

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

Sarah M. Perman, MD, MSCE, FAHA, Vice Chair; Jonathan Elmer, MD, MS; Carolina B. Maciel, MD, MSCR; Anezi Uzendu, MD; Teresa May, DO; Bryn E. Mumma, MD, MAS; Jason A. Bartos, MD, PhD; Amber J. Rodriguez, PhD; Michael C. Kurz, MD, MS, FAHA; Ashish R. Panchal, MD, PhD; Jon C. Rittenberger, MD, MS, Chair; on behalf of the American Heart Association

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.

© 2023 American Heart Association, Inc.

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

- 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.
- 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.
- 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 De-

velopment” 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	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) Benefit >>> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none">Is recommendedIs indicated/useful/effective/beneficialShould be performed/administered/otherComparative-Effectiveness Phrases†:<ul style="list-style-type: none">Treatment/strategy A is recommended/indicated in preference to treatment BTreatment A should be chosen over treatment B	LEVEL A <ul style="list-style-type: none">High-quality evidence‡ from more than 1 RCTMeta-analyses of high-quality RCTsOne or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) Benefit >> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none">Is reasonableCan be useful/effective/beneficialComparative-Effectiveness Phrases†:<ul style="list-style-type: none">Treatment/strategy A is probably recommended/indicated in preference to treatment BIt is reasonable to choose treatment A over treatment B	LEVEL B-R (Randomized) <ul style="list-style-type: none">Moderate-quality evidence‡ from 1 or more RCTsMeta-analyses of moderate-quality RCTs
CLASS 2b (WEAK) Benefit ≥ Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none">May/might be reasonableMay/might be consideredUsefulness/effectiveness is unknown/unclear/uncertain or not well-established	LEVEL B-NR (Nonrandomized) <ul style="list-style-type: none">Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studiesMeta-analyses of such studies
CLASS 3: No Benefit (MODERATE) Benefit = Risk (Generally, LOE A or B use only) Suggested phrases for writing recommendations: <ul style="list-style-type: none">Is not recommendedIs not indicated/useful/effective/beneficialShould not be performed/administered/other	LEVEL C-LD (Limited Data) <ul style="list-style-type: none">Randomized or nonrandomized observational or registry studies with limitations of design or executionMeta-analyses of such studiesPhysiological or mechanistic studies in human subjects
Class 3: Harm (STRONG) Risk > Benefit Suggested phrases for writing recommendations: <ul style="list-style-type: none">Potentially harmfulCauses harmAssociated with excess morbidity/mortalityShould not be performed/administered/other	LEVEL C-EO (Expert Opinion) <ul style="list-style-type: none">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

REFERENCES

1. Magid DJ, Aziz K, Cheng A, Hazinski MF, Hoover AV, Mahgoub M, Panchal AR, Sasson C, Topjian AA, Rodriguez AJ, et al. Part 2: evidence evaluation and guidelines development: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(suppl 2):S358–S365. doi: 10.1161/CIR.0000000000000898

2. Levine GN, O’Gara PT, Beckman JA, Al-Khatib SM, Birtcher KK, Cigarroa JE, de Las Fuentes L, Deswal A, Fleisher LA, Gentile F, et al. Recent innovations, modifications, and evolution of ACC/AHA clinical practice guidelines: an update for our constituencies: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Circulation*. 2020;141:e34]. *Circulation*. 2019;139:e879–e886. doi: 10.1161/CIR.0000000000000651

3. Panchal AR, Bartos JA, Cabanas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, et al; on behalf of the Adult Basic and Advanced Life Support Writing Group. Part 3: adult basic and advanced life support: 2020 American Heart Association Guidelines for car-

diopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916

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}

CLINICAL STATEMENTS AND GUIDELINES

Downloaded from <http://ahajournals.org> by on April 26, 2024

Recommendation-Specific Supportive Text

- 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.
- 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.
- 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
- 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}
- 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

- 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}

REFERENCES

- Jacobs IG, Finn JC, Jelinek GA, Oxer HF, Thompson PL. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation*. 2011;82:1138–1143. doi: 10.1016/j.resuscitation.2011.06.029
- Perkins GD, Ji C, Deakin CD, Quinn T, Nolan JP, Scamperin C, Regan S, Long J, Slowther A, Pocock H, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. *N Engl J Med*. 2018;379:711–721. doi: 10.1056/NEJMoa1806842
- Holmberg MJ, Issa MS, Moskowitz A, Morley P, Welsford M, Neumar RW, Paiva EF, Coker A, Hansen CK, Andersen LW, et al. Vasopressors during adult cardiac arrest: a systematic review and meta-analysis. *Resuscitation*. 2019;139:106–121. doi: 10.1016/j.resuscitation.2019.04.008
- Aves T, Chopra A, Patel M, Lin S. Epinephrine for out-of-hospital cardiac arrest: an updated systematic review and meta-analysis. *Crit Care Med*. 2020;48:225–229. doi: 10.1097/CCM.0000000000004130
- Finn J, Jacobs I, Williams TA, Gates S, Perkins GD. Adrenaline and vasopressin for cardiac arrest. *Cochrane Database Syst Rev*. 2019;1:CD003179. doi: 10.1002/14651858.CD003179.pub2
- Abdelazeem B, Awad AK, Manasrah N, Elbadawy MA, Ahmad S, Savarapu P, Abbas KS, Kunadi A. The effect of vasopressin and methylprednisolone on return of spontaneous circulation in patients with in-hospital cardiac arrest: a systematic review and meta-analysis of randomized controlled trials. *Am J Cardiovasc Drugs*. 2022;22:523–533. doi: 10.1007/s40256-022-00522-z
- Brown CG, Martin DR, Pepe PE, Stueven H, Cummins RO, Gonzalez E, Jastremski M. A comparison of standard-dose and high-dose epinephrine in cardiac arrest outside the hospital: the Multicenter High-Dose Epinephrine Study Group. *N Engl J Med*. 1992;327:1051–1055. doi: 10.1056/NEJM199210083271503
- Choux C, Gueugniaud PY, Barbieux A, Pham E, Lae C, Dubien PY, Petit P. Standard doses versus repeated high doses of epinephrine in cardiac arrest outside the hospital. *Resuscitation*. 1995;29:3–9. doi: 10.1016/0300-9572(94)00810-3
- Gueugniaud PY, Mols P, Goldstein P, Pham E, Dubien PY, Deweerdt C, Vergnion M, Petit P, Carli P. A comparison of repeated high doses and repeated standard doses of epinephrine for cardiac arrest outside the hospital: European Epinephrine Study Group. *N Engl J Med*. 1998;339:1595–1601. doi: 10.1056/NEJM199811263392204
- Lindner KH, Ahnefeld FW, Prengel AW. Comparison of standard and high-dose adrenaline in the resuscitation of asystole and electromechanical dissociation. *Acta Anaesthesiol Scand*. 1991;35:253–256. doi: 10.1111/j.1399-6576.1991.tb03283.x
- Lipman J, Wilson W, Kobilski S, Scribante J, Lee C, Kraus P, Cooper J, Barr J, Moyes D. High-dose adrenaline in adult in-hospital asystolic cardiopulmonary resuscitation: a double-blind randomised trial. *Anaesth Intensive Care*. 1993;21:192–196. doi: 10.1177/0310057X9302100210
- Sherman BW, Munger MA, Foulke GE, Rutherford WF, Panacek EA. High-dose versus standard-dose epinephrine treatment of cardiac arrest after failure of standard therapy. *Pharmacotherapy*. 1997;17:242–247.
- Stiell IG, Hebert PC, Weitzman BN, Wells GA, Raman S, Stark RM, Higginson LA, Ahuja J, Dickinson GE. High-dose epinephrine in adult cardiac arrest. *N Engl J Med*. 1992;327:1045–1050. doi: 10.1056/NEJM199210083271502
- Callahan M, Madsen CD, Barton CW, Saunders CE, Pointer J. A randomized clinical trial of high-dose epinephrine and norepinephrine vs standard-dose epinephrine in prehospital cardiac arrest. *JAMA*. 1992;268:2667–2672.

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

- Administration of amiodarone or lidocaine to patients with OHCA was last formally reviewed in 2018² 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.

- 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.
- 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
- 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
- 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

REFERENCES

1. Panchal AR, Bartos JA, Cabanas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, 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(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916

2. Panchal AR, Berg KM, Kudenchuk PJ, Del Rios M, Hirsch KG, Link MS, Kurz MC, Chan PS, Cabanas JG, Morley PT, et al. 2018 American Heart Association focused update on advanced cardiovascular life support use of antiarrhythmic drugs during and immediately after cardiac arrest: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2018;138:e740–e749. doi: 10.1161/CIR.0000000000000613

3. Kudenchuk PJ, Brown SP, Daya M, Rea T, Nichol G, Morrison LJ, Leroux B, Vaillancourt C, Wittwer L, Callaway CW, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med*. 2016;374:1711–1722. doi: 10.1056/NEJMoa1514204

4. Chowdhury A, Fernandes B, Melhuish TM, White LD. Antiarrhythmics in cardiac arrest: a systematic review and meta-analysis. *Heart Lung Circ*. 2018;27:280–290. doi: 10.1016/j.hlc.2017.07.004

5. Batul SA, Gopinathannair R. Intravenous sotalol: reintroducing a forgotten agent to the electrophysiology therapeutic arsenal. *J Atr Fibrillation*. 2017;9:1499. doi: 10.4022/jafib.1499

6. Markel DT, Gold LS, Allen J, Fahrenbruch CE, Rea TD, Eisenberg MS, Kudenchuk PJ. Procainamide and survival in ventricular fibrillation out-of-hospital cardiac arrest. *Acad Emerg Med*. 2010;17:617–623. doi: 10.1111/j.1553-2712.2010.00763.x

7. Tsai MS, Chuang PY, Yu PH, Huang CH, Tang CH, Chang WT, Chen WJ. Glucocorticoid use during cardiopulmonary resuscitation may be beneficial for cardiac arrest. *Int J Cardiol*. 2016;222:629–635.

8. Tsai MS, Huang CH, Chang WT, Chen WJ, Hsu CY, Hsieh CC, Yang CW, Chiang WC, Ma MH, Chen SC. The effect of hydrocortisone on the outcome of out-of-hospital cardiac arrest patients: a pilot study. *Am J Emerg Med*. 2007;25:318–325.

9. Kette F, Ghuman J, Parr M. Calcium administration during cardiac arrest: a systematic review. *Eur J Emerg Med*. 2013;20:72–78. doi: 10.1097/MEJ.0b013e328358e336

10. Vallentin MF, Granfeldt A, Meilandt C, Povlsen AL, Sindberg B, Holmberg MJ, Iversen BN, Maerkedahl R, Mortensen LR, Nyboe R, et al. Effect of intravenous or intraosseous calcium vs saline on return of spontaneous circulation in adults with out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2021;326:2268–2276. doi: 10.1001/jama.2021.20929

11. Vukmir RB, Katz L; Sodium Bicarbonate Study Group. Sodium bicarbonate improves outcome in prolonged prehospital cardiac arrest. *Am J Emerg Med*. 2006;24:156–161. doi: 10.1016/j.ajem.2005.08.016

12. Ahn S, Kim YJ, Sohn CH, Seo DW, Lim KS, Donnino MW, Kim WY. Sodium bicarbonate on severe metabolic acidosis during prolonged cardiopulmonary resuscitation: a double-blind, randomized, placebo-controlled pilot study. *J Thorac Dis*. 2018;10:2295–2302. doi: 10.21037/jtd.2018.03.124

13. Kawano T, Grunau B, Scheuermeyer FX, Gibo K, Dick W, Fordyce CB, Dorian P, Stenstrom R, Straight R, Christenson J. Prehospital sodium bicarbonate use could worsen long term survival with favorable neurological recovery among patients with out-of-

hospital cardiac arrest. *Resuscitation*. 2017;119:63–69. doi: 10.1016/j.resuscitation.2017.08.008

14. Fatovich DM, Prentice DA, Dobb GJ. Magnesium in cardiac arrest (the MAGIC trial). *Resuscitation*. 1997;35:237–241. doi: 10.1016/s0300-9572(97)00062-2

15. Allegra J, Lavery R, Cody R, Birnbaum G, Brennan J, Hartman A, Horowitz M, Nashed A, Yablonski M. Magnesium sulfate in the treatment of refractory ventricular fibrillation in the prehospital setting. *Resuscitation*. 2001;49:245–249. doi: 10.1016/s0300-9572(00)00375-0

16. Hassan TB, Jagger C, Barnett DB. A randomised trial to investigate the efficacy of magnesium sulphate for refractory ventricular fibrillation. *Emerg Med J*. 2002;19:57–62. doi: 10.1136/emj.19.1.57

17. Thel MC, Armstrong AL, McNulty SE, Califf RM, O'Connor CM. Randomised trial of magnesium in in-hospital cardiac arrest: Duke Internal Medicine Housestaff. *Lancet*. 1997;350:1272–1276. doi: 10.1016/s0140-6736(97)05048-4

18. Manz M, Jung W, Luderitz B. Effect of magnesium on sustained ventricular tachycardia [in German]. *Herz*. 1997;22(suppl 1):51–55. doi: 10.1007/BF03042655

EXTRACORPOREAL CPR

ECPR		
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 trial⁹ (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 Trial¹⁰ 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.

REFERENCES

1. Panchal AR, Bartos JA, Cabanas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, 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(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916

2. Yannopoulos D, Bartos JA, Martin C, Raveendran G, Missov E, Conterato M, Frascone RJ, Trembley A, Sippell K, John R, et al. Minnesota Resuscitation Consortium's advanced perfusion and reperfusion cardiac life support strategy for out-of-hospital refractory ventricular fibrillation. *J Am Heart Assoc*. 2016;5:e003732. doi: 10.1161/JAHA.116.003732

3. Bartos JA, Carlson K, Carlson C, Raveendran G, John R, Aufderheide TP, Yannopoulos D. Surviving refractory out-of-hospital ventricular fibrillation cardiac arrest: critical care and extracorporeal membrane oxygenation management. *Resuscitation*. 2018;132:47–55. doi: 10.1016/j.resuscitation.2018.08.030

4. Bartos JA, Grunau B, Carlson C, Duval S, Ripeckij A, Kalra R, Raveendran G, John R, Conterato M, Frascone RJ, et al. Improved survival with extracorporeal cardiopulmonary resuscitation despite progressive metabolic derangement associated with prolonged resuscitation. *Circulation*. 2020;141:877–886. doi: 10.1161/CIRCULATIONAHA.119.042173

5. Kim SJ, Kim HJ, Lee HY, Ahn HS, Lee SW. Comparing extracorporeal cardiopulmonary resuscitation with conventional cardiopulmonary resuscitation: a meta-analysis. *Resuscitation*. 2016;103:106–116. doi: 10.1016/j.resuscitation.2016.01.019

6. Lamhaut L, Hutin A, Puymirat E, Jouan J, Raphalen JH, Jouffroy R, Jaffry M, Dagron C, An K, Dumas F, et al. A pre-hospital extracorporeal cardiopulmonary resuscitation (ECPR) strategy for treatment of refractory out hospital cardiac arrest: an observational study and propensity analysis. *Resuscitation*. 2017;117:109–117. doi: 10.1016/j.resuscitation.2017.04.014

7. Stub D, Bernard S, Pellegrino V, Smith K, Walker T, Sheldrake J, Hockings L, Shaw J, Duffy SJ, Burrell A, et al. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial). *Resuscitation*. 2015;86:88–94. doi: 10.1016/j.resuscitation.2014.09.010

8. Sakamoto T, Morimura N, Nagao K, Asai Y, Yokota H, Nara S, Hase M, Tahara Y, Atsumi T; SAVE-J Study Group. Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with out-of-hospital cardiac arrest: a prospective observational study. *Resuscitation*. 2014;85:762–768. doi: 10.1016/j.resuscitation.2014.01.031

9. Yannopoulos D, Bartos J, Raveendran G, Walser E, Connett J, Murray TA, Collins G, Zhang L, Kalra R, Kosmopoulos M, et al. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. *Lancet*. 2020;396:1807–1816. doi: 10.1016/S0140-6736(20)32338-2

10. Belohlavek J, Smalcova J, Rob D, Franek O, Smid O, Pokorna M, Horak J, Mrazek V, Kovarnik T, Zemanek D, et al. Effect of intra-arrest transport, extracorporeal cardiopulmonary resuscitation, and immediate invasive assessment and treatment on functional neurologic outcome in refractory out-of-hospital cardiac arrest: a randomized clinical Trial. *JAMA*. 2022;327:737–747. doi: 10.1001/jama.2022.1025

PERCUTANEOUS CORONARY INTERVENTION AFTER CARDIAC ARREST

Percutaneous Coronary Intervention After Cardiac Arrest		
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 rhythm¹³; 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.

REFERENCES

1. Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JF, Carli P. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med*. 1997;336:1629–1633. doi: 10.1056/NEJM199706053362302

2. Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, Empana JP, Carli P, Mira JP, Jouven X, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac Arrest) registry. *Circ Cardiovasc Interv*. 2010;3:200–207. doi: 10.1161/CIRCINTERVENTIONS.109.913665

3. Davies MJ. Anatomic features in victims of sudden coronary death coronary artery pathology. *Circulation*. 1992;85(suppl):119–124.

4. Yannopoulos D, Bartos JA, Aufderheide TP, Callaway CW, Deo R, Garcia S, Halperin HR, Kern KB, Kudenchuk PJ, Neumar RW, et al; on behalf of the American Heart Association Emergency Cardiovascular Care Committee. 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:e530–e552. doi: 10.1161/CIR.0000000000000630

5. Kern KB, Lotun K, Patel N, Mooney MR, Hollenbeck RD, McPherson JA, McMullan PW, Unger B, Hsu CH, Seder DB, et al. Outcomes of comatose cardiac arrest survivors with and without ST-segment elevation myocardial infarction: importance of coronary angiography. *JACC Cardiovasc Interv*. 2015;8:1031–1040. doi: 10.1016/j.jcin.2015.02.021

6. Yannopoulos D, Bartos JA, Raveendran G, Conterato M, Frascione RJ, Trembley A, John R, Connett J, Benditt DG, Lurie KG, et al. Coronary artery disease in patients with out-of-hospital refractory ventricular fibrillation cardiac arrest. *J Am Coll Cardiol*. 2017;70:1109–1117. doi: 10.1016/j.jacc.2017.06.059

7. Dumas F, Bougouin W, Geri G, Lamhaut L, Rosencher J, Pene F, Chiche JD, Varenne O, Carli P, Jouven X, et al. Emergency percutaneous coronary intervention in post-cardiac arrest patients without ST-segment elevation pattern: insights from the PROCAT II Registry. *JACC Cardiovasc Interv*. 2016;9:1011–1018. doi: 10.1016/j.jcin.2016.02.001

8. Garcia S, Drexel T, Bekwelem W, Raveendran G, Caldwell E, Hodgson L, Wang Q, Adabag S, Mahoney B, Frascione R, 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:e002670. doi: 10.1161/JAHA.115.002670

9. Geri G, Dumas F, Bougouin W, Varenne O, Daviaud F, Pene F, Lamhaut L, Chiche JD, Spaulding C, Mira JP, 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:e002303. doi: 10.1161/CIRCINTERVENTIONS.114.002303

10. Zanuttini D, Armellini I, Nucifora G, Carchietti E, Trillo G, Spedicato L, Bernardi G, Proclemer A. Impact of emergency coronary angiography on in-hospital outcome of unconscious survivors after out-of-hospital cardiac arrest. *Am J Cardiol*. 2012;110:1723–1728. doi: 10.1016/j.amjcard.2012.08.006

11. Sideris G, Voicu S, Yannopoulos D, Dillinger JG, Adedji J, Deye N, Gueye P, Manzo-Silberman S, Malissin I, Logeart D, et al. Favourable 5-year postdischarge survival of comatose patients resuscitated from out-of-hospital cardiac arrest, managed with immediate coronary angiogram on admission. *Eur Heart J Acute Cardiovasc Care*. 2014;3:183–191. doi: 10.1177/2048872614523348

12. Panchal AR, Bartos JA, Cabanas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, 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(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916

13. Lemkes JS, Janssens GN, van der Hoeven NW, Jewbali LSD, Dubois EA, Meuwissen M, Rijpsma TA, Bosker HA, Blans MJ, Bleeker GB, et al. Coronary angiography after cardiac arrest without ST-segment elevation. *N Engl J Med*. 2019;380:1397–1407. doi: 10.1056/NEJMoa1816897

14. Desch S, Freund A, Akin I, Behnes M, Preusch MR, Zelniker TA, Skurk C, Landmesser U, Graf T, Eitel I, et al. Angiography after out-of-hospital cardiac arrest without ST-segment elevation. *N Engl J Med*. 2021;385:2544–2553. doi: 10.1056/NEJMoa2101909

15. Hauw-Berlemont C, Lamhaut L, Diehl JL, Andreotti C, Varenne O, Leroux P, Lascarrou JB, Guerin P, Loeb T, Roupie E, 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;7:700–707. doi: 10.1001/jamacardio.2022.1416

16. Kern KB, Radsel P, Jentzer JC, Seder DB, Lee KS, Lotun K, Janardhanan R, Stub D, Hsu CH, Noc M. 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;142:2002–2012. doi: 10.1161/CIRCULATIONAHA.120.049569

17. Bro-Jeppesen J, Kjaergaard J, Wanscher M, Pedersen F, Holmvang L, Lippert FK, Møller JE, Kober L, Hassager C. Emergency coronary angiography in comatose cardiac arrest patients: do real-life experiences support the guidelines? *Eur Heart J Acute Cardiovasc Care*. 2012;1:291–301. doi: 10.1177/2048872612465588

18. 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:e002321. doi: 10.1161/CIRCINTERVENTIONS.114.002321

19. Waldo SW, Armstrong EJ, Kulkarni A, Hoffmayer K, Kinlay S, Hsue P, Ganz P, McCabe JM. Comparison of clinical characteristics and outcomes of cardiac arrest survivors having versus not having coronary angiography. *Am J Cardiol*. 2013;111:1253–1258. doi: 10.1016/j.amjcard.2013.01.267

20. Hosmane VR, Mustafa NG, Reddy VK, Reese CL, DiSabatino A, Kolm P, Hopkins JT, Weintraub WS, Rahman E. Survival and neurologic recovery in patients with ST-segment elevation myocardial infarction resuscitated from cardiac arrest. *J Am Coll Cardiol*. 2009;53:409–415. doi: 10.1016/j.jacc.2008.08.076

21. Hollenbeck RD, McPherson JA, Mooney MR, Unger BT, Patel NC, McMullan PW Jr, Hsu CH, Seder DB, Kern KB. Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. *Resuscitation*. 2014;85:88–95. doi: 10.1016/j.resuscitation.2013.07.027

22. Khan MS, Shah SMM, Mubashir A, Khan AR, Fatima K, Schenone AL, Khosa F, Samady H, Menon V. 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. doi: 10.1016/j.resuscitation.2017.10.019

23. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in *Circulation*. 2014;130:e431–e432]. *Circulation*. 2014;130:2354–2394. doi: 10.1161/CIR.0000000000000133

24. Lee L, Bates ER, Pitt B, Walton JA, Laufer N, O'Neill WW. Percutaneous transluminal coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogenic shock. *Circulation*. 1988;78:1345–1351. doi: 10.1161/01.cir.78.6.1345

25. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock: SHOCK Investigators: Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. *N Engl J Med*. 1999;341:625–634. doi: 10.1056/NEJM199908263410901

TEMPERATURE CONTROL

Indications for Temperature Control		
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 Non-shockable 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 review⁴ supported the ILCOR CoSTR⁶ 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		
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.

REFERENCES

1. Lascarrou JB, Merdji H, Le Gouge A, Colin G, Grillet G, Girardie P, Coupez E, Dequin PF, Cariou A, Boulain T, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. *N Engl J Med*. 2019;381:2327–2337. doi: 10.1056/NEJMoa1906661
2. Dankiewicz J, Cronberg T, Lilja G, Jakobsen JC, Levin H, Ullen S, Rylander C, Wise MP, Oddo M, Cariou A, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. *N Engl J Med*. 2021;384:2283–2294. doi: 10.1056/NEJMoa2100591
3. Le May M, Osborne C, Russo J, So D, Chong AY, Dick A, Froeschl M, Glover C, Hibbert B, Marquis JF, et al. Effect of moderate vs mild therapeutic hypothermia on mortality and neurologic outcomes in comatose survivors of out-of-hospital cardiac arrest: the CAPITAL CHILL randomized clinical trial. *JAMA*. 2021;326:1494–1503. doi: 10.1001/jama.2021.15703
4. Granfeldt A, Holmberg MJ, Nolan JP, Soar J, Andersen LW; International Liaison Committee on Resuscitation Advanced Life Support Task Force. Targeted temperature management in adult cardiac arrest: systematic review and meta-analysis. *Resuscitation*. 2021;167:160–172. doi: 10.1016/j.resuscitation.2021.08.040
5. Panchal AR, Bartos JA, Cabanas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, 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(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916
6. Wyckoff MH, Greif R, Morley PT, Ng KC, Olasveengen TM, Singletary EM, Soar J, Cheng A, Drennan IR, Liley HG, et al. 2022 International Consensus on

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: summary from the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces. *Circulation*. 2022;146:e483–e557. doi: 10.1161/CIR.0000000000001095

7. Kirkegaard H, Soreide E, de Haas I, Pettila V, Taccone FS, Arus U, Storm C, Hassager C, Nielsen JF, Sorensen CA, et al. Targeted temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2017;318:341–350. doi: 10.1001/jama.2017.8978

8. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, Horn J, Hovdenes J, Kjaergaard J, Kuiper M, et al. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med*. 2013;369:2197–2206. doi: 10.1056/NEJMoa1310519

9. Bouwes A, Robillard LB, Binnekade JM, de Pont AC, Wieske L, Hartog AW, Schultz MJ, Horn J. The influence of rewarming after therapeutic hypothermia on outcome after cardiac arrest. *Resuscitation*. 2012;83:996–1000. doi: 10.1016/j.resuscitation.2012.04.006

10. Bisschops LL, Hoedemaekers CW, Mollnes TE, van der Hoeven JG. Rewarming after hypothermia after cardiac arrest shifts the inflammatory balance. *Crit Care Med*. 2012;40:1136–1142. doi: 10.1097/CCM.0b013e3182377050

11. Lascarrou JB, Guichard E, Reignier J, Le Gouge A, Pouplet C, Martin S, Lacherade JC, Colin G, After R. Impact of rewarming rate on interleukin-6 levels in patients with shockable cardiac arrest receiving targeted temperature management at 33 degrees C: the ISOCRATE pilot randomized controlled trial. *Crit Care*. 2021;25:434. doi: 10.1186/s13054-021-03842-9

12. Nordberg P, Taccone FS, Truhlar A, Forsberg S, Hollenberg J, Jonsson M, Cuny J, Goldstein P, Vermeersch N, Higuete A, et al. Effect of trans-nasal evaporative intra-arrest cooling on functional neurologic outcome in out-of-hospital cardiac arrest: the PRINCESS randomized clinical trial. *JAMA*. 2019;321:1677–1685. doi: 10.1001/jama.2019.4149

13. Kim F, Nichol G, Maynard C, Hallstrom A, Kudenchuk PJ, Rea T, Copass MK, Carlborn D, Deem S, Longstreth WT Jr, et al. Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: a randomized clinical trial. *JAMA*. 2014;311:45–52. doi: 10.1001/jama.2013.282173

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 non-sedating 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 Continuum¹

Hyperexcitable phenomenon	Diagnostic criteria
Electrographic seizure	1. Epileptiform discharges averaging >2.5 Hz for ≥10 s* or 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 or 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 or 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,^{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 review¹⁴ 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 settings¹⁵ and is prudent after cardiac arrest. Myoclonus is a particularly common clinical manifestation of hypoxic-ischemic brain injury, identified in $\approx 20\%$ 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 anti-seizure 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 nonseizure 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.

REFERENCES

1. Rittenberger JC, Popescu A, Brenner RP, Guyette FX, Callaway CW. Frequency and timing of nonconvulsive status epilepticus in comatose post-cardiac arrest subjects treated with hypothermia. *Neurocrit Care*. 2012;16:114–122. doi: 10.1007/s12028-011-9565-0
2. Legriel S, Hilly-Ginoux J, Resche-Rigon M, Merceron S, Pinoteau J, Henry-Lagarrigue M, Bruneel F, Nguyen A, Guezennec P, Troche G, et al. Prognostic value of electrographic postanoxic status epilepticus in comatose cardiac-arrest survivors in the therapeutic hypothermia era. *Resuscitation*. 2013;84:343–350. doi: 10.1016/j.resuscitation.2012.11.001
3. Dragancea I, Backman S, Westhall E, Rundgren M, Friberg H, Cronberg T. Outcome following postanoxic status epilepticus in patients with targeted temperature management after cardiac arrest. *Epilepsy Behav*. 2015;49:173–177. doi: 10.1016/j.yebeh.2015.04.043
4. Ruijter BJ, van Putten MJ, Hofmeijer J. Generalized epileptiform discharges in postanoxic encephalopathy: quantitative characterization in relation to outcome. *Epilepsia*. 2015;56:1845–1854. doi: 10.1111/epi.13202
5. Lybeck A, Friberg H, Aneman A, Hassager C, Horn J, Kjaergaard J, Kuiper M, Nielsen N, Ullen S, Wise MP, et al. Prognostic significance of clinical seizures after cardiac arrest and target temperature management. *Resuscitation*. 2017;114:146–151. doi: 10.1016/j.resuscitation.2017.01.017
6. Beretta S, Coppo A, Bianchi E, Zanchi C, Carone D, Stabile A, Padovano G, Sulmina E, Grassi A, Bogliun G, et al. Neurologic outcome of postanoxic refractory status epilepticus after aggressive treatment. *Neurology*. 2018;91:e2153–e2162. doi: 10.1212/WNL.0000000000006615
7. Hirsch LJ, Fong MWK, Leitinger M, LaRoche SM, Beniczky S, Abend NS, Lee JW, Wusthoff CJ, Hahn CD, Westover MB, et al. American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol*. 2021;38:1–29. doi: 10.1097/WNP.0000000000000806
8. Lybeck A, Friberg H, Nielsen N, Rundgren M, Ullen S, Zetterberg H, Blennow K, Cronberg T, Westhall E. Postanoxic electrographic status epilepticus and serum biomarkers of brain injury. *Resuscitation*. 2021;158:253–257. doi: 10.1016/j.resuscitation.2020.10.027
9. Rossetti AO, Logroscino G, Liaudet L, Ruffieux C, Ribordy V, Schaller MD, Despland PA, Oddo M. Status epilepticus: an independent outcome predictor after cerebral anoxia. *Neurology*. 2007;69:255–260. doi: 10.1212/01.wnl.0000265819.36639.e0
10. Lamartine Monteiro M, Taccone FS, Depoent C, Lamanna I, Gaspard N, Ligot N, Mavroudis N, Naeije G, Vincent JL, Legros B. The prognostic value of 48-h continuous EEG during therapeutic hypothermia after cardiac arrest. *Neurocrit Care*. 2016;24:153–162. doi: 10.1007/s12028-015-0215-9
11. Elmer J, Rittenberger JC, Faro J, Molyneux BJ, Popescu A, Callaway CW, Baldwin M; Pittsburgh Post-Cardiac Arrest Service. Clinically distinct electroencephalographic phenotypes of early myoclonus after cardiac arrest. *Ann Neurol*. 2016;80:175–184. doi: 10.1002/ana.24697
12. Beretta S, Coppo A, Bianchi E, Zanchi C, Carone D, Stabile A, Padovano G, Sulmina E, Grassi A, Bogliun G, et al. Neurological outcome of postanoxic refractory status epilepticus after aggressive treatment. *Epilepsy Behav*. 2019;101:106374. doi: 10.1016/j.yebeh.2019.06.018
13. Westhall E, Rosen I, Rundgren M, Bro-Jeppesen J, Kjaergaard J, Hassager C, Lindehammar H, Horn J, Ullen S, Nielsen N, et al. Time to epileptiform activity and EEG background recovery are independent predictors after cardiac arrest. *Clin Neurophysiol*. 2018;129:1660–1668. doi: 10.1016/j.clinph.2018.05.016
14. Soar J, Berg KM, Andersen LW, Bottiger BW, Cacciola S, Callaway CW, Couper K, Cronberg T, D'Arrigo S, Deakin CD, et al. Adult advanced life support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2020;156:A80–A119. doi: 10.1016/j.resuscitation.2020.09.012
15. Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the Guideline Committee of the American Epilepsy Society. *Epilepsy Curr*. 2016;16:48–61. doi: 10.5698/1535-7597-16.1.48
16. Crane J, Pearce N, Flatt A, Burgess C, Jackson R, Kwong T, Ball M, Beasley R. Prescribed fenoterol and death from asthma in New Zealand, 1981–83: case-control study. *Lancet*. 1989;1:917–922. doi: 10.1016/s0140-6736(89)92505-1
17. Reynolds AS, Rohaut B, Holmes MG, Robinson D, Roth W, Velazquez A, Couch CK, Presciutti A, Brodie D, Moitra VK, et al. Early myoclonus following anoxic brain injury. *Neurol Clin Pract*. 2018;8:249–256. doi: 10.1212/CPJ.0000000000000466
18. Barbella G, Lee JW, Alvarez V, Novy J, Oddo M, Beers L, Rossetti AO. Prediction of regaining consciousness despite an early epileptiform EEG after cardiac arrest. *Neurology*. 2020;94:e1675–e1683. doi: 10.1212/WNL.0000000000009283
19. Elmer J, Coppler PJ, Solanki P, Westover MB, Struck AF, Baldwin ME, Kurz MC, Callaway CW. Sensitivity of continuous electroencephalography to detect ictal activity after cardiac arrest. *JAMA Netw Open*. 2020;3:e203751. doi: 10.1001/jamanetworkopen.2020.3751
20. Crepeau AZ, Fugate JE, Mandrekar J, White RD, Wijdicks EF, Rabinstein AA, Britton JW. Value analysis of continuous EEG in patients during therapeutic hypothermia after cardiac arrest. *Resuscitation*. 2014;85:785–789. doi: 10.1016/j.resuscitation.2014.01.019
21. Fatuzzo D, Beuchat I, Alvarez V, Novy J, Oddo M, Rossetti AO. Does continuous EEG influence prognosis in patients after cardiac arrest? *Resuscitation*. 2018;132:29–32. doi: 10.1016/j.resuscitation.2018.08.023
22. Rossetti AO, Schindler K, Sutter R, Ruegg S, Zubler F, Novy J, Oddo M, Warpelin-Decrausaz L, Alvarez V. Continuous vs routine electroencephalogram in critically ill adults with altered consciousness and no recent seizure: a multicenter randomized clinical trial. *JAMA Neurol*. 2020;77:1225–1232. doi: 10.1001/jamaneurol.2020.2264
23. Ruijter BJ, Keijzer HM, Tjepkema-Cloostermans MC, Blans MJ, Beishuizen A, Tromp SC, Scholten E, Horn J, van Rootselaar AF, Admiraal MM, et al. Treating rhythmic and periodic EEG patterns in comatose survivors of cardiac arrest. *N Engl J Med*. 2022;386:724–734. doi: 10.1056/NEJMoa2115998
24. Rosenthal ES, Claassen J, Wainwright MS, Husain AM, Vaitkevicius H, Raines S, Hoffmann E, Colquhoun H, Doherty JJ, Kanes SJ. Brexanolone as adjunctive therapy in super-refractory status epilepticus. *Ann Neurol*. 2017;82:342–352. doi: 10.1002/ana.25008
25. Kapur J, Elm J, Chamberlain JM, Barsan W, Cloyd J, Lowenstein D, Shinnar S, Conwit R, Meinzer C, Cock H, et al. Randomized trial of three anticonvulsant medications for status epilepticus. *N Engl J Med*. 2019;381:2103–2113. doi: 10.1056/NEJMoa1905795
26. Brain Resuscitation Clinical Trial I Study Group. Randomized clinical study of thiopental loading in comatose survivors of cardiac arrest. *N Engl J Med*. 1986;314:397–403. doi: 10.1056/NEJM198602133140701
27. Longstreth WT Jr, Fahrenbruch CE, Olsufka M, Walsh TR, Copass MK, Cobb LA. Randomized clinical trial of magnesium, diazepam, or both after out-of-hospital cardiac arrest. *Neurology*. 2002;59:506–514. doi: 10.1212/wnl.59.4.506
28. Monsalve F, Rucabado L, Ruano M, Cunat J, Lacueva V, Vinales A. The neurologic effects of thiopental therapy after cardiac arrest. *Intensive Care Med*. 1987;13:244–248. doi: 10.1007/BF00265112

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.

REFERENCES

1. US Department of Health and Human Services. Organ Procurement and Transplantation Network. Accessed July 20, 2022. <https://optn.transplant.hrsa.gov/>
2. Elmer J, Molyneaux BJ, Shutterly K, Stuart SA, Callaway CW, Darby JM, Weisgerber AR. Organ donation after resuscitation from cardiac arrest. *Resuscitation*. 2019;145:63–69. doi: 10.1016/j.resuscitation.2019.10.013
3. Pilcher D, Gladkis L, Arcia B, Bailey M, Cook D, Cass Y, Opdam H. Estimating the number of organ donors in Australian hospitals: implications for monitoring organ donation practices. *Transplantation*. 2015;99:2203–2209. doi: 10.1097/TP.0000000000000716
4. Cheetham OV, Thomas MJ, Hadfield J, O'Higgins F, Mitchell C, Rooney KD. Rates of organ donation in a UK tertiary cardiac arrest centre following out-of-hospital cardiac arrest. *Resuscitation*. 2016;101:41–43. doi: 10.1016/j.resuscitation.2016.01.003
5. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, Boehme AK, Buxton AE, Carson AP, Commodore-Mensah Y, et al. Heart disease and stroke statistics—2022 update: a report from the American Heart Association [published correction appears in *Circulation*. 2022;146:e141]. *Circulation*. 2022;145:e153–e639. doi: 10.1161/CIR.0000000000001052
6. Sandroni C, D'Arrigo S, Callaway CW, Cariou A, Dragancea I, Taccone FS, Antonelli M. The rate of brain death and organ donation in patients resuscitated from cardiac arrest: a systematic review and meta-analysis. *Intensive Care Med*. 2016;42:1661–1671. doi: 10.1007/s00134-016-4549-3
7. Casadio MC, Coppo A, Vargiolu A, Villa J, Rota M, Avalli L, Citerio G. Organ donation in cardiac arrest patients treated with extracorporeal CPR: a single centre observational study. *Resuscitation*. 2017;118:133–139. doi: 10.1016/j.resuscitation.2017.06.001
8. Elmer J, Weisgerber AR, Wallace DJ, Horne E, Stuart SA, Shutterly K, Callaway CW. Between-hospital variability in organ donation after resuscitation from out-of-hospital cardiac arrest. *Resuscitation*. 2021;167:372–379. doi: 10.1016/j.resuscitation.2021.07.038
9. Achana F, Petrou S, Madan J, Khan K, Ji C, Hossain A, Lall R, Slowther AM, Deakin CD, Quinn T, et al. Cost-effectiveness of adrenaline for out-of-hospital cardiac arrest. *Crit Care*. 2020;24:579. doi: 10.1186/s13054-020-03271-0
10. Soar J, Callaway CW, Aibiki M, Bottiger BW, Brooks SC, Deakin CD, Donnino MW, Drajer S, Kloeck W, Morley PT, et al. Part 4: advanced life support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2015;95:e71–e120. doi: 10.1016/j.resuscitation.2015.07.042
11. Morrison LJ, Sandroni C, Grunau B, Parr M, Macneil F, Perkins GD, Aibiki M, Censullo E, Lin S, Neumar RW, Brooks SC, on behalf of the International Liaison Committee on Resuscitation. Organ donation after out-of-hospital cardiac arrest: a scientific statement from the International Liaison Committee on Resuscitation. *Circulation*. 2023;148:e120–e146. doi: 10.1161/CIR.0000000000001125
12. Hoyer DP, Paul A, Saner F, Gallinat A, Mathe Z, Treckmann JW, Schulze M, Kaiser GM, Canbay A, Molmenti E, et al. Safely expanding the donor pool: brain dead donors with history of temporary cardiac arrest. *Liver Int*. 2015;35:1756–1763. doi: 10.1111/liv.12766
13. Mohite PN, Zych B, Sabashnikov A, Popov AF, Garcia-Saez D, Patil NP, Koch A, Zerihou M, Rahmanian PB, Dhar D, et al. Effect of donor cardiac arrest and arrest duration on outcomes of lung transplantation. *Clin Transplant*. 2016;30:421–428. doi: 10.1111/ctr.12704
14. West S, Soar J, Callaway CW. The viability of transplanting organs from donors who underwent cardiopulmonary resuscitation: a systematic review. *Resuscitation*. 2016;108:27–33. doi: 10.1016/j.resuscitation.2016.07.029
15. Hinzmann J, Grzella S, Lengenfeld T, Pillokeit N, Hummels M, Vaihinger HM, Westhoff TH, Viebahn R, Schenker P. Impact of donor cardiopulmonary resuscitation on the outcome of simultaneous pancreas-kidney transplantation: a retrospective study. *Transpl Int*. 2020;33:644–656. doi: 10.1111/tri.13588
16. Messner F, Etra JW, Yu Y, Massie AB, Jackson KR, Brandacher G, Schneeberger S, Margreiter C, Segev DL. Outcomes of simultaneous

pancreas and kidney transplantation based on donor resuscitation. *Am J Transplant*. 2020;20:1720–1728. doi: 10.1111/ajt.15808

17. Echterdiek F, Kitterer D, Dippon J, Paul G, Schwenger V, Latus J. Impact of cardiopulmonary resuscitation on outcome of kidney transplantations from braindead donors aged ≥ 65 years. *Clin Transplant*. 2021;35:e14452. doi: 10.1111/ctr.14452

18. Mehdiani A, Immohr MB, Sipahi NF, Boettger C, Dalyanoglu H, Scheiber D, Westenfeld R, Aubin H, Lichtenberg A, Boeken U, et al. Successful heart transplantation after cardiopulmonary resuscitation of donors. *Thorac Cardiovasc Surg*. 2021;69:504–510. doi: 10.1055/s-0040-1713351

19. Greer DM, Shemie SD, Lewis A, Torrance S, Varelas P, Goldenberg FD, Bernat JL, Souter M, Topcuoglu MA, Alexandrov AW, et al. Determination of brain death/death by neurologic criteria: the World Brain Death Project. *JAMA*. 2020;324:1078–1097. doi: 10.1001/jama.2020.11586

20. Etheredge HR. Assessing global organ donation policies: opt-in vs opt-out. *Risk Manag Healthc Policy*. 2021;14:1985–1998. doi: 10.2147/RMHP.S270234

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

REFERENCES

1. Kim C, Fahrenbruch CE, Cobb LA, Eisenberg MS. Out-of-hospital cardiac arrest in men and women. *Circulation*. 2001;104:2699–2703. doi: 10.1161/hc4701.099784
2. Bosson N, Kaji AH, Fang A, Thomas JL, French WJ, Shavelle D, Niemann JT. Sex differences in survival from out-of-hospital cardiac arrest in the era of regionalized systems and advanced post-resuscitation care. *J Am Heart Assoc*. 2016;5:e004131. doi: 10.1161/JAHA.116.004131
3. Blom MT, Oving I, Berdowski J, van Valkengoed IGM, Bardai A, Tan HL. Women have lower chances than men to be resuscitated and survive out-of-hospital cardiac arrest. *Eur Heart J*. 2019;40:3824–3834. doi: 10.1093/eurheartj/ehz297
4. Morris NA, Mazzeffi M, McArdle P, May TL, Burke JF, Bradley SM, Agarwal S, Badjatia N, Perman SM; CARES Surveillance Group. Women receive less targeted temperature management than men following out-of-hospital cardiac arrest due to early care limitations: a study from the CARES Investigators. *Resuscitation*. 2021;169:97–104. doi: 10.1016/j.resuscitation.2021.10.036
5. Blewer AL, Schmicker RH, Morrison LJ, Aufderheide TP, Daya M, Starks MA, May S, Idris AH, Callaway CW, Kudenchuk PJ, et al. Variation in bystander cardiopulmonary resuscitation delivery and subsequent survival from out-of-hospital cardiac arrest based on neighborhood-level ethnic characteristics. *Circulation*. 2020;141:34–41. doi: 10.1161/CIRCULATIONAHA.119.041541
6. Starks MA, Schmicker RH, Peterson ED, May S, Buick JE, Kudenchuk PJ, Drennan IR, Herren H, Jasti J, Sayre M, et al. Association of neighborhood demographics with out-of-hospital cardiac arrest treatment and outcomes: where you live may matter. *JAMA Cardiol*. 2017;2:1110–1118. doi: 10.1001/jamacardio.2017.2671
7. Garcia RA, Spertus JA, Girotra S, Nallamothu BK, Kennedy KF, McNally BF, Breathett K, Del Rios M, Sasson C, Chan PS. Racial and ethnic differences in bystander CPR for witnessed cardiac arrest. *N Engl J Med*. 2022;387:1569–1578. doi: 10.1056/NEJMoa2200798
8. Sasson C, Magid DJ, Chan P, Root ED, McNally BF, Kellermann AL, Haukoos JS, Group CS. Association of neighborhood characteristics with bystander-initiated CPR. *N Engl J Med*. 2012;367:1607–1615. doi: 10.1056/NEJMoa1110700
9. Huebinger R, Chavez S, Abella BS, Al-Araji R, Witkov R, Panczyk M, Villa N, Bobrow B. Race and ethnicity disparities in post-arrest care in Texas. *Resuscitation*. 2022;176:99–106. doi: 10.1016/j.resuscitation.2022.04.001
10. Jadhav S, Gaddam S. Gender and location disparities in prehospital bystander AED usage. *Resuscitation*. 2021;158:139–142. doi: 10.1016/j.resuscitation.2020.11.006
11. Mumma BE, Umarov T. Sex differences in the prehospital management of out-of-hospital cardiac arrest. *Resuscitation*. 2016;105:161–164. doi: 10.1016/j.resuscitation.2016.05.029
12. Casey SD, Mumma BE. Sex, race, and insurance status differences in hospital treatment and outcomes following out-of-hospital cardiac arrest. *Resuscitation*. 2018;126:125–129. doi: 10.1016/j.resuscitation.2018.02.027
13. May T, Skinner K, Unger B, Mooney M, Patel N, Dupont A, McPherson J, McMullan P, Nielsen N, Seder DB, et al. Coronary angiography and intervention in women resuscitated from sudden cardiac death. *J Am Heart Assoc*. 2020;9:e015629. doi: 10.1161/JAHA.119.015629
14. Perman SM, Beaty BL, Daugherty SL, Havranek EP, Haukoos JS, Juarez-Colunga E, Bradley SM, Fendler TJ, Chan PS; American Heart Association Get With The Guidelines–Resuscitation Investigators. Do sex differences exist in the establishment of "do not attempt resuscitation" orders and survival in patients successfully resuscitated from in-hospital cardiac arrest? *J Am Heart Assoc*. 2020;9:e014200. doi: 10.1161/JAHA.119.014200
15. Vogelsson MA, May T, Agarwal S, Cronberg T, Dankiewicz J, Dupont A, Friberg H, Hand R, McPherson J, Mlynash M, et al. Influence of sex on survival, neurologic outcomes, and neurodiagnostic testing after out-of-hospital cardiac arrest. *Resuscitation*. 2021;167:66–75. doi: 10.1016/j.resuscitation.2021.07.037
16. Le May M, Osborne C, Russo J, So D, Chong AY, Dick A, Froeschl M, Glover C, Hibbert B, Marquis JF, et al. Effect of moderate vs mild therapeutic hypothermia on mortality and neurologic outcomes in comatose survivors of out-of-hospital cardiac arrest: the CAPITAL CHILL randomized clinical trial. *JAMA*. 2021;326:1494–1503. doi: 10.1001/jama.2021.15703
17. Dankiewicz J, Cronberg T, Lilja G, Jakobsen JC, Levin H, Ullen S, Rylander C, Wise MP, Oddo M, Cariou A, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. *N Engl J Med*. 2021;384:2283–2294. doi: 10.1056/NEJMoa2100591
18. Nordberg P, Taccone FS, Truhlar A, Forsberg S, Hollenberg J, Jonsson M, Cuny J, Goldstein P, Vermeersch N, Higuete A, et al. Effect of transnasal evaporative intra-arrest cooling on functional neurologic outcome in out-of-hospital cardiac arrest: the PRINCESS randomized clinical trial. *JAMA*. 2019;321:1677–1685. doi: 10.1001/jama.2019.4149
19. Lascarrou JB, Merdji H, Le Gouge A, Colin G, Grillet G, Girardie P, Coupez E, Dequin PF, Cariou A, Boulain T, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. *N Engl J Med*. 2019;381:2327–2337. doi: 10.1056/NEJMoa1906661
20. Lopez-de-Sa E, Juarez M, Armada E, Sanchez-Salado JC, Sanchez PL, Loma-Orsio P, Sionis A, Monedero MC, Martinez-Selles M, Martin-Benitez JC, et al. A multicentre randomized pilot trial on the effectiveness of different levels of cooling in comatose survivors of out-of-hospital cardiac arrest: the FROST-I trial. *Intensive Care Med*. 2018;44:1807–1815. doi: 10.1007/s00134-018-5256-z
21. Look X, Li H, Ng M, Lim ETS, Pothiwala S, Tan KBK, Sewa DW, Shahidah N, Pek PP, Ong MEH. Randomized controlled trial of internal and external targeted temperature management methods in post-cardiac arrest patients. *Am J Emerg Med*. 2018;36:66–72. doi: 10.1016/j.ajem.2017.07.017
22. Scales DC, Cheskes S, Verbeek PR, Pinto R, Austin D, Brooks SC, Dainty KN, Goncharenko K, Mamdani M, Thorpe KE, et al. Prehospital cooling to improve successful targeted temperature management after cardiac arrest: a randomized controlled trial. *Resuscitation*. 2017;121:187–194. doi: 10.1016/j.resuscitation.2017.10.002
23. Kirkegaard H, Soreide E, de Haas I, Pettita V, Taccone FS, Arus U, Storm C, Hassager C, Nielsen JF, Sorensen CA, et al. Targeted temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2017;318:341–350. doi: 10.1001/jama.2017.8978
24. Grejs AM, Nielsen BRR, Juhl-Olsen P, Gjedsted J, Sloth E, Heiberg J, Frederiksen CA, Jeppesen AN, Duez CHV, Hamre PD, et al. Effect of prolonged targeted temperature management on left ventricular myocardial function after out-of-hospital cardiac arrest: a randomised, controlled trial. *Resuscitation*. 2017;115:23–31. doi: 10.1016/j.resuscitation.2017.03.021
25. Bernard SA, Smith K, Finn J, Hein C, Grantham H, Bray JE, Deasy C, Stephenson M, Williams TA, Straney LD, et al. Induction of therapeutic hypothermia during out-of-hospital cardiac arrest using a rapid infusion of cold

saline: the RINSE trial (Rapid Infusion of Cold Normal Saline). *Circulation*. 2016;134:797–805. doi: 10.1161/CIRCULATIONAHA.116.021989

26. Desch S, Freund A, Akin I, Behnes M, Preusch MR, Zelniker TA, Skurk C, Landmesser U, Graf T, Eitel I, et al. Angiography after out-of-hospital cardiac arrest without ST-segment elevation. *N Engl J Med*. 2021;385:2544–2553. doi: 10.1056/NEJMoa2101909

27. Lemkes JS, Janssens GN, van der Hoeven NW, Jewbali LSD, Dubois EA, Meuwissen MM, Rijpsma TA, Bosker HA, Blans MJ, Bleeker GB, et al. Coronary angiography after cardiac arrest without ST segment elevation: one-year outcomes of the COACT randomized clinical trial. *JAMA Cardiol*. 2020;5:1358–1365. doi: 10.1001/jamacardio.2020.3670

28. Kern KB, Radsel P, Jentzer JC, Seder DB, Lee KS, Lotun K, Janardhanan R, Stub D, Hsu CH, Noc M. 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;142:2002–2012. doi: 10.1161/CIRCULATIONAHA.120.049569

29. Hauw-Berlemont C, Lamhaut L, Diehl JL, Andreotti C, Varenne O, Leroux P, Lascarrou JB, Guerin P, Loeb T, Roupie E, 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;7:700–707. doi: 10.1001/jamacardio.2022.1416

30. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, Crews DC, Doria A, Estrella MM, Froissart M, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385:1737–1749. doi: 10.1056/NEJMoa2102953

31. Segar MW, Hall JL, Jhund PS, Powell-Wiley TM, Morris AA, Kao D, Fonarow GC, Hernandez R, Ibrahim NE, Rutan C, et al. Machine learning-based models incorporating social determinants of health vs traditional models for predicting in-hospital mortality in patients with heart failure. *JAMA Cardiol*. 2022;7:844–854. doi: 10.1001/jamacardio.2022.1900

32. Meddings JF, Reichert H, Smith SN, Iwashyna TJ, Langa KM, Hofer TP, McMahon LF Jr. The impact of disability and social determinants of health on condition-specific readmissions beyond Medicare risk adjustments: a cohort study. *J Gen Intern Med*. 2017;32:71–80. doi: 10.1007/s11606-016-3869-x

33. US Department of Health and Human Services, US Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Enhancing the diversity of clinical trial populations—eligibility criteria, enrollment practices, and trial designs guidance for industry. Accessed February 8, 2023. <https://fda.gov/media/127712/download>

34. Moise N, Cene CW, Tabak RG, Young DR, Mills KT, Essien UR, Anderson CAM, Lopez-Jimenez F, et al; on behalf of the American

Heart Association Council on Epidemiology and Prevention; Council on Hypertension; and Stroke Council. Leveraging implementation science for cardiovascular health equity: a scientific statement from the American Heart Association. *Circulation*. 2022;146:e260–e278. doi: 10.1161/CIR.0000000000001096

35. Boehmer U, Kressin NR, Berlowitz DR, Christiansen CL, Kazis LE, Jones JA. Self-reported vs administrative race/ethnicity data and study results. *Am J Public Health*. 2002;92:1471–1472. doi: 10.2105/ajph.92.9.1471

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

The expert peer review of AHA-commissioned documents (eg, scientific statements, clinical practice guidelines, systematic reviews) is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit <https://professional.heart.org/statements>. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development"

Permissions: Multiple copies, modification, alteration, enhancement, and distribution of this document are not permitted without the express permission of the American Heart Association. Instructions for obtaining permission are located at <https://www.heart.org/permissions>. A link to the "Copyright Permissions Request Form" appears in the second paragraph (<https://www.heart.org/en/about-us/>)

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
Jon C. Rittenberger	Guthrie Medical Center	None	None	None	None	None	None	None
Sarah M. Perman	University of Colorado, School of Medicine	NIH/NHLBI (K23 HL138164)†	None	None	None	None	None	None
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
Carolina B. Maciel	University of Florida	None	None	None	None	None	None	None

(Continued)

Appendix 1. Writing Group Disclosures Continued

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Teresa May	Maine Medical Center	NIH/NINDS R01NS119825 (co-I on PRECICECAP [Precision Care in Cardiac Arrest–ICECAP], which is an ancillary of ICECAP. This deals with precision medicine in the setting of temperature management after cardiac arrest.)*	None	None	None	None	None	None
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
Katherine M. Berg	Beth Israel Deaconess Medical Center	None	None	None	None	None	AHA/ILCOR†	None
Cameron Dezfulian	Baylor College of Medicine	None	None	None	None	None	None	None
Dana P. Edelson	University of Chicago	None	None	None	None	AgileMD†	None	None
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.