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AHA FOCUSED UPDATE

# 2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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**ABSTRACT:** Cardiac arrest is common and deadly, affecting up to 700 000 people in the United States annually. Advanced cardiac life support measures are commonly used to improve outcomes. This "2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support" summarizes the most recent published evidence for and recommendations on the use of medications, temperature management, percutaneous coronary angiography, extracorporeal cardiopulmonary resuscitation, and seizure management in this population. We discuss the lack of data in recent cardiac arrest literature that limits our ability to evaluate diversity, equity, and inclusion in this population. Last, we consider how the cardiac arrest population may make up an important pool of organ donors for those awaiting organ transplantation.

**Key Words:** AHA Scientific Statements ■ advanced cardiac life support ■ angiography ■ heart arrest ■ resuscitation

## TOP 10 TAKE-HOME MESSAGES FOR THE 2023 FOCUSED UPDATE ON ADULT ADVANCED CARDIOVASCULAR LIFE SUPPORT

1. It is important for researchers to develop and implement methods to improve representation of participants from diverse backgrounds and to improve the accuracy of reporting study subject demographics.
2. Routine administration of calcium for treatment of cardiac arrest is not recommended.
3. Use of extracorporeal cardiopulmonary resuscitation for patients with cardiac arrest refractory to standard advanced cardiovascular life support is reasonable in select patients when provided within an appropriately trained and equipped system of care.
4. Emergency coronary angiography is not recommended over a delayed or selective strategy in patients with return of spontaneous circulation after cardiac arrest unless they exhibit ST-segment–elevation myocardial infarction, shock, electrical instability, signs of significant myocardial damage, or ongoing ischemia.
5. We recommend that all adults who do not follow commands after return of spontaneous circulation, regardless of arrest location or presenting rhythm, receive treatment that includes a deliberate strategy for temperature control.
6. We recommend selecting and maintaining a constant temperature between 32°C and 37.5°C during postarrest temperature control.
7. There is insufficient evidence to recommend a specific therapeutic temperature for different subgroups of patients with cardiac arrest.

Supplemental Material is available at www.ahajournals.org/journal/doi/suppl/10.1161/CIR.0000000000001194.

*Circulation* is available at www.ahajournals.org/journal/circ

8. Patients with spontaneous hypothermia after return of spontaneous circulation who do not follow commands should not be routinely actively or passively rewarmed faster than 0.5°C per hour.
9. A therapeutic trial of a nonsedating antiseizure medication may be reasonable in adult survivors of cardiac arrest with electroencephalography patterns on the ictal-interictal continuum.
10. Organ donation is an important outcome that should be considered in the development and evaluation of systems of care.

# INTRODUCTION

## Scope of the Guidelines

This 2023 focused update to the American Heart Association (AHA) advanced cardiovascular life support (ACLS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care is based on the expert writing group review of the relevant International Liaison Committee on Resuscitation (ILCOR) Consensus on Science With Treatment Recommendations (CoSTR) documents and the studies included in the systematic reviews, as well as new evidence updates conducted by the writing group. The writing group discussion and evidence reviews were conducted within the context of the clinical environments in which out-of-hospital and in-hospital resuscitations occur, with special consideration for the health care professionals who use these ACLS guidelines.

## Organization of the Writing Group

The Advanced Life Support (ALS) Focused Update Writing Group included a diverse group of experts with backgrounds in emergency medicine, pulmonary/critical care, neurocritical care, interventional cardiology, and emergency medical services. Group members were appointed by the AHA Emergency Cardiovascular Care Science Subcommittee and approved by the AHA Manuscript Oversight Committee. Writing group members were selected to represent diverse backgrounds in clinical medicine and research expertise and to form a group that was institutionally diverse and inclusive of women, underrepresented racial and ethnic groups, and early-career participants.

The AHA has rigorous conflict of interest policies and procedures to minimize the risk of bias or improper influence during the development of guidelines. Before appointment, writing group members disclosed all relevant commercial relationships and other potential (including intellectual) conflicts. These procedures are described more fully in "Part 2: Evidence Evaluation and Guidelines Development" of the "2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[1] Appendix 1 of this document lists the writing group members' relevant relationships with industry.

## Abbreviations

| | |
|---|---|
| ACLS | advanced cardiovascular life support |
| AHA | American Heart Association |
| ALS | advanced life support |
| COR | Class of Recommendation |
| CoSTR | Consensus on Science With Treatment Recommendations |
| CPR | cardiopulmonary resuscitation |
| DCD | donation after circulatory death |
| ECPR | extracorporeal cardiopulmonary resuscitation |
| EEG | electroencephalography |
| ILCOR | International Liaison Committee on Resuscitation |
| LOE | Level of Evidence |
| OHCA | out-of-hospital cardiac arrest |
| RCT | randomized controlled trial |
| ROSC | return of spontaneous circulation |

# METHODOLOGY AND EVIDENCE REVIEW

The writing group members evaluated the current list of patient, intervention, comparison, and outcome questions included in current ALS guidelines. Patient, intervention, comparison, and outcome questions with novel evidence were revisited by the writing group through systematic review as described. For each targeted patient, intervention, comparison, and outcome question, writing group members created a search strategy, used a previously created ILCOR search strategy when available, or reviewed the evidence from the ILCOR CoSTRs. Search strategies were internally peer reviewed and executed in Medline and Excerpta Medica Database (Embase), using the Ovid search interface, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search` strategies and details about article selection are provided in the Supplemental Appendix. Final searches were executed in July 2022. Search results were not limited by language or year. Two writing group members performed dual screening of the titles and abstracts of all articles identified from each search and identified articles for full-text review. Screening conflicts were resolved between the 2 writing group members and writing group leadership before full-text review. Two writing group members reviewed the full text of all selected articles and applied the information contained to develop treatment recommendations appropriate for each clinical question. Each draft recommendation was created by a group of 2 or 3 writing group members and then reviewed and refined by all writing group members during regular virtual meetings. The final manuscript was reviewed and approved by all writing group members.

## Class of Recommendation and Level of Evidence

As with all AHA guidelines, each recommendation in this focused update is assigned a Class of Recommendation

(COR) according to the strength and consistency of the evidence, alternative treatment options, and impact on patients and society (Table 1). The Level of Evidence (LOE) is based on the quality, quantity, relevance, and consistency of the available evidence. For each recommendation, the writing group discussed and approved specific recommendation wording and the COR and LOE assignments. In determining the COR, the writing group considered the LOE and other factors, including systems issues, economic factors, and ethical factors such as equity, acceptability, and feasibility. These evidence-review methods, including specific criteria used to determine COR and LOE, are described more fully in "Part 2: Evidence Evaluation and Guidelines Development" of the 2020 guidelines.[1] The writing group members had final authority over and formally approved these recommendations.

## Guideline Structure

The guidelines in this focused update are organized into knowledge chunks, grouped into discrete modules of information on specific topics or management issues.[2] Each modular knowledge chunk includes a table of recommendations that uses standard AHA nomenclature of COR and LOE. A brief introduction is provided to put the recommendations into context with important background information and overarching management

**Table 1. Applying the American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated May 2019)**

| CLASS (STRENGTH) OF RECOMMENDATION | |
|---|---|
| **CLASS 1 (STRONG)** | **Benefit >>> Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is recommended<br>• Is indicated/useful/effective/beneficial<br>• Should be performed/administered/other<br>• Comparative-Effectiveness Phrases†:<br>– Treatment/strategy A is recommended/indicated in preference to treatment B<br>– Treatment A should be chosen over treatment B | |
| **CLASS 2a (MODERATE)** | **Benefit >> Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is reasonable<br>• Can be useful/effective/beneficial<br>• Comparative-Effectiveness Phrases†:<br>– Treatment/strategy A is probably recommended/indicated in preference to treatment B<br>– It is reasonable to choose treatment A over treatment B | |
| **CLASS 2b (WEAK)** | **Benefit ≥ Risk** |
| **Suggested phrases for writing recommendations:**<br>• May/might be reasonable<br>• May/might be considered<br>• Usefulness/effectiveness is unknown/unclear/uncertain or not well-established | |
| **CLASS 3: No Benefit (MODERATE)**<br>**(Generally, LOE A or B use only)** | **Benefit = Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is not recommended<br>• Is not indicated/useful/effective/beneficial<br>• Should not be performed/administered/other | |
| **Class 3: Harm (STRONG)** | **Risk > Benefit** |
| **Suggested phrases for writing recommendations:**<br>• Potentially harmful<br>• Causes harm<br>• Associated with excess morbidity/mortality<br>• Should not be performed/administered/other | |

| LEVEL (QUALITY) OF EVIDENCE‡ | |
|---|---|
| **LEVEL A** | |
| • High-quality evidence‡ from more than 1 RCT<br>• Meta-analyses of high-quality RCTs<br>• One or more RCTs corroborated by high-quality registry studies | |
| **LEVEL B-R** | **(Randomized)** |
| • Moderate-quality evidence‡ from 1 or more RCTs<br>• Meta-analyses of moderate-quality RCTs | |
| **LEVEL B-NR** | **(Nonrandomized)** |
| • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies<br>• Meta-analyses of such studies | |
| **LEVEL C-LD** | **(Limited Data)** |
| • Randomized or nonrandomized observational or registry studies with limitations of design or execution<br>• Meta-analyses of such studies<br>• Physiological or mechanistic studies in human subjects | |
| **LEVEL C-EO** | **(Expert Opinion)** |
| • Consensus of expert opinion based on clinical experience | |

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

or treatment concepts. Recommendation-specific text clarifies the rationale and key study data supporting the recommendations. When appropriate, additional tables are included.

This 2023 document updates the recommendations for the use of vasopressors and calcium intra-arrest, extracorporeal cardiopulmonary resuscitation (ECPR), coronary angiography and percutaneous coronary intervention, temperature control, seizure management, and organ donation after cardiac arrest. In addition, this document introduces the concept of diversity, equity, and inclusion into the formal guideline document.

## Document Review and Approval

These guidelines were submitted for blinded peer review to 5 subject matter experts nominated by the AHA. Before appointment, all peer reviewers were required to disclose relationships with industry and any other conflicts of interest, and all disclosures were reviewed by the AHA staff. Peer reviewer feedback was provided for guidelines in draft format and again in final format. All guidelines were reviewed and approved for publication by the AHA Science Advisory and Coordinating Committee and the AHA Executive Committee. Comprehensive disclosure information for peer reviewers is listed in Appendix 2.

These recommendations supersede the last full set of AHA recommendations for ALS made in 2020.[3] These are the first formal updates since the publication of the 2020 guidelines. All other recommendations and algorithms published in "Part 3: Adult Basic and Advanced Cardiovascular Life Support" in the 2020 guidelines remain the official recommendations of the AHA Emergency Cardiovascular Care Science Subcommittee and writing groups.[3] This 2023 focused update to the 2020 guidelines is based on the evidence identified in systematic reviews performed by ILCOR and this writing group addressing novel data that have been published since the formal release of the 2020 AHA ALS guidelines for cardiopulmonary resuscitation.[3]

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## VASOPRESSOR MEDICATIONS DURING CARDIAC ARREST

| Vasopressor Management in Cardiac Arrest | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| 1 | B-R | 1. We recommend that epinephrine be administered for patients in cardiac arrest. |
| 2a | B-R | 2. It is reasonable to administer epinephrine 1 mg every 3 to 5 minutes for cardiac arrest. |
| 2a | C-LD | 3. With respect to timing, for cardiac arrest with a nonshockable rhythm, it is reasonable to administer epinephrine as soon as feasible. |
| 2b | B-R | 4. Vasopressin alone or vasopressin+ methylprednisolone in combination with epinephrine may be considered in cardiac arrest but offers no advantage as a substitute for epinephrine. |
| 2b | C-LD | 5. With respect to timing, for cardiac arrest with a shockable rhythm, it may be reasonable to administer epinephrine after initial defibrillation attempts have failed. |
| 3: No Benefit | B-R | 6. High-dose epinephrine is not recommended for routine use in cardiac arrest. |

## Synopsis

Epinephrine has been hypothesized to have beneficial effects during cardiac arrest primarily because of its α-adrenergic effects, leading to increased coronary and cerebral perfusion pressure during CPR. Conversely, the β-adrenergic effects may increase myocardial oxygen demand, reduce subendocardial perfusion, and be proarrhythmic. Two randomized, placebo-controlled trials enrolling >8500 patients evaluated the efficacy of epinephrine for out-of-hospital cardiac arrest (OHCA).[1,2] Systematic reviews and meta-analyses of these and other studies[3–5] concluded that epinephrine significantly increased return of spontaneous circulation (ROSC) and survival to hospital discharge. Epinephrine did not increase survival with favorable or unfavorable neurological outcome at 3 months, although both of these outcomes occurred slightly more frequently in the epinephrine group.[2] Observational data suggest better outcomes when epinephrine is given sooner, and the low survival with favorable neurological outcome in the available trials may be due in part to the median time of 21 minutes from arrest to receipt of epinephrine. This time delay is a consistent issue in OHCA trials. Time to drug in in-hospital cardiac arrest is generally much shorter; therefore, the effect of epinephrine on outcomes in the in-hospital cardiac arrest population may be different. No trials to date have found any benefit of either higher-dose epinephrine or other vasopressors over standard-dose epinephrine during CPR.[4,5]

## Recommendation-Specific Supportive Text

1. Administration of epinephrine is a 2020 recommendation based on systematic reviews and meta-analyses[3–5] that included results of 2 randomized trials of epinephrine for OHCA, one of which included >8000 patients,[1,2] showing that epinephrine increased ROSC and short-term survival. At 3 months—the time point felt to be most meaningful for neurological recovery—there was a nonsignificant increase in survivors with both favorable and unfavorable neurological outcome in the epinephrine group.[2] Any drug that increases the rate of ROSC and short-term survival but is given after several minutes of downtime will likely increase long-term survival with both favorable and unfavorable neurological outcomes. Determining the likelihood of favorable or unfavorable neurological outcome at the time of arrest is currently not feasible. Therefore, continuing to use a drug that has been shown to increase survival while focusing our broader efforts on shortening time to drug for all patients so that more survivors will have a favorable neurological outcome seems to be the most beneficial approach. Relevant literature published subsequent to the 2020 guidelines was evaluated for this focused update.
2. The existing trials have used a protocol of epinephrine 1 mg every 3 to 5 minutes. Operationally, administering epinephrine every second cycle of CPR after the initial dose may also be reasonable.
3. Of 16 observational studies on timing in the recent systematic review, all found an association between earlier epinephrine and ROSC for patients with nonshockable rhythms, although improvements in survival were not universally seen.[3]
4. Systematic reviews[3–5] found no difference in outcomes in trials testing vasopressin alone or vasopressin combined with epinephrine compared with epinephrine alone for cardiac arrest, although these studies were underpowered. A recent placebo-controlled, randomized clinical trial including 501 patients with in-hospital cardiac arrest demonstrated that administering 20 IU vasopressin plus 40 mg methylprednisolone after the first dose of epinephrine was associated with an increase in ROSC, with a risk difference of 9.6% (95% CI, 1.1%–18%; $P$=0.03). No differences in survival or favorable neurological outcomes were found at 30 days; however, the study was not sufficiently powered for these secondary end points. These findings were supported by subsequent meta-analyses.[5,6]
5. For shockable rhythms, trial protocols have directed that epinephrine be given after the third shock.[1,2] The literature supports prioritizing defibrillation and CPR initially and giving epinephrine if initial attempts with CPR and defibrillation are not successful.[3]
6. Multiple randomized controlled trials (RCTs) have been done comparing high-dose with standard-dose epinephrine, and although some have shown higher rates of ROSC with high-dose epinephrine, none have shown improvement in survival to discharge or any longer-term outcomes.[7–14]

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## NONVASOPRESSOR MEDICATIONS DURING CARDIAC ARREST

| Nonvasopressor Medications | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| 2b | B-R | 1. Amiodarone or lidocaine may be considered for ventricular fibrillation/pulseless ventricular tachycardia that is unresponsive to defibrillation. |
| 2b | C-LD | 2. For patients with OHCA, use of steroids during CPR is of uncertain benefit. |
| 3: No Benefit | B-R | 3. Routine administration of calcium for treatment of cardiac arrest is not recommended. |
| 3: No Benefit | B-R | 4. Routine use of sodium bicarbonate is not recommended for patients in cardiac arrest. |
| 3: No Benefit | B-R | 5. Routine use of magnesium for cardiac arrest is not recommended. |

### Synopsis

Pharmacological treatment of cardiac arrest is typically deployed when CPR with or without attempted defibrillation fails to achieve ROSC. This may include vasopressor agents such as epinephrine (discussed in Vasopressor Medications During Cardiac Arrest) and drugs without direct hemodynamic effects such as antiarrhythmic medications, magnesium, sodium bicarbonate, calcium, or steroids. Although theoretically attractive and of some proven benefit in animal studies, no nonvasopressor pharmacological treatment has definitively been proven to improve overall survival after cardiac arrest, although some may have benefit in selected populations or special circumstances.

Recommendations for the treatment of cardiac arrest attributable to hyperkalemia, including the use of calcium and sodium bicarbonate, are presented in the 2020 guidelines.[1]

### Recommendation-Specific Supportive Text

1. Administration of amiodarone or lidocaine to patients with OHCA was last formally reviewed in 2018[2] and demonstrated improved survival to hospital admission but did not improve overall survival to hospital discharge or survival with good neurological outcome.[2,3] However, amiodarone and lidocaine each significantly improved survival to hospital discharge in a prespecified subgroup of patients with bystander-witnessed arrest, potentially arguing for a time-dependent benefit and a group for whom these drugs may be more useful. Other antiarrhythmic agents were not specifically addressed in the most recent evidence review and merit further evaluation. These include bretylium tosylate, which was recently reintroduced in the United States for treatment of immediately life-threatening ventricular arrhythmias but without any new information on its effectiveness or safety.[4] Sotalol requires administration as a slow infusion, rendering it impractical to use in cardiac arrest.[5] Similar limitations also apply to procainamide, although it has been given by rapid infusion as a second-line agent in cardiac arrest with uncertain benefit.[6] The efficacy of antiarrhythmic drugs when given in combination for cardiac arrest has not been systematically addressed and remains a knowledge gap.
2. Nonrandomized studies of intra-arrest corticosteroid administration, in addition to standard resuscitation, show mixed outcomes.[7,8] It remains unclear whether steroids alone are beneficial during cardiac arrest because the only studies suggesting benefit evaluated steroids with other bundles of interventions, and observational data have shown conflicting results. Additional insights concerning steroid use when given as a bundle with vasopressors are addressed in Vasopressor Medications During Cardiac Arrest.
3. A 2013 systematic review found little evidence to support the routine use of calcium in undifferentiated cardiac arrest, although the evidence was weak because of the lack of clinical trials and the tendency to use calcium as a last-resort medication in refractory cardiac arrest.[9] Since the prior guideline statement, 1 randomized, double-blinded, placebo-controlled trial evaluated administration of intravenous or intraosseous calcium and its effect on sustained ROSC, demonstrating no difference between the calcium treatment (19%) and saline control (27%; risk ratio, 0.72 [95% CI, 0.49–1.03]; risk difference, −7.6% [95% CI, −16% to 0.8%]; $P$=0.09).[10] Of note, these data suggest that the routine administration of calcium, outside of special circumstances, may trend toward the potential for harm. Administration of calcium in special circumstances such as known hyperkalemia and calcium blocker overdose is addressed in the 2020 guidelines.[1]
4. Clinical trials and observational studies since the "2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" have yielded no new evidence that routine administration of sodium bicarbonate improves outcomes from undifferentiated cardiac arrest, and evidence suggests that it may worsen survival and neurological recovery.[11–13] The use of sodium bicarbonate in special circumstances such as hyperkalemia and drug overdose is addressed in the 2020 guidelines.[1]
5. The role of magnesium as an antiarrhythmic agent was last addressed by the 2018 AHA focused

update on ACLS use of antiarrhythmic drugs,[2] and no recent literature has revealed additional information since that publication. RCTs have not found magnesium to improve return of circulation, survival, or neurological outcome, regardless of the presenting cardiac arrest rhythm,[14–17] nor is it useful for monomorphic ventricular tachycardia.[18] Anecdotal reports and small case series attest to the efficacy of magnesium in the treatment of torsades de pointes.[1]

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# EXTRACORPOREAL CPR

| ECPR | | |
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| **COR** | **LOE** | **Recommendation** |
| **2a** | **B-R** | 1. Use of ECPR for patients with cardiac arrest refractory to standard ACLS is reasonable in select patients when provided within an appropriately trained and equipped system of care. |

## Synopsis

ECPR refers to the initiation of cardiopulmonary bypass during the resuscitation of a patient in cardiac arrest. This involves the cannulation of a large vein and artery and initiation of venoarterial extracorporeal membrane oxygenation. The goal of ECPR is to support end-organ perfusion while potentially reversible conditions are addressed. ECPR is a complex intervention that requires a highly trained team, specialized equipment, and multidisciplinary support within a health care system. An effective program achieves excellence along the other links in the Chain of Survival, develops strategic partnerships, secures resources, and perfects the clinical skill necessary to proficiently deliver and maintain this therapy in an equitable fashion. In the last review in 2020, the AHA guidelines addressed the use of ECPR for cardiac arrest and noted insufficient evidence to recommend the routine use of ECPR in cardiac arrest. However, consideration of ECPR was suggested in select cases of cardiac arrest with potentially reversible pathogenesis that would benefit from temporary cardiorespiratory support.[1] Multiple observational studies were available supporting the use of ECPR,[2–8] but no randomized clinical trials were available at the time of guideline publication in 2020. Two randomized clinical trials have since been published that provide additional evidence concerning the use of ECPR for patients with refractory cardiac arrest.[9,10]

## Recommendation-Specific Supportive Text

1. Two RCTs have been published comparing patients with refractory cardiac arrest treated with ongoing standard ACLS versus ECPR. The ARREST trial[9] (Advanced Reperfusion Strategies for Refractory Cardiac Arrest) demonstrated significantly improved survival to discharge and 6-month survival for patients receiving ECPR for refractory cardiac arrest with shockable presenting rhythms. Although the trial randomized only 30 patients, the Data and Safety Monitoring Board unanimously decided to terminate the trial, citing ethical concerns in the face of strong evidence for efficacy. The Hyperinvasive Trial[10] did not meet the primary end point of 180-day neurologically favorable survival, although it did demonstrate significant benefit in 30-day survival with favorable neurological recovery. It is important to note that the Hyperinvasive Trial included patients with all presenting rhythms and required only 5 minutes of ACLS before enrollment. The ARREST trial randomized after a mean 47 minutes of ACLS compared with 24 minutes of ACLS in the Hyperinvasive Trial. The Hyperinvasive Trial demonstrated a 22% 180-day neurologically favorable survival in the standard ACLS group compared with 7% observed in the standard ACLS group in the ARREST trial. Further data related to optimal patient selection criteria, including age, presenting rhythm, and timing of transition from standard ACLS to ECPR, are needed.

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# PERCUTANEOUS CORONARY INTERVENTION AFTER CARDIAC ARREST

| Percutaneous Coronary Intervention After Cardiac Arrest | | |
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| **COR** | **LOE** | **Recommendation** |
| 1 | B-NR | 1. Coronary angiography should be performed emergently for all cardiac arrest patients with suspected cardiac cause of arrest and ST-segment elevation on electrocardiogram. |
| 2a | B-NR | 2. Emergent coronary angiography is reasonable for selected adult patients without ST-elevation on electrocardiogram but with elevated risk of significant coronary artery disease where revascularization may provide benefit, such as those with shock, electrical instability, signs of significant ongoing myocardial damage, or ongoing ischemia. |
| 2a | C-LD | 3. Independent of a patient's neurologic status, coronary angiography is reasonable in all post–cardiac arrest patients for whom coronary angiography is otherwise indicated. |
| 3: No Benefit | B-R | 4. Emergent coronary angiography is not recommended over a delayed or selective strategy in patients with ROSC after cardiac arrest in the absence of ST-segment elevation, shock, electrical instability, signs of significant myocardial damage, and ongoing ischemia. |

## Synopsis

The contribution of coronary artery disease and acute coronary syndromes to the epidemiology of OHCA and the role/timing of revascularization have been areas of rigorous investigation. Previous registry and observational data demonstrated a high incidence of acute coronary lesions in patients resuscitated after cardiac arrest.[1–4] This incidence was even higher among those with shockable presenting rhythms and those with ST-segment elevation on their postarrest electrocardiogram.[2,5] Patients with shockable presenting rhythms refractory to ACLS demonstrated high rates of significant

coronary artery disease.[6] Timely revascularization for postarrest patients appeared to be associated with a mortality benefit that persisted after attempts to control for confounders.[2,7–11] Thus, the prior recommendations, leveraging these best available data, recommended emergency coronary angiography for patients with ST-segment elevation and suggested emergency angiography in select patients (eg, hemodynamically and electrically unstable) without ST-segment elevation.[12] Notably, no recommendation was made for stable patients without ST-segment elevation.

A review of the ILCOR CoSTR and an independent search indicated that new RCT data conflict with the previously described observational data. Since the 2020 guidelines, 4 RCTs in this population have been published: COACT (Coronary Angiography After Cardiac Arrest Without ST-Segment Elevation), which was limited to patients with shockable rhythm[13]; TOMAHAWK (Angiography after Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation) and EMERGE (Emergency vs Delayed Coronary Angiogram in Survivors of Out-of-Hospital Cardiac Arrest), which included all presenting rhythms[14,15]; and PEARL (Randomized Pilot Clinical Trial of Early Coronary Angiography Versus No Early Coronary Angiography After Cardiac Arrest Without ST-Segment Elevation), which also included all presenting rhythms but was terminated early because of the pace of enrollment.[16] Despite variations in intervention and outcome definitions, protocols, and locations, these trials consistently found no difference between the intervention (emergency or early coronary angiography) and control arms. However, important patient populations were excluded from these clinical trials. Patients with ST-segment elevation, cardiogenic shock, signs of significant myocardial damage, electrical instability, and ongoing ischemia were excluded or permitted to cross over to the emergency arm. Thus, these studies demonstrate that there is no benefit of emergency coronary angiography over delayed coronary angiography for stable patients resuscitated from cardiac arrest without ST-segment elevation. Although it still might be reasonable, we do not urge emergency coronary angiography for patients who present and remain hemodynamically stable without signs of ischemia.

Randomized data are lacking for patients with ST-segment elevation or cohorts permitted to cross over in RCTs because of the presence of cardiogenic shock, signs of significant myocardial damage, electrical instability, or ongoing ischemia. Given the paucity of cardiac arrest–specific data and the clear benefits of emergency revascularization in patients without cardiac arrest with ST-segment–elevation myocardial infarction, patients with high-risk acute coronary syndrome, and patients with cardiogenic shock, we recommend considering emergency coronary angiography and revascularization in these patient populations.

## Recommendation-Specific Supportive Text

1. Multiple observational studies have demonstrated improved neurologically favorable survival when early coronary angiography is performed followed by percutaneous coronary intervention in patients with cardiac arrest who have an ST-segment–elevation myocardial infarction.[5,17–20] This led to a Class 1 recommendation in the 2020 guidelines that has not been contradicted by any other recent studies. This recommendation is consistent with global recommendations for all patients with ST-segment–elevation myocardial infarction.
2. Multiple observational studies have shown an association between emergency coronary angiography and percutaneous coronary intervention and improved neurological outcomes in patients without ST-segment elevation.[5,8,17,18,21] A meta-analysis also supported the use of early coronary angiography in patients without ST-segment elevation.[22] Although no randomized trials have addressed the use of emergency coronary angiography in patients with shock, hemodynamic or electrical instability, significant myocardial damage, or signs of ongoing cardiac ischemia, use of emergency coronary angiography in these situations is to identify patients in whom revascularization could improve outcomes by preventing rearrest or supporting cardiac recovery. In the absence of cardiac arrest, there is overwhelming benefit for early revascularization in patients with acute coronary syndrome with cardiovascular instability[23–25]; thus, the writing group felt it was reasonable to extrapolate to unstable postarrest patients.
3. Evidence suggests that comatose patients with ROSC benefit from invasive angiography, when indicated, as do patients who are awake.[4,17,21] Therefore, the use of invasive coronary angiography is reasonable, regardless of neurological status.
4. Multiple RCTs similarly demonstrated no benefit of emergency coronary angiography over delayed coronary angiography for patients with ROSC but without ST-segment elevation, shock, electrical instability, signs of significant ongoing myocardial damage, or ongoing ischemia.[13–16] If patients develop instability or signs of ongoing ischemia early in their treatment course, emergency coronary angiography can be reconsidered. Of note, the power of RCTs to detect small improvements in cardiac outcome may be affected by significant numbers of patients who died of a neurological cause with devastating neurological injury after cardiac arrest, in whom cardiac recovery has limited impact.

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# TEMPERATURE CONTROL

| Indications for Temperature Control | | |
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| **COR** | **LOE** | **Recommendation** |
| **1** | **B-R** | 1. We recommend all adults who do not follow commands after ROSC, irrespective of arrest location or presenting rhythm, receive treatment that includes a deliberate strategy for temperature control. |

## Synopsis

Temperature management has been a focus of post-arrest care for several decades. In recent years, clinical trials have rigorously tested the effect of target temperature on mortality and functional outcomes for patients with cardiac arrest. The 2020 ALS Guideline Committee reviewed data, including the HYPERION trial

(Therapeutic Hypothermia After Cardiac Arrest in Nonshockable Rhythm).[1] Two notable trials were published since completion of the 2020 ALS guidelines. The TTM2 trial (Targeted Temperature Management 2) randomized 1900 patients to 33°C or to normothermia with early treatment of fever (37.8°C) for 28 hours after randomization.[2] There was no difference in the primary outcome of Cerebral Performance Category 1 or 2 at 6 months. The CAPITAL CHILL trial (Effect of Moderate vs Mild Therapeutic Hypothermia on Mortality and Neurologic Outcomes in Comatose Survivors of Out-of-Hospital Cardiac Arrest) randomized 389 patients to moderate (31°C) versus mild (34°C) therapeutic hypothermia for 24 hours.[3] The primary outcome of mortality or poor neurological outcome (Disability Rating Scale score >5) at 6 months did not differ across arms in the primary or prespecified subgroup analyses. In both studies, most enrolled patients had primary cardiac causes of arrest.

In 2021, The ILCOR CoSTR task force updated their 2015 systematic review to include key trials published up to October of 2022, including TTM2.[4] This review found no outcome differences after temperature management to 32°C to 34°C compared with normothermia among the populations studied.

## Recommendation-Specific Supportive Text

1. Recently completed trials have strengthened our understanding that a range of target temperatures for postarrest temperature control is safe. With the addition of TTM2, the recommended range of target temperature has expanded since the publication of the 2020 guidelines.[5] A 2021 systematic review[4] supported the ILCOR CoSTR[6] incorporating the latest available trial data and recommended preventing fever, acknowledging the uncertainty of whether subpopulations benefit from hypothermia to 32°C to 34°C. This revised statement reflects this approach but acknowledges the lack of benefit of selecting a higher versus a lower temperature target within the population studied. There was insufficient evidence to change the lower range of target temperature, which remains at 32°C. This revised statement also consolidates the distinctions among in-hospital cardiac arrest, OHCA, shockable rhythms, and nonshockable rhythms compared with the AHA 2020 ALS guidelines.

   Several important considerations need to be emphasized when our current knowledge from clinical trials is applied to the general population receiving postresuscitation care. It is important to recognize that most enrolled patients in the aforementioned trials had shockable rhythms with primary cardiac causes of arrest, despite eligibility criteria comprising both shockable and nonshockable rhythms. These do not reflect the general population of postarrest patients who survive to hospital admission in the United States, where most initial arrest rhythms are nonshockable and arrests due to respiratory failure, drug overdose, sepsis, and other noncardiac causes are prevalent.

## Performance of Temperature Control

| Performance of Temperature Control | | |
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| **COR** | **LOE** | **Recommendations** |
| 1 | B-R | 1. We recommend selecting and maintaining a constant temperature between 32°C and 37.5°C during postarrest temperature control. |
| 1 | B-NR | 2. We recommend hospitals develop protocols for postarrest temperature control. |
| 2a | B-NR | 3. It is reasonable that temperature control be maintained for at least 24 h after achieving target temperature. |
| 2b | B-NR | 4. There is insufficient evidence to recommend a specific therapeutic temperature for different subgroups of cardiac arrest patients. |
| 2b | C-LD | 5. It may be reasonable to actively prevent fever in patients unresponsive to verbal commands after initial temperature control. |
| 2b | C-EO | 6. Patients with spontaneous hypothermia after ROSC unresponsive to verbal commands should not routinely be actively or passively rewarmed faster than 0.5°C per hour. |
| 2b | B-R | 7. The benefit of strategies other than rapid infusion of cold intravenous fluids for prehospital cooling is unclear. |
| 3: No Benefit | B-R | 8. We do not recommend the routine use of rapid infusion of cold intravenous fluids for prehospital cooling of patients after ROSC. |

## Recommendation-Specific Supportive Text

1. In agreement with the ILCOR CoSTR statement, terminology is shifting away from targeted temperature management in favor of temperature control, which encompasses hypothermic temperature control, normothermic temperature control, and temperature control with fever prevention.[6] The upper limit of temperature control was raised to 37.5°C to reflect findings of no difference between patients treated with a target temperature of 33°C and those treated with a target temperature of 37.5°C in the TTM2 trial.[2]
2. Recent trials have set strict criteria for temperature control and required continuous temperature monitoring and systematic application of protocolized interventions to maintain goal temperature. Half of patients in the normothermia arm of TTM2 required a device for active temperature management, and almost a third required neuromuscular blockade.[2] Even those who did not require a cooling device were cared for in a system that was able to offer this treatment if needed. Therefore, all hospitals providing postresuscitation care need to have a system that supports routine use of temperature control for these patients.

3. The duration of temperature control has been understudied compared with the ranges of target temperature. The ongoing ICECAP study (Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients) aims to identify the optimal duration of hypothermic temperature control at 33°C for patients with both shockable and nonshockable rhythms (NCT04217551). This will supplement the prior study reviewed as part of the 2020 guidelines, which showed no difference in temperature management between 24 and 48 hours in 335 patients.[7]
4. It is unknown whether trial results in a primary cardiac cause cohort generalize to other subpopulations of cardiac arrest survivors. Similarly, it is unknown whether other patient characteristics measured early after resuscitation such as severity of initial neurological injury or organ failure alter optimal target temperature. The most recent systematic review did not find evidence favoring temperature control with hypothermia in multiple single-variable subgroups.[4] However, robust risk-adjusted patient-level pooled data analysis is not available, the potential for heterogeneity of treatment effect within RCTs was not fully addressed, and single trials have conflicting data.[1]
5. As stated in the 2020 guidelines, fever after ROSC is associated with poor outcome in patients not treated with temperature control, but it has not been shown that prevention of fever is associated with improved outcomes. Given the lack of additional data in this area, treatment or prevention of fever beyond the initial temperature-control phase continues to be recommended as a reasonable approach.
6. Rewarming in the post–cardiac arrest period may occur during the initial phase of temperature control to a higher target temperature in patients who are spontaneously hypothermic. Rewarming also occurs when patients are transitioning to the controlled normothermia phase. Patients presenting with spontaneous hypothermia after ROSC may have more severe injury and be more susceptible to secondary injury with active rewarming. It is unclear whether passive uncontrolled rewarming (potentially at rates above 0.25°C–0.5°C per hour) is better or worse than slow, controlled rewarming. In the TTM and TTM2 trials, patients with temperatures between 30°C and 33°C assigned to hypothermic arms were actively rewarmed to 33°C, and those with temperatures of 30°C to 36°C who were assigned to higher temperature arms were allowed to passively rewarm to that goal; the rate of rewarming was not specified.[2,8] The HYPERION trial used active controlled rewarming to 37°C at 0.25°C to 0.5°C per hour for patients who were spontaneously below target at randomization.[1] Passive versus controlled rewarming after temperature control has been studied, and controlled warming may be beneficial.[9,10] A pilot study failed to demonstrate differences in interleukin-6 levels and neurological outcome with rewarming rates after controlled hypothermia between 0.25°C and 0.5°C per hour.[11] We conservatively recommend rewarming to the prespecified target temperature at 0.25°C to 0.5°C per hour, regardless of the phase of temperature control. In the setting of severe trauma and active bleeding, faster rewarming may be appropriate. Patients with profound bradycardia or other electrical cardiac instability arriving with severe hypothermia may warrant faster rewarming until instability improves.
7. According to animal studies, time to achieve target temperature may have an important impact on outcome. It has been difficult to extrapolate these data to humans. A recent randomized trial measured the impact of prehospital transnasal evaporative intra-arrest cooling versus postadmission targeted temperature management on survival in 671 patients. The effectiveness of obtaining a core temperature <34°C was higher in the intervention group; however, the primary outcome of Cerebral Performance Category 1 to 2 at 90 days was not different between the 2 groups (16.6% in the treatment group and 13.5% in the control group).[12]
8. Prehospital cooling with rapid infusion of cold fluids has been evaluated as a method to improve time to target temperature in patients with shockable rhythm, and there was no clear benefit to this approach. This may be due to fewer personnel, reduced monitoring capabilities, and potentially unsecured airways.[13] This recommendation has remained unchanged since the 2015 guidelines statement.

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## SEIZURE AND OTHER EPILEPTIFORM ACTIVITY

| Diagnosis and Management of Seizure and Other Epileptiform Activity | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| 1 | C-LD | 1. We recommend treatment of clinically apparent seizures in adult survivors of cardiac arrest. |
| 1 | C-LD | 2. We recommend promptly performing and interpreting electroencephalography (EEG) for the diagnosis of seizures in patients who do not follow commands after ROSC. |
| 2a | C-LD | 3. Monitoring EEG repeatedly or continuously is reasonable for patients who do not follow commands after ROSC. |
| 2a | B-R | 4. Treatment of nonconvulsive seizures (diagnosed by EEG only) is reasonable in adult survivors of cardiac arrest. |
| 2b | C-EO | 5. A therapeutic trial of a nonsedating antiseizure medication may be reasonable in adult survivors of cardiac arrest with EEG patterns on the ictal-interictal continuum. |
| 2b | C-LD | 6. The same antiseizure medications used for treatment of seizures caused by other etiologies may be considered for seizures detected after cardiac arrest. |
| 3: No Benefit | B-R | 7. Seizure prophylaxis in adult survivors of cardiac arrest is not recommended. |

**Table 2. American Clinical Neurophysiology Society Criteria for Electrographic Seizures, Status Epilepticus, and Ictal-Interictal Continuum[1]**

| Hyperexcitable phenomenon | Diagnostic criteria |
|---|---|
| Electrographic seizure | 1. Epileptiform discharges averaging >2.5 Hz for ≥10 s*<br>or<br>2. Any pattern with definite evolution† lasting ≥10 s* |
| Electrographic status epilepticus | 1. Any pattern qualifying for electrographic seizure for ≥10 continuous min‡ or for a total duration of ≥20% of any 60-min‡ period of monitoring |
| Ictal-interictal continuum (ie, possible electrographic status epilepticus. If an unequivocal electrographic and clinical response seen after therapeutic trial=electroclinical status epilepticus) | 1. Any periodic discharges or spike/sharp-wave pattern averaging >1.0 and ≤2.5 Hz over 10 s<br>or<br>2. Any periodic discharges or spike/sharp-wave pattern averaging ≥0.5 Hz and ≤1.0 Hz over 10 s with either a plus modifier§ or fluctuation‖<br>or<br>3. Any lateralized rhythmic delta activity averaging >1 Hz over 10 s with either a plus modifier§ or fluctuation‖ |

*The minimum duration of 10 seconds does not apply if a consistent clinical correlate is in lockstep to the electrographic pattern (ie, electroclinical seizure).

†Evolution: at least 2 unequivocal, sequential changes in frequency, morphology, or location.

‡The minimum duration for bilateral tonic-clonic motor activity is 5 continuous minutes (ie, electroclinical convulsive status epilepticus).

§Plus modifier: additional feature that renders the pattern more ictal in appearance (+F [superimposed fast activity], +R [superimposed rhythmic activity], +S [superimposed sharp waves or spikes, or sharply contoured]).

‖Fluctuation: ≥3 changes, all within 1 minute in frequency, morphology, or location but not qualifying as evolution.

Data from Hirsch et al.[7]

## Synopsis

Seizures occur in 10% to 35% of patients with cardiac arrest who do not follow commands after ROSC.[1–6] Postanoxic hyperexcitability can manifest as a wide range of electroclinical findings, from seizures with overt clinical signs such as convulsions to EEG patterns with or without impairment of consciousness that may or may not reach strict thresholds to meet criteria for status epilepticus (Table 2).[7] Neuronal hyperexcitability may exacerbate mismatches between neuronal bioenergetic supply and demand, thereby contributing to secondary brain injury.[8] Indications for and intensity of antiseizure medications vary in clinical practice and across studies according to the specific manifestation of postanoxic hyperexcitability. Although the occurrence of postanoxic status epilepticus has been associated with a poor outcome in observational studies,[2,9,10] reports of survival with functional independence in some subgroups have accumulated over the past decade.[3,6,11,12] For example, cardiac arrest survivors who have continuous cortical background activity and those who develop epileptiform abnormalities >24 hours after ROSC are more likely to recover.[13] Marked heterogeneity in the definitions of status epilepticus used across studies challenges interpretation of available data.

## Recommendation-Specific Supportive Text

1. A 2020 ILCOR systematic review[14] and our updated search identified no controlled studies comparing treatment of clinically apparent seizures with no treatment in adult cardiac arrest patients. Despite the lack of high-level evidence, untreated clinically apparent seizure activity is thought to be potentially harmful to the brain; therefore, treatment of seizures is recommended in other settings[15] and is prudent after cardiac arrest. Myoclonus is a particularly common clinical manifestation of hypoxic-ischemic brain injury, identified in ≈20% of cardiac arrest survivors.[5,16] Myoclonus may occur in lockstep with epileptiform abnormalities such as burst suppression with identical bursts, develop without an EEG correlate (ie, subcortical myoclonus), or develop in patients with continuous cortical background activity.[17] These are important distinctions because some patients (eg, those with subcortical myoclonus) may not warrant aggressive treatment with antiseizure medications if the myoclonus is not interfering with mechanical ventilation.
2. EEG in post–cardiac arrest patients who are unable to follow commands can inform neurological prognostication, detect nonconvulsive seizures and status epilepticus, and distinguish among different types of myoclonus.[11,17] The role of EEG in neuroprognostication is not included in this focused update. There is no direct evidence that EEG used to detect nonconvulsive seizures improves outcomes. This recommendation is informed by the high prevalence of nonconvulsive seizures and other epileptiform activity in postarrest patients.[5] Whether treatment of nonconvulsive seizures affects outcome in this setting remains uncertain. An ILCOR systematic review done for 2020 did not specifically address the timing and method of obtaining EEGs in post–cardiac arrest patients who remain unresponsive.
3. There are several approaches to EEG monitoring that vary in duration (ie, from short 20- to 40-minute recordings to continuous monitoring for several days) and electrode arrangement (ie, from full 21 electrodes to simplified 6- to 10-electrode montages). Myoclonus, seizures, and epileptiform abnormalities may occur immediately after ROSC or emerge several days after initial resuscitation.[13,18] Continuous EEG, although costly and labor intensive, may increase sensitivity to detect epileptiform activity, including seizures and status epilepticus, after cardiac arrest compared with brief intermittent recordings[19,20] because of the episodic and unpredictable nature of these events. However, use of continuous EEG was not associated with survival or functional outcomes in observational cardiac arrest cohorts[20,21] or in the CERTA trial (Continuous EEG Randomized Trial in Adults), a multicenter pragmatic study in critically ill patients with impaired consciousness, of whom nearly one-third had been resuscitated from cardiac arrest.[22]
4. The clinical impact of aggressive suppression of EEG patterns meeting American Clinical Neurophysiology Society criteria for nonconvulsive seizures and status epilepticus (Table 2) may be different from other rhythmic or periodic patterns. The TELSTAR trial (Treatment of Electroencephalographic Status Epilepticus After Cardiopulmonary Resuscitation) is the first randomized clinical trial of protocolized tiered treatment targeting suppression of EEG rhythmic or periodic patterns in adults who had a Glasgow Coma Scale score ≤8 after ROSC versus standard of care in which antiseizure regimen was left to the discretion of the treatment team.[23] This trial was published after the 2020 guidelines and is therefore new to this statement. The trial randomized 172 subjects whose baseline characteristics were comparable between allocation arms. Rates of poor neurological outcome (Cerebral Performance Category 3–5) between treatment arms did not differ at 3 months (90% in intervention versus 92% in control; difference, 2 percentage points [95% CI, −7 to 11]; $P$=0.68). Although the trial was not powered for subgroup analyses, patients with unequivocal electrographic seizures (ie, frequencies reaching at least 2.5 Hz) or evolving patterns and those with nongeneralized periodic discharges (even at 0.5–2.5 Hz) were noted to fare better with protocolized, tiered antiseizure treatment.
5. Anoxic pathogenesis of seizures and status epilepticus is frequently an exclusion criterion in randomized clinical trials[24,25]; consequently, therapeutic algorithms are largely extrapolated from other settings, including guidelines for generalized convulsive status epilepticus. The 2020 CoSTR recommended that seizures be treated when diagnosed in post–cardiac arrest patients.[14] No specific agents were recommended.
6. The American Clinical Neurophysiology Society defines the ictal-interictal continuum as rhythmic or periodic patterns that are considered to be possible seizure or status epilepticus even without fulfilling strict electrographic criteria (ie, >2.5 Hz or any pattern with definite evolution and lasting ≥10 seconds for seizures or ≥10 minutes for status epilepticus).[7] Patients with patterns on the ictal-interictal continuum who exhibit

positive electrographic and clinical response to a therapeutic trial with a loading dose of a parenteral nonsedating antiseizure medication (ie, not benzodiazepine) are considered to have electroclinical status epilepticus; thus, therapeutic trials of antiseizure medication may be considered regardless of cardiac arrest being the cause of the seizures.[7]

7. Primary seizure prophylaxis did not improve outcomes after cardiac arrest in 2 prospective RCTs[26,27] and 1 nonrandomized prospective clinical trial with historical control subjects.[28] Primary prophylaxis was also not effective in preventing subsequent seizures in the post–cardiac arrest period.[26–28] Of note, these studies examine medications not commonly deployed as first-line agents in seizure treatment in current clinical care.

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# ORGAN DONATION AFTER CARDIAC ARREST

| Organ Donation After Cardiac Arrest | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| 1 | B-NR | 1. Organ donation should be considered in all patients resuscitated from cardiac arrest who meet neurological criteria for death. |
| 1 | B-NR | 2. Organ donation should be considered in all patients resuscitated from cardiac arrest before planned withdrawal of life-sustaining therapies. |
| 1 | C-EO | 3. Decisions about organ donation should follow local legal and regulatory requirements. |
| 1 | C-EO | 4. Organ donation is an important outcome that should be considered in the development and evaluation of systems of care. |

## Synopsis

Organ transplantation wait times in the United States are lengthening as increases in patients in need of transplant outpace available organs.[1] Thousands die annually waiting for organ transplantation.[1] Patients with cardiac arrest make up an important growing pool of potential organ donors[2–4] because cardiac arrest is common and a substantial proportion of those who cannot recover from cardiac arrest are still able to become organ donors.[2,5–9] However, organ donation is rarely reported as an outcome in cardiac arrest clinical trials or as a metric in large registry data.

Deceased organ donation may occur after death is determined by neurological criteria (donation after brain death) or circulatory criteria (donation after circulatory death [DCD]). After sudden cardiac arrest, DCD can be pursued in patients with ROSC after planned withdrawal of life-sustaining therapies and the transition to comfort-oriented care, called controlled DCD, or in patients who fail to achieve ROSC after unsuccessful resuscitation, called uncontrolled DCD. Uncontrolled DCD has unique logistic, ethical, and legal requirements—factors that hinder its widespread application in many settings.

## Recommendation-Specific Supportive Text

A 2015 ILCOR CoSTR scientific statement, updated in 2023, is the basis for these recommendations.[10,11]

1, 2. Numerous observational studies demonstrate that allograft function and recipient outcomes are similar when transplanted organs are recovered from patients with cardiac arrest compared with other deceased donors[12–18]; this holds true for donation after brain death and controlled DCD.

3. Laws and regulations governing the determination of death and organ donation vary between countries.[19,20] Clinicians must follow local requirements.

4. A 2023 ILCOR CoSTR scientific statement focused on the importance of increasing organ availability after cardiac arrest.[11] It recognizes organ donation as an important outcome of cardiac arrest. Organ donation after cardiac arrest directly benefits recipient patients.

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## DIVERSITY, EQUITY, AND INCLUSION

| Diversity, Equity, and Inclusion | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **2a** | **C-EO** | 1. It is reasonable for researchers studying cardiac arrest to develop and implement methods to promote recruitment and representation of participants from diverse backgrounds. |
| **2a** | **C-EO** | 2. It is beneficial for researchers studying cardiac arrest to collect and report complete demographic data. |

### Synopsis

Patients with cardiac arrest deserve equitable care through each step of the Chain of Survival, regardless of their demographic characteristics and social determinants of health. The Chain of Survival framework recognizes the dependence of each link to the ultimate survival and quality of life for patients with cardiac arrest. Current research suggests that there are inequities in this chain.

Cardiac arrest prevalence, characteristics, and treatments differ by sex and between racial groups.[1–4] Residents of predominantly Black and Hispanic neighborhoods are less likely to receive bystander CPR and less likely to survive to hospital discharge.[5–8] Female patients are less likely to receive bystander CPR and automated external defibrillator use[9,10] and to receive guideline-recommended prehospital interventions.[3,11] After cardiac arrest, female patients and people of color are less likely to receive cardiac catheterization and targeted temperature management, less likely to survive, and less likely to have good neurological recovery.[2,4,12,13] Last, female patients are more likely to receive a "do not resuscitate" order within 24 hours of admission[4,12,14] and withdrawal of life-sustaining treatments despite comparable rates of neurodiagnostic testing.[15] Further quantification of these disparities and elucidation of their underlying causes are critical to developing interventions that will eliminate them.

An important part of research translation is understanding who is participating in research and how the composition of the study population affects the generalizability of the study. Historically, people of color and women have been underrepresented in clinical trials. Although this may stem from trial site location or study design and not from systematic exclusion, it still impairs result generalizability and is modifiable with intentional design and implementation. To characterize the frequency at which sex, gender, race, and ethnicity are currently reported and analyzed in post–resuscitation care research, we conducted a structured review of the major randomized clinical trials published from 2016 through 2022, studying 2 important cornerstones of post–cardiac arrest care: targeted temperature management and coronary angiography timing. We found 14 randomized clinical trials meeting our criteria and assessed their inclusion, analysis, and reporting of sex, gender, race, and ethnicity.[16–29] Sex or gender was reported in every trial. In the 2 trials in which gender was reported instead of sex, the terms were used interchangeably, and biological sex was inaccurately reported as gender. Nine studies included sex in their analysis, either as a subgroup analysis or as an independent variable in multivariable analyses. Race was reported in 2 of the trials, and ethnicity was reported in none. None of the studies performed subgroup or multivariable analyses by race or ethnicity to characterize potential disparities.

Although we focused on race, ethnicity, sex, and gender diversity in this statement, equity and inclusion encompass a growing number of issues for the scientific community to consider. Globally, it is also important to acknowledge the interaction between these factors and social determinants of health. Social determinants of health include conditions in the environments in which people are born, live, learn, work, and play that affect a wide range of health risks and outcomes. These factors contribute to health disparities and inequities. The extent to which social determinants of health drive disparities in racial and ethnic groups should be carefully considered in the analysis and interpretation of research done in this area to avoid misclassification.[30–32]

### Recommendation-Specific Supportive Text

1. The US Food and Drug Administration's "Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry" recommends that clinical trials for new therapies recruit a sample representative of the population in which the therapy will be used.[33] To improve inclusion of currently underrepresented populations, diversity, equity, and inclusion need to be considered early in trial development. Community engagement in all stages of cardiac arrest research is a reasonable approach to improving representation.[34] Because centers can enroll only patients cared for in their institutions, intentional selection of sites in diverse neighborhoods to ensure recruitment of a representative sample is a reasonable approach. Ideally,

researchers should perform continuous evaluation of enrollment demographics throughout the study. The scientific community should prioritize the difficult work that goes into ensuring a representative population as part of performing high-quality and generalizable research. The responsibility for this task falls not only on investigators but also on funding agencies and publishers of the data.

2. To quantify cardiac arrest disparities, ensure enrollment of diverse populations, and develop targeted interventions, researchers need to capture sufficient data to accurately describe patient demographics, including but not limited to gender, sex, race, and ethnicity. As described in the Synopsis of this section, the most recent major trials dictating the landscape of cardiac arrest care contained sparse information on gender, race, and ethnicity. Researchers should make a concerted effort to capture these data elements. One important consideration related to the reporting of race, ethnicity, sex, and gender in cardiac arrest research is the assignment of these classifications. When feasible, patients (or surrogates) should self-identify their race, ethnicity, and gender. Self-identification not only improves the accuracy of assignment but also ensures a patient-centered approach to research.[35]

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## ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This focused update was approved by the American Heart Association Science Advisory and Coordinating Committee on August 22, 2023, and the American Heart Association Executive Committee on October 25, 2023. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com

The American Heart Association requests that this document be cited as follows: Perman SM, Elmer J, Maciel CB, Uzendu A, May T, Mumma BE, Bartos JA, Rodriguez AJ, Kurz MC, Panchal AR, Rittenberger JC; on behalf of the American Heart Association. 2023 American Heart Association focused update on adult advanced cardiovascular life support: an update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2024;149:e254–e273. doi: 10.1161/CIR.0000000000001194

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## Disclosures

### Appendix 1. Writing Group Disclosures

| Writing group member | Employment | Research grant | Other research support | Speakers' bureau/ honoraria | Expert witness | Ownership interest | Consultant/ advisory board | Other |
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| Jason A. Bartos | University of Minnesota | NIH (grant funding: LV physiology on ECMO)†; NIH (grant funding: artificial intelligence)†; Helmsley charitable trust (grant: Minnesota AED)†; Helmsley charitable trust (grant: ECPR in the Twin Cities of MN)† | None | None | None | None | None | None |
| Jonathan Elmer | University of Pittsburgh | None | None | None | None | None | None | None |
| Michael C. Kurz | University of Alabama at Birmingham | NIH (multiple NIH grants to study cardiac arrest that go directly to UAB)† | None | None | None | None | None | None |
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(*Continued*)

**Appendix 1. Writing Group Disclosures Continued**

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| Bryn E. Mumma | University of California Davis | None | None | None | None | None | Roche* | None |
| Ashish R. Panchal | The Ohio State University Wexner Medical Center | None | None | None | None | None | None | None |
| Amber J. Rodriguez | American Heart Association | None | None | None | None | None | None | None |
| Anezi Uzendu | St. Luke's Mid America Heart Institute | None | None | None | None | None | None | None |

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

**Appendix 2. Reviewer Disclosures**

| Reviewer | Employment | Research grant | Other research support | Speakers' bureau/ honoraria | Expert witness | Ownership interest | Consultant/ advisory board | Other |
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| Joshua R. Lupton | Oregon Health & Science University | Society for Academic Emergency Medicine (research training grant related to cardiac arrest)*; Zoll Foundation (completed grant related to cardiac arrest care)* | None | None | None | None | None | None |

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.