the cause of death? *Resuscitation*. 2008;77(2): 207–210.
21. Martínez-Losas P, Salinas P, Ferrera C, et al. Coronary angiography findings in cardiac arrest patients with non-diagnostic post-resuscitation electrocardiogram: a comparison of shockable and non-shockable initial rhythms. *World J Cardiol*. 2017;9(8):702–709.
22. 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(2):312–318.
23. Garcia-Tejada J, Jurado-Román A, Rodríguez J, et al. Post-resuscitation electrocardiograms, acute coronary findings and in-hospital prognosis of survivors of out-of-hospital cardiac arrest. *Resuscitation*. 2014;85(9):1245–1250.
24. Joffre J, Varenne O, Bougouin W, Rosencher J, Mira JP, Cariou A. Stent thrombosis: an increased adverse event after angioplasty following resuscitated cardiac arrest. *Resuscitation*. 2014;85(6):769–773.
25. Steg PG, Popovic B. Emergency coronary angiography after out-of-hospital cardiac arrest: is it essential or futile? *Circ Cardiovasc Interv*. 2018;11(6), e006804.
26. Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. *Intensive Care Med*. 2004;30(11): 2126–2128.
27. Harhash AA, May T, Hsu CH, et al. Incidence of cardiac interventions and associated cardiac arrest outcomes in patients with nonshockable initial rhythms and no ST elevation post resuscitation. *Resuscitation*. 2021;167:188–197.
28. Verma BR, Sharma V, Shekhar S, et al. Coronary angiography in patients with out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis. *JACC Cardiovasc Interv*. 2020;13(19):2193–2205.
29. 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(1):88–95.
30. Kleissner M, Sramko M, Kohoutek J, Kautzner J, Kettner J. Impact of urgent coronary angiography on mid-term clinical outcome of comatose out-of-hospital cardiac arrest survivors presenting without ST-segment elevation. *Resuscitation*. 2015;94:61–66.
31. Dankiewicz J, Nielsen N, Annborn M, et al. Survival in patients without acute ST elevation after cardiac arrest and association with early coronary angiography: a post hoc analysis from the TTM trial. *Intensive Care Med*. 2015;41(5):856–864.
32. Elfwén L, Lagedal R, James S, et al. Coronary angiography in out-of-hospital cardiac arrest without ST elevation on ECG-short- and long-term survival. *Am Heart J*. 2018; 200:90–95.
33. Kim YJ, Kim YH, Lee BK, et al. Immediate versus early coronary angiography with targeted temperature management in out-of-hospital cardiac arrest survivors without ST-segment elevation: a propensity score-matched analysis from a multicenter registry. *Resuscitation*. 2019;135:30–36.
34. 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(4):291–301.
35. Reynolds JC, Rittenberger JC, Toma C, Callaway CW. 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(9):1232–1239.
36. Vyas A, Chan PS, Cram P, Nallamothu BK, McNally B, Girotra S. Early coronary angiography and survival after out-of-hospital cardiac arrest. *Circ Cardiovasc Interv*. 2015;8(10):e002321.
37. Geri G, Dumas F, Bougouin W, et al. Immediate percutaneous coronary intervention is associated with improved short- and long-term survival after out-of-hospital cardiac arrest. *Circ Cardiovasc Interv*. 2015;8(10):e002321.
38. Staudacher II , den Uil C, Jewbali L, et al. Timing of coronary angiography in survivors of out-of-hospital cardiac arrest without obvious extracardiac causes. *Resuscitation*. 2018;123:98–104.
39. Jentzer JC, Scutella M, Pike F, et al. Early coronary angiography and percutaneous coronary intervention are associated with improved outcomes after out of hospital cardiac arrest. *Resuscitation*. 2018;123:15–21.
40. Song H, Kim HJ, Park KN, et al. Which out-of-hospital cardiac arrest patients without ST-segment elevation benefit from early coronary angiography? Results from the Korean Hypothermia Network Prospective Registry. *J Clin Med*. 2021;10(3):439.
41. Vedamurthy D, Singh S, Subedi K, Garratt KN, Wimmer NJ. Outcomes with early cardiac catheterization in out of hospital cardiac arrest survivors and utility of a prognostic scoring system. *Cureus*. 2021;13(7), e16775.
42. Lim SL, Lau YH, Chan MY, et al. Early coronary angiography is associated with improved 30-day outcomes among patients with out-of-hospital cardiac arrest. *J Clin Med*. 2021;10(21):5191.
43. Lemkes JS, Janssens GN, van der Hoeven NW, et al. Coronary angiography after cardiac arrest without ST segment elevation: one-year outcomes of the COACT randomized clinical trial. *JAMA Cardiol*. 2020;5(12):1358–1365.
44. Andrew E, Nehme Z, Wolfe R, Bernard S, Smith K. Long-term survival following out-of-hospital cardiac arrest. *Heart*. 2017;103(14):1104–1110.
45. Desch S, Freund A, Akin I, et al. Angiography after out-of-hospital cardiac arrest without ST-segment elevation. *N Engl J Med*. 2021;385(27):2544–2553.
46. Kern KB, Radsel P, Jentzer JC, et al. Randomized pilot clinical trial of early coronary angiography versus no early coronary angiography after cardiac arrest without ST-segment elevation: the PEARL study. *Circulation*. 2020;142(21):2002–2012.
47. Hauw-Berlemont C, Lamhaut L, Diehl JL, et al. Emergency vs delayed coronary angiogram in survivors of out-of-hospital cardiac arrest: results of the randomized, multicentric EMERGE trial. *JAMA Cardiol*. 2022;7(7):700–707.
48. Viana-Tejedor A, Ariza-Solé A, Martínez-Sellés M, et al. Role of coronary angiography in patients with a non-diagnostic electrocardiogram following out-of hospital cardiac arrest: rationale and design of the multicentre randomized controlled COUPE trial. *Eur Heart J Acute Cardiovasc Care*. 2020;9(suppl 4): S131–S137.
49. Elfwén L, Lagedal R, Nordberg P, et al. Direct or subacute coronary angiography in out-of-hospital cardiac arrest (DISCO)—an initial pilot-study of a randomized clinical trial. *Resuscitation*. 2019;139:253–261.
50. Elfwén L, Lagedal R, Rubertsson S, et al. Post-resuscitation myocardial dysfunction in out-of-hospital cardiac arrest patients randomized to immediate coronary angiography versus standard of care. *Int J Cardiol Heart Vasc*. 2020;27:100483.
51. Welsford M, Bossard M, Shortt C, Pritchard J, Natarajan MK, Belley-Côté EP. Does early coronary angiography improve survival after out-of-hospital cardiac arrest? A systematic review with meta-analysis. *Can J Cardiol*. 2018;34(2):180–194.
52. Patel JK, Thippeswamy G, Kataya A, Loeb CA, Parikh PB. Predictors of obstructive coronary disease and mortality in adults having cardiac arrest. *Am J Cardiol*. 2018; 122(1):12–16.
53. Larsen JM, Ravkilde J. Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—a systematic review and meta-analysis. *Resuscitation*. 2012; 83(12):1427–1433.
54. Nielsen N, Hovdenes J, Nilsson F, et al. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand*. 2009;53(7):926–934.
55. Merchant RM, Abella BS, Khan M, et al. Cardiac catheterization is underutilized after in-hospital cardiac arrest. *Resuscitation*. 2008;79(3):398–403.
56. Reynolds JC, Callaway CW, El Khoudary SR, Moore CG, Alvarez RJ, Rittenberger JC. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. *J Intensive Care Med*. 2009;24(3): 179–186.
57. Casella G, Carinci V, Cavallo P, et al. Combining therapeutic hypothermia and emergent coronary angiography in out-of-hospital cardiac arrest survivors: optimal post-arrest care for the best patient. *Eur Heart J Acute Cardiovasc Care*. 2015; 4(6):579–588.
58. Shin J, Ko E, Cha WC, et al. Impact of early coronary angiography on the survival to discharge after out-of-hospital cardiac arrest. *Clin Exp Emerg Med*. 2017;4(2):65–72.
59. Khan MS, Shah SM, Mubashir A, et al. Early coronary angiography in patients resuscitated from out of hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis. *Resuscitation*. 2017;121:127–134.
60. Barbarawi M, Zayed Y, Kheiri B, et al. Optimal timing of coronary intervention in patients resuscitated from cardiac arrest without ST-segment elevation myocardial infarction (NSTEMI): a systematic review and meta-analysis. *Resuscitation*. 2019; 144:137–144.
61. Subahi A, Kheiri B, Yassin AS, Ali OE. Coronary angiography in patients resuscitated from cardiac arrest without ST-segment elevation: does it confer survival benefit? *Cardiovasc Revasc Med*. 2020;21(8):989–991.
62. Yang MC, Meng-Jun W, Xiao-Yan X, Peng KL, Peng YG, Wang RR. Coronary angiography or not after cardiac arrest without ST segment elevation: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(41):e22197.
63. Abusnina W, Al-Abdouh A, Latif A, et al. Timing of coronary angiography in patients following out-of-hospital cardiac arrest without ST-segment elevation: a systematic review and meta-analysis of randomized trials. *Cardiovasc Revasc Med*. 2022;40:92–98.

64. Nolan JP, Maconochie I, Soar J, et al. Executive summary: 2020 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Circulation*. 2020;142(16_suppl 1):S2–S27.
65. Rab T, Kern KB, Tamis-Holland JE, et al. Cardiac arrest: a treatment algorithm for emergent invasive cardiac procedures in the resuscitated comatose patient. *J Am Coll Cardiol*. 2015;66(1):62–73.
66. Reynolds JC, Frisch A, Rittenberger JC, Callaway CW. Duration of resuscitation efforts and functional outcome after out-of-hospital cardiac arrest: when should we change to novel therapies? *Circulation*. 2013;128(23):2488–2494.
67. Harhash AA, May TL, Hsu CH, et al. Risk stratification among survivors of cardiac arrest considered for coronary angiography. *J Am Coll Cardiol*. 2021;77(4):360–371.
68. Bascom KE, Dziodzio J, Vasaiwala S, et al. Derivation and validation of the CREST model for very early prediction of circulatory etiology death in patients without ST-segment-elevation myocardial infarction after cardiac arrest. *Circulation*. 2018; 137(3):273–282.
69. Baldi E, Schnaubelt S, Caputo ML, et al. Association of timing of electrocardiogram acquisition after return of spontaneous circulation with coronary angiography findings in patients with out-of-hospital cardiac arrest. *JAMA Netw Open*. 2021; 4(1):e2032875.
70. Jentzer JC, Herrmann J, Prasad A, Barsness GW, Bell MR. Utility and challenges of an early invasive strategy in patients resuscitated from out-of-hospital cardiac arrest. *JACC Cardiovasc Interv*. 2019;12(8):697–708.