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Part 11: Post–Cardiac Arrest Care: 2025 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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ABSTRACT: Cardiac arrest is common and deadly, affecting up to 700 000 people in the United States annually. Advanced cardiac life support measures are commonly employed to improve outcomes. This 2025 guideline on adult post–cardiac arrest care from the American Heart Association summarizes the most recent published evidence for and recommendations on several important areas of post–cardiac arrest management. Based on structured evidence reviews, guidelines are provided for initial blood pressure, oxygen, ventilation, and glucose goals. Evidence evaluating the routine use of antibiotics after return of spontaneous circulation is reviewed. The update also reviews diagnostic testing modalities, temperature control goals and duration, and the use of percutaneous coronary intervention and mechanical circulatory support in the patient resuscitated from cardiac arrest. New data regarding the detection and management of seizures have been incorporated, along with updates regarding the timing and modalities used in neuroprognostication. These guidelines now differentiate prognostication for favorable versus unfavorable outcome. New sections on the utility of advanced neuromonitoring, along with definitions and treatment options for myoclonus, are included to guide the clinician. Expanded recommendations regarding how to optimize survivorship for patients, caregivers, and rescuers are reviewed. Finally, the potential role of organ donation in the patient resuscitated from cardiac arrest is reviewed.

Key Words: AHA Scientific Statements ■ advanced cardiac life support ■ blood pressure ■ electroencephalography ■ heart arrest ■ hypothermia ■ percutaneous coronary intervention ■ survivorship

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TOP 10 TAKE-HOME MESSAGES FOR ADULT ADVANCED CARDIOVASCULAR LIFE SUPPORT

1. The section on neuroprognostication was updated to include predictors of favorable outcome, and neurofilament light chain (NfL) was added as a serum biomarker: When performed in combination with other prognostic tests, it may be reasonable to consider high serum values of neuron-specific enolase (NSE) or NfL within 72 hours after cardiac arrest to support the prognosis of unfavorable neurological outcome in patients who remain comatose.
2. It is reasonable that temperature control be maintained for at least 36 hours in adult patients who remain unresponsive to verbal commands after return of spontaneous circulation (ROSC).
3. It may be reasonable to perform computed tomography (CT) for adult patients after ROSC to investigate the etiology of cardiac arrest and complications from resuscitation, and it may be reasonable to perform echocardiography or point-of-care cardiac ultrasound for adult patients after ROSC to identify clinically significant diagnoses requiring intervention.
4. Coronary angiography is recommended prior to hospital discharge in adult cardiac arrest survivors

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with suspected cardiac etiology, particularly in the presence of an initial shockable rhythm, unexplained left ventricular systolic dysfunction, or evidence of severe myocardial ischemia.
5. Hypotension should be avoided in adults after ROSC by maintaining a minimum mean arterial pressure (MAP) of at least 65 mm Hg, though there is insufficient evidence to recommend a specific vasopressor to treat low blood pressure in adult patients after cardiac arrest.
6. In adult patients with cardiogenic shock (CS) after cardiac arrest and ROSC, temporary mechanical circulatory support (MCS) should not be routinely used, though in highly selected adult patients with refractory CS after cardiac arrest and ROSC, temporary MCS may be considered.
7. A new section dedicated to diagnosis and management of myoclonus after cardiac arrest was developed and includes the following: Treatment to suppress myoclonus without an electroencephalography (EEG) correlate is not recommended in adult survivors of cardiac arrest.
8. A therapeutic trial of a nonsedating antiseizure medication may be reasonable in adult patients who do not follow commands after ROSC with EEG patterns on the ictal-interictal continuum.
9. It is recommended that cardiac arrest survivors and their caregivers have structured assessment and treatment/referral for emotional distress after medical stabilization and before hospital discharge.
10. Interventions to address health care professional burnout may be beneficial.

INTRODUCTION

Scope of the Guidelines

This 2025 post–cardiac arrest care (PCAC) guideline from the American Heart Association (AHA) 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 PCAC guidelines.

Organization of the Writing Group

The PCAC Focused Update Writing Group included a diverse group of experts with backgrounds in emergency medicine, neurocritical care, interventional and critical care cardiology, psychology, and pulmonary critical care. 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 as well as to form a group that was institutionally diverse.

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.

METHODOLOGY AND EVIDENCE REVIEW

The writing group members evaluated the current list of patient, intervention, comparison, and outcome questions included in current PCAC guidelines. Patient, intervention, comparison, and outcome questions with novel evidence were revisited by the writing group. For each targeted patient, intervention, comparison, and outcome question, writing group members created a search strategy or utilized a previously created ILCOR search strategy when available. Search strategies were internally peer reviewed. This search was executed in Medline and Excerpta Medica Database using the Ovid search interface and in the Cochrane Central Register of Controlled Trials. Final searches were executed in November 2024. 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.

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Table 1. Applying 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 December 2024)*

CLASS (STRENGTH) OF RECOMMENDATION

Class 1 (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

Class 2a (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

Class 2b (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

Class 3: No Benefit (MODERATE) — Benefit = Risk (Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

Class 3: HARM (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

Level A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

Level B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

Level B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

Level C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

Level C-EO (Expert Opinion)
- Consensus of expert opinion based on clinical experience

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

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

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

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

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

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

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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) based on the strength and consistency of the evidence, alternative treatment options, and the 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 like equity, acceptability, and feasibility. These evidence-review methods, including specific criteria used to determine COR and LOE, are described more fully in "Part 2: Evidence Evaluation and Guidelines Development" of the 2025 guidelines.[1] The writing group members had final authority over and formally approved these recommendations.

Guideline Structure

The guidelines 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 synopsis is provided to put the recommendations into context with important background information and overarching management or treatment concepts. Recommendation-specific supportive text clarifies the rationale and key study data supporting the recommendations. When appropriate, additional tables are included.

This 2025 document updates the recommendations for the use of MCS, vasopressor choice, ventilatory goals, coronary angiography and percutaneous coronary intervention (PCI), temperature control, seizure management (with a new section on postarrest myoclonus), and survivorship after cardiac arrest (Figure 1). This 2025 update is based on the evidence identified in systematic reviews performed by ILCOR and this writing group addressing novel data that has been published since the formal release of the 2020 AHA advanced life support guidelines for cardiopulmonary resuscitation and the 2023 AHA Focused Update on Adult Advanced Cardiovascular Life Support.[1,3]

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 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.

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OXYGENATION TARGETS IN ADULT PATIENTS AFTER CARDIAC ARREST

Recommendations for Oxygenation Targets in Adult Patients After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	B-R	1. The use of 100% inspired oxygen is recommended until the arterial oxygen saturation (Spo_2) or the partial pressure of arterial oxygen (Pao_2) can be reliably measured in adult patients after ROSC.
1	B-NR	2. Hypoxemia should be avoided in adult patients after ROSC.
2a	B-R	3. Once reliable measurement of oxygen saturation is available, it is reasonable to avoid hyperoxemia and hypoxemia by titrating the fraction of inspired oxygen (Fio_2) to target oxygen saturation of 90% to 98% (Pao_2, 60–105 mm Hg) in adult patients after ROSC.
2b	C-LD	4. When relying on pulse oximetry, health care professionals should be aware of the increased risk of inaccuracy that may conceal hypoxemia in patients with darker skin pigmentation.

Synopsis

Delivery of oxygen to the brain and other vital organs is critical in resuscitation. There are theoretical risks associated with both hyperoxemia and hypoxemia.[1,2] Hyperoxemia may contribute to the development of reactive oxygen species in ischemic tissue, worsening oxidative injury and cell death.[3] Hypoxemia may

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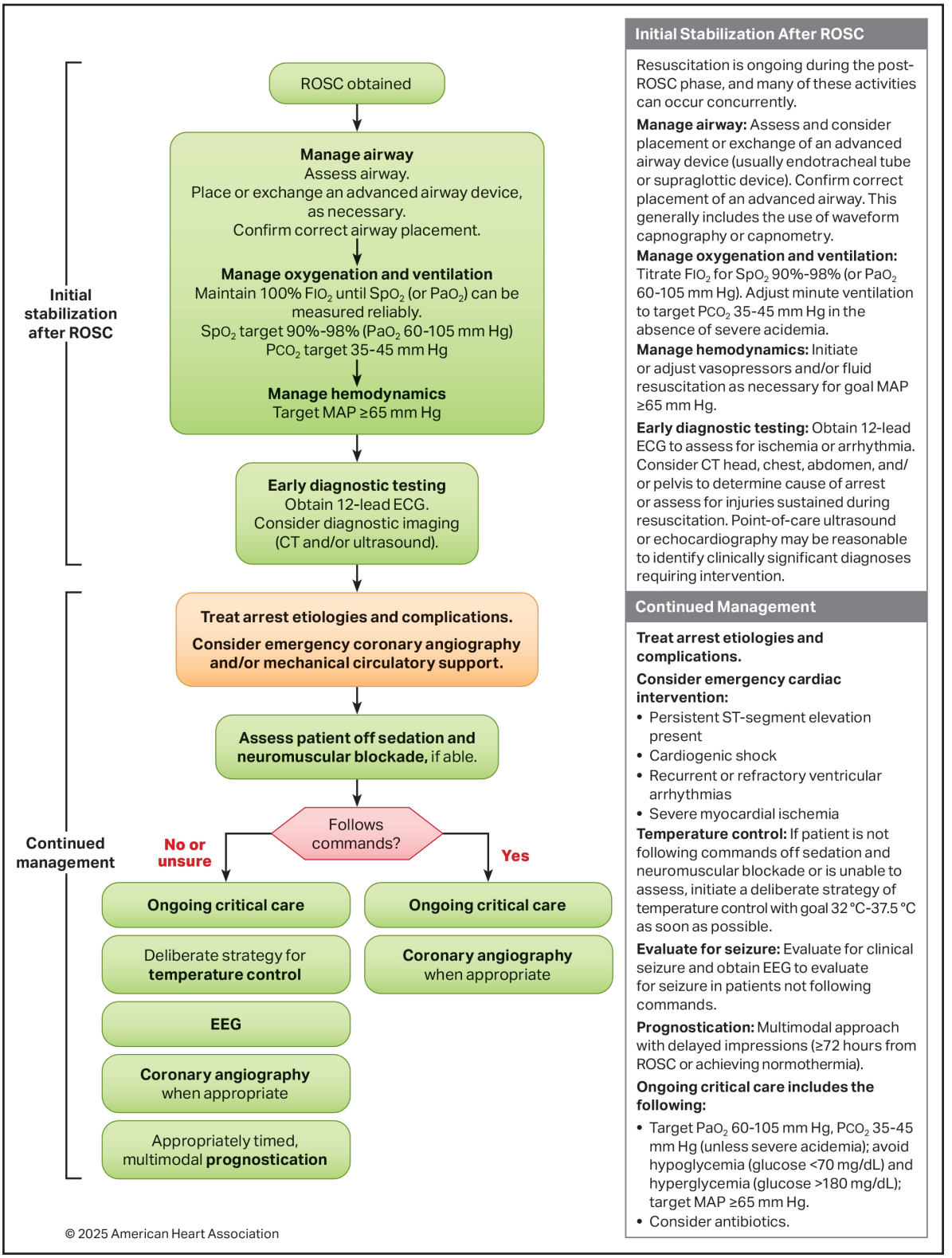


Figure 1. Adult Post–Cardiac Arrest Care Algorithm.
CT indicates computed tomography; MAP, mean arterial pressure; and ROSC, return of spontaneous circulation.

cause additional injury to end-organs and exacerbate the ischemic injury caused by the initial cardiac arrest.[4] Limitations in the ability to accurately measure oxygen saturation (Spo_2) after cardiac arrest can occur due to technological limitations in the prehospital setting and poor perfusion.[5] Additionally, pulse oximetry may be less accurate in patients with darker skin pigmentation.[6,7]

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Recommendation-Specific Supportive Text

1. In settings where accurate measures of Spo_2 or Pao_2 cannot be obtained, maintaining an Fio_2 of 100% until a reliable measure of oxygenation is obtained can help avoid hypoxemia. Administration of 100% oxygen immediately after ROSC until oxygen saturation can reliably be measured is supported by the EXACT (Reduction of Oxygen After Cardiac Arrest) randomized trial.[5] This study found an increase in hypoxemic events in the prehospital setting when Fio_2 was adjusted to maintain lower as compared to a higher Spo_2 target.[5]
2. Hypoxia increases the risk of end-organ damage, and hypoxemia is a widely available surrogate for hypoxia. Observational studies are mixed, with at least one study showing worse outcomes in patients experiencing post-ROSC hypoxemia.[8] These observational data are supported by the EXACT randomized trial, which demonstrated that lower oxygen targets in the prehospital and emergency department setting led to more hypoxemic episodes and lower survival.[5,9]
3. Several clinical trials have compared different Spo_2 and Pao_2 targets after ROSC in a variety of clinical settings with no superior or inferior target identified.[5,10,11] An Spo_2 target of 90% to 98% (Pao_2 target, 60–105 mm Hg) reflects the ranges studied in key randomized trials. In a prespecified subgroup of patients with hypoxic-ischemic encephalopathy in one clinical trial, patients randomized to a conservative oxygen therapy arm emphasizing protocolized reduction of Fio_2 had better outcomes than those in a usual care arm.[12] Observational studies have found an association between severe hyperoxemia (Pao_2 >250 mm Hg) and worse outcomes.[13]
4. Patients with darker skin pigmentation may develop "occult hypoxemia," wherein the Spo_2 on pulse oximeter reads in the normal range but the Pao_2 is in the hypoxemic range.[7,14–16]

VENTILATION TARGETS IN ADULT PATIENTS AFTER CARDIAC ARREST

Recommendations for Ventilation Targets in Adult Patients After Cardiac Arrest

COR	LOE	Recommendations
1	B-R	1. Arterial partial pressure of carbon dioxide ($Paco_2$) should be maintained within a normal physiologic range (generally 35–45 mm Hg) in adult patients who remain comatose after ROSC.
2b	B-NR	2. It may be reasonable to obtain a blood gas measurement to assess $Paco_2$ in mechanically ventilated adult patients after ROSC.

Synopsis

Management of carbon dioxide during the postarrest phase is necessary given its role in regulating cerebral blood flow. Hypocapnia-induced vasoconstriction may lead to cerebral ischemia, while hypercapnia may exacerbate elevated intracranial pressure (ICP) through increased cerebral blood volume associated with vasodilation.

Recommendation-Specific Supportive Text

1. Although a strategy of mild permissive hypercapnia (target $Paco_2$, of 50–55 mm Hg) might improve brain perfusion, observational studies have demonstrated mixed results on patient outcomes.[8,17–19] The TAME (Targeted Therapeutic Mild Hypercapnia after Resuscitated Cardiac Arrest) randomized trial compared the maintenance of normocapnia ($Paco_2$, 35–45 mm Hg) to mild hypercapnia ($Paco_2$, 50–55 mm Hg) for 24 hours in patients who remained comatose after cardiac arrest and found no difference in neurologic outcome at 6 months or in other secondary outcomes.[20] Although there was no outcome difference overall, the intervention in the TAME trial was stopped more often in the mild hypercapnia arm, possibly in response to severe acidemia because the protocol recommended suspending the intervention if pH <7.1 and base excess <—6 mmol/L. As a result, maintaining the $Paco_2$ within a normal physiologic range (generally, 35–45 mm Hg) is supported. Whether targets should be individualized based on individual patient physiology remains unknown.
2. The ability to measure $Paco_2$ after arrest is limited without blood gas measurement, and observational studies[21–24] suggest that end-tidal carbon dioxide levels may be falsely low and may not accurately reflect $Paco_2$ levels in post–cardiac arrest patients.

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BLOOD PRESSURE TARGETS IN ADULTS AFTER CARDIAC ARREST

Recommendation for Blood Pressure Targets in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendation**
1	B-R	1. Hypotension should be avoided in adults after ROSC by maintaining a minimum MAP of at least 65 mm Hg.

Synopsis

Adequate blood pressure is important after cardiac arrest to maintain end-organ perfusion, including to the brain and heart. Determining the optimal blood pressure for an individual patient can be influenced by characteristics like the degree of myocardial dysfunction, the prearrest baseline blood pressure, the cause of hypotension, and the degree of neurologic injury.[1] The physiologic rationale for considering a higher MAP after cardiac arrest relates to impaired cerebral blood flow autoregulation, which can potentially impair the ability of the brain to maintain perfusion, even at normal MAP.

Recommendation-Specific Supportive Text

1. Hypotension and shock occur in at least two thirds of patients after cardiac arrest. Observational studies have associated hypotension with worse overall survival and lower rates of favorable neurologic outcome after cardiac arrest.[2–6] Four randomized trials including over 1000 patients compared lower (a cutoff of ≤70 mm Hg) to higher (≥71 mm Hg) MAP targets after out-of-hospital cardiac arrest (OHCA).[7–10] These studies did not demonstrate better overall survival or favorable neurologic outcome with higher MAP targets.[11] The median MAP achieved in the lower MAP arms was approximately 65 mm Hg, which is the standard minimum MAP recommended for other forms of critical illness, including CS and sepsis. Collectively, these trials do not provide evidence for a different MAP goal in patients after cardiac arrest.[11–13] The safety of a lower MAP target (eg, 60–65 mm Hg) has not been evaluated in post–cardiac arrest patients.[14] It is also unknown if a higher MAP target (eg, 80–100 mm Hg) may be beneficial for some

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patients. Because the referenced trials used MAP targets and not systolic blood pressure, the recommendation is updated to remove a previous systolic blood pressure target.

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DIAGNOSTIC STUDIES FOR ADULTS AFTER CARDIAC ARREST

Recommendations for Diagnostic Studies for Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	B-NR	1. A 12-lead electrocardiogram (ECG) should be obtained as soon as feasible for all adult patients after ROSC.
2b	B-NR	2. It may be reasonable to perform head-to-pelvis CT for adult patients after ROSC to investigate the etiology of cardiac arrest and complications from resuscitation.
2b	C-LD	3. It may be reasonable to perform echocardiography or point-of-care cardiac ultrasound for adult patients after ROSC to identify clinically significant diagnoses requiring intervention.

Synopsis

Diagnosis and treatment of the underlying cause of cardiac arrest as well as identification and treatment of complications from cardiac arrest and cardiopulmonary resuscitation (CPR) are important considerations in postarrest care. Twelve-lead ECG, echocardiography, point-of-care cardiac ultrasound, and CT imaging are used in postarrest patients to identify clinically significant diagnoses requiring intervention. These diagnostic modalities are complementary, with patients often receiving multiple studies. While the majority of patients resuscitated from cardiac arrest have abnormal findings on these studies, these are not always diagnostic for the specific etiology of cardiac arrest and may not change clinical management.[1–7] The performance, timing, and interpretation of each study is guided by the clinical context. It is also important to note that the considerations regarding diagnostic imaging for an in-hospital cardiac arrest may differ from those in OHCA and that most of the available literature focuses on OHCA.

Recommendation-Specific Supportive Text

1. A 12-lead ECG obtained after ROSC can identify arrhythmia, ST-segment elevation myocardial infarction (STEMI), and other diagnoses associated with cardiac arrest for which treatment or monitoring is indicated. While the ECG is critical in identifying patients with STEMI or STEMI-equivalent patterns,[8,9] its accuracy for these diagnoses in the immediate post-ROSC period has limitations.[1,10–14] Electrocardiograms

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performed within the first 8 minutes following ROSC have been shown to have higher false positive rates for STEMI than those performed later.[1,10] In one study, approximately two thirds of STEMI patterns on the immediate post-ROSC ECG evolved to non-STEMI patterns on repeat ECG performed a median of 30 minutes later.[10] Optimal timing of an initial and repeat ECG following ROSC are not well defined. Furthermore, the absence of ST-segment elevation does not rule out an intervenable coronary lesion.[11,15–18]

2. Full body CT scan (ie, head to pelvis) can diagnose pathologies contributing to cardiac arrest, including but not limited to intracerebral hemorrhage, pulmonary embolism, cardiac tamponade, aortic dissection, and pneumothorax. A 2019 systematic review evaluating post–cardiac arrest imaging to determine arrest etiology included 17 observational studies and found that, despite heterogeneity in the CT protocols, the diagnostic yield of CT scans for clinically significant diagnoses and injuries ranges from 8% to 54%,[3] with several studies indicating an approximate yield of 30%.[7] This review was limited by the small number of patients included in the individual studies and the fact that few studies are prospective and that none were randomized.

   CT imaging can also identify complications of cardiac arrest or resuscitation, such as fractures, aspiration, pulmonary contusions, pneumothorax, and hemorrhage, which may inform subsequent medical interventions.[3–7,19,20] Small observational studies showed that patients resuscitated from OHCA may have CPR injuries identifiable by CT,[21–23] including a small proportion of time-critical injuries, such as liver/splenic lacerations and pneumothoraces.[6]

   CT imaging carries risks such as contrast-associated nephropathy. Transporting critically ill patients also carries the risks of hemodynamic instability, dislodging medical equipment, and delaying other interventions[24,25] that are weighed against the benefits of obtaining additional diagnostic information.[3–7]

   Head CT for neuroprognostication is discussed elsewhere.

3. Echocardiography and point-of-care cardiac ultrasound have been studied in the intra-arrest setting for a variety of purposes, including identification of a reversible cause for cardiac arrest. Available data suggest that these modalities can also contribute to elucidating the etiology of cardiac arrest in the postarrest setting. Diagnoses that have been evaluated with echocardiography or point-of-care ultrasound include pericardial effusion, pericardial tamponade, right ventricular dilation suggestive of pulmonary embolism, aortic dissection, cardiac regional wall motion abnormalities suggestive of myocardial infarction, cardiomyopathy, and hypovolemia.[3,26–35] An important limitation of most studies is that echocardiography or point-of-care ultrasound diagnoses were not compared to a reference standard[32]; thus, the accuracy of these studies for most diagnoses cannot be quantified.[3,36] Data are limited on whether cardiac regional wall motion abnormalities have an additional benefit when ECG and cardiac troponin results are considered.[29,37] Noncardiac point-of-care ultrasound protocols have been described, but limited data are available on their yield and accuracy.[38–40] The optimal time frame, operator, and technique for performing ECG or point-of-care cardiac ultrasound following ROSC remain uncertain.[36] Ultrasound is operator dependent, and recommendations for sonographer training and competencies are available from other organizations.[41–43]

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TEMPERATURE CONTROL AFTER CARDIAC ARREST IN ADULTS

Recommendations for Temperature Control After Cardiac Arrest in Adults

COR	LOE	Recommendations
1	B-R	1. A deliberate, protocolized strategy of temperature control is recommended for all adults who are unresponsive to verbal commands after ROSC, irrespective of arrest location or presenting rhythm.
1	B-R	2. Maintaining a temperature between 32 °C and 37.5 °C in patients unresponsive to verbal commands after ROSC is recommended for adults.
2a	B-R	3. It is reasonable that temperature control be maintained for at least 36 h in adult patients who remain unresponsive to verbal commands after ROSC.
2b	B-R	4. The benefit of strategies other than rapid infusion of cold intravenous fluids for prehospital cooling is unclear.
2b	B-R	5. It may be reasonable to avoid rapid (faster than 0.5 °C/h) rewarming in adult patients who have spontaneous hypothermia after ROSC or who are warming after hypothermic temperature control.
2b	B-NR	6. It is unclear if maintenance of a specific temperature (hypothermia versus normothermia) improves outcomes in subgroups of adult patients with higher illness severity.
3: No Benefit	B-R	7. Routine rapid infusion of intravenous fluids for prehospital hypothermic temperature control in adult patients after ROSC is not recommended.

Synopsis

Temperature control has been a focus of PCAC for several decades, reflecting strong physiologic rationale, evidence of benefit from preclinical and observational studies, and benefit in some randomized trials.[1–4] In 2023, the AHA published a focused update on temperature control that revised recommendations based upon newly published clinical trial data including the TTM2 (Targeted Temperature Management 2) trial and the CAPITAL CHILL (Moderate vs Mild Therapeutic Hypothermia in Comatose Survivors of OHCA) trial.[5–7] A recent systematic review and meta-analysis published in 2023 summarizes the multiple randomized trials conducted in various domains of temperature control.[8]

Temperature control refers to the period of active temperature management to a hypothermic target or to a normothermic target. In settings in which a hypothermic target is used, a period of fever prevention or temperature control to a normothermic target may follow the hypothermic period. The entire duration of active temperature management is considered temperature control.

Recommendation-Specific Supportive Text

1. Multiple randomized trials have tested various approaches to temperature control after cardiac arrest, including surface, intravascular, and intranasal cooling. Most of these trials specified deliberate temperature control strategies in both the intervention and control arms.[6,7,9–11]
2. A 2023 updated ILCOR systematic review[8] incorporates 6 additional randomized trials published between 2021 and 2023. All trial arms controlled temperature to between 31 °C and 37.7 °C. In the meta-analysis, there was no difference in survival when applying temperature control at 32 °C to 34 °C versus 36 °C or normothermia; however, the confidence intervals did not exclude a potential beneficial effect of temperature control at colder temperatures.[8] None of the included trials found worse outcomes with lower temperature goals. Observational studies have found that adopting higher temperature targets may result in an increased risk of fever and potentially worse outcomes, though confounders are likely present.[12–14]
3. The optimal overall duration of temperature control, including hypothermic temperature control (32 °C–34 °C) and normothermic or fever-prevention temperature control (36 °C–37.5 °C), is an important area of ongoing investigation. In one randomized trial, there was no difference in outcomes comparing hypothermic temperature control for 24 versus 48 hours, although the trial may have been underpowered and effect estimates favored longer temperature control durations.[10] In another recent randomized trial, there was no difference in outcomes comparing a period of device-based fever prevention of 12 versus 48 hours after an initial 24-hour period of temperature control to 36 °C (ie, 36 versus 72 total hours of temperature control, respectively).[15] The 2 large TTM randomized trials protocolized patients to 72 hours of total temperature control.[6,9] Recognizing evolution of evidence and definitions with respect to temperature control, 36 hours of total temperature control is the shortest recommended duration. Multiple observational studies have found strong associations between post–cardiac arrest fever and poor outcomes, including for fevers occurring after an initial 24-hour period of temperature control.[16–19] Results of the ICECAP (Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients) trial, which aimed to identify the optimal duration of hypothermic temperature control for patients with both shockable and nonshockable rhythms, are pending after the study was stopped in June 2025.[20]
4. A randomized trial measured the impact of prehospital transnasal evaporative intra-arrest cooling

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versus postadmission temperature control on survival in 671 patients and found no difference in the primary outcome of neurologically favorable survival at 90 days (16.6% in the treatment group and 13.5% in the control group).[21] The ongoing PRINCESS-2 trial aims to study a similar approach in patients with shockable rhythm, a subgroup of interest in earlier trials.[22] Cooling through surface or intravascular methods are reasonable alternatives.

5. In one small, randomized trial, there was no difference in the primary outcome of interleukin-6 level or other outcomes comparing rewarming from temperature control at 33 °C at a rate of 0.25 °C per hour as compared to 0.5 °C per hour.[23] Recent randomized trials of temperature control used rewarming rates ranging from 0.25 °C to 0.5 °C per hour when transitioning out of temperature control to colder target temperatures.[6,7,9–11] Patients presenting with spontaneous hypothermia after ROSC may have more severe neurologic injury and be more susceptible to secondary injury with rewarming. In these cases, it is unclear whether passive, uncontrolled rewarming (potentially at rates above 0.5 °C per hour) results in worse outcomes as compared to slow, controlled rewarming. Approaches to warming of patients presenting at temperatures below target in randomized trials have varied from allowing either active or passive warming[6] to active, controlled warming at 0.25 °C to 0.5 °C per hour.[11]
6. Most patients enrolled in temperature control trials had shockable rhythms with primary cardiac causes of arrest, despite eligibility criteria including both shockable and nonshockable rhythms.[6,7,9,10] A patient level meta-analysis including patients with nonshockable rhythms from the TTM2 and HYPERION trials found no difference between hypothermic and normothermic temperature control.[24] Patients who do not meet eligibility criteria for randomized trials or who suffer cardiac arrest in the United States as compared to other parts of the world may have differences in important characteristics like arrest etiology, initial rhythm, witness status, bystander CPR, and downtime.[25,26] Some observational studies suggest benefit with temperature control to lower temperatures for patients with higher illness and brain injury severity.[27,28]
7. There was no clear benefit to prehospital initiation of temperature control with cold intravenous fluids and signals of potential harm in one large randomized clinical trial.[29]

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ADDITIONAL TREATMENTS IN ADULTS AFTER CARDIAC ARREST

Recommendations for Additional Treatments in Adults After Cardiac Arrest

COR	LOE	Recommendations
2b	B-R	1. The routine use of prophylactic antibiotics in adult patients after ROSC is of uncertain benefit.
2b	B-R	2. The effectiveness of agents to mitigate neurological injury in adult patients who remain comatose after ROSC is uncertain.

Recommendations for Additional Treatments in Adults After Cardiac Arrest (Continued)

COR	LOE	Recommendations
2b	B-R	3. The routine use of steroids for adult patients with shock after ROSC is of uncertain value.
2b	B-NR	4. In adult patients with ROSC after cardiac arrest, it may be reasonable to avoid hypoglycemia (glucose <70 mg/dL) as well as hyperglycemia (glucose >180 mg/dL).

Synopsis

Patients with cardiac arrest often remain critically ill in the immediate post–cardiac arrest period, though treatments for general critical care populations may not be universally applicable to the post–cardiac arrest patient population. One important area in post–cardiac arrest therapies where new observational data have emerged is glucose control for post–cardiac arrest patients, and this has also been studied more extensively in general critical care populations. Patients are at risk of developing pneumonia after cardiac arrest, which is often caused by aspiration during the cardiac arrest and resuscitation. Thus, there is rationale to evaluate whether empiric antibiotic treatment can improve outcomes. Steroids are also of physiologic interest in patients after cardiac arrest due to their broad effects, including reducing inflammation and possibly supporting hemodynamics. Similarly, neuroprotective agents that act through a broad range of possible mechanisms continue to be an area of clinical and research interest.

Recommendation-Specific Supportive Text

1. A 2020 ILCOR systematic review[1] identified 2 randomized controlled trials (RCTs) that found no difference in survival or neurological outcome[2,3] in patients treated with early prophylactic antibiotics after cardiac arrest. One RCT[2] did find lower incidence of early pneumonia in those who received prophylactic antibiotics, but this did not translate to a difference in other outcomes. Since then, one observational study similarly demonstrated a reduction of early ventilator-associated pneumonia with prophylactic antibiotics[4] but no differences in other patient-oriented outcomes (ie, short-term mortality, duration of mechanical ventilation, or intensive care unit length of stay). Given the need for general antibiotic stewardship and the findings of the above studies, there is insufficient evidence to suggest the use of antibiotics routinely after cardiac arrest.
2. A recent systematic review[5] evaluated neuroprotective drugs and their effect on mortality and functional outcome. Nineteen RCTs of drugs categorized as neuroprotective agents and 16 studies of drugs categorized as anti-inflammatory

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or antioxidant were included. Multiple agents, including magnesium, nimodipine, inhaled gases (hydrogen, nitric oxide, and xenon), coenzyme Q10 (ubiquinol), thiamine, and others, were evaluated. Most studies were single-center trials with low numbers of participants. The heterogeneity of intervention agents and trial designs limited the ability to perform meta-analyses, and there was overall low certainty of evidence, thus, limiting the ability to recommend any specific agent.

3. One small RCT including 50 patients compared steroids to placebo for post–cardiac arrest shock.[6] Time to shock reversal and other outcomes did not differ between groups. A large retrospective observational study found that steroid use after cardiac arrest was associated with survival.[7] A recent systematic review evaluating drug therapy compared with placebo[5] included 2 RCTs using hydrocortisone after arrest as part of a multidrug protocol.[8,9] There was insufficient evidence to perform a meta-analysis for steroids after ROSC and insufficient evidence to recommend any specific drug treatment after ROSC. This topic does not address intra-arrest steroids.
4. One small RCT evaluating strict versus moderate glucose control in patients resuscitated from cardiac arrest due to ventricular fibrillation (VF)[10] found no difference in survival, though the therapeutic ranges for their control and experimental arms are no longer congruent with current critical care management. Many subsequent observational studies have demonstrated an association between hyperglycemia or hypoglycemia in the post–cardiac arrest period and worse neurological outcomes and mortality, though these were not evaluating active glucose management interventions.[11–16] While no RCTs have evaluated glucose targets in broad populations of post–cardiac arrest patients, treatment of blood glucose using insulin in the general critical care population improves mortality and is recommended in other guidelines, acknowledging risks of hypoglycemia when lower blood glucose ranges are targeted.[17–19] Given the observational findings in post–cardiac arrest patients, the RCT findings in general critical care populations, and that post–cardiac arrest patients are often critically ill, this recommendation is updated to address avoidance of hypoglycemia and hyperglycemia without giving a specific target glucose range.

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USE OF VASOPRESSORS IN ADULTS AFTER CARDIAC ARREST

Recommendation for Use of Vasopressors in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendation**
2b	B-NR	1. There is insufficient evidence to recommend a specific vasopressor to treat low blood pressure in adult patients after cardiac arrest.

Synopsis

Hypotension requiring vasopressors occurs in up to 75% of post–cardiac arrest patients.[1,2] After cardiac arrest, shock is often caused by multiple etiologies, and the shock phenotype may evolve from initial low-output CS from post–cardiac arrest myocardial dysfunction to a later vasodilatory shock from inflammatory vasoplegia.[2] Vasopressors are commonly used to support blood pressure and cardiac output in the setting of hypotension after cardiac arrest. Vasopressors have dose-dependent differences in cardiac (inotropic), vascular (vasoconstrictive), and adverse (tissue ischemia, cardiac arrhythmia) effects, which influence their efficacy and safety across individuals.[3]

Recommendation-Specific Supportive Text

1. No large-scale RCTs have compared clinical outcomes between different vasopressors in post–cardiac arrest patients.[4] A small prehospital RCT (n=40) comparing epinephrine and norepinephrine after cardiac arrest did not show a difference in safety or clinical outcomes.[5] Some, but not all, observational studies with a high risk of bias and residual confounding have suggested worse outcomes in postarrest patients who received epinephrine versus norepinephrine.[4,6] In patients with CS, many of whom had cardiac arrest, epinephrine and dopamine have been associated with a less favorable safety profile and potentially worse outcomes than norepinephrine; the presence of cardiac arrest did not influence this effect in one meta-analysis comparing epinephrine to other drug regimens.[7–9] In non–cardiac arrest patients with vasodilatory or septic shock, epinephrine was associated with more arrhythmias and metabolic abnormalities but similar survival while dopamine was associated with worse outcomes.[10] Accordingly, norepinephrine is suggested as the first-line vasopressor for patients with CS or septic shock, but whether this recommendation applies to undifferentiated post–cardiac arrest patients remains unproven.[11–13]

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PERCUTANEOUS CORONARY INTERVENTION IN ADULTS AFTER CARDIAC ARREST

Recommendations for PCI in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	B-NR	1. Coronary angiography should be performed emergently after cardiac arrest for all patients with suspected cardiac cause of arrest and persistent ST-segment elevation on ECG, regardless of the presence of coma.
1	B-NR	2. Coronary angiography is recommended prior to hospital discharge in adult cardiac arrest survivors with suspected cardiac etiology, particularly in the presence of an initial shockable rhythm, unexplained left ventricular systolic dysfunction, or evidence of severe myocardial ischemia.
2a	B-NR	3. Emergency coronary angiography is reasonable for selected adult patients after cardiac arrest with suspected cardiac etiology without ST-segment elevation on ECG in the presence of CS, recurrent ventricular arrhythmias, or evidence of significant ongoing myocardial ischemia, regardless of the presence of coma.
3: No Benefit	B-R	4. In adult comatose patients with ROSC after cardiac arrest, emergency coronary angiography is not recommended over a delayed or selective strategy in the absence of ST-segment elevation, shock, electrical instability, or evidence of significant ongoing myocardial ischemia.
3: No Benefit	B-R	5. In the setting of multivessel coronary artery disease (CAD) in adult patients with shock after cardiac arrest, immediate revascularization of non–infarct-related coronary lesions is not recommended over initial revascularization of only the infarct-related artery.

Synopsis

Coronary artery disease is identified in up to two thirds[1] of patients with OHCA from a presumed cardiac etiology who undergo invasive coronary angiography, including acute culprit lesions in one third of these patients; the prevalence is higher in patients with VF, particularly refractory VF receiving extracorporeal CPR (ECPR).[2] Identifying and treating unstable CAD has been shown to improve outcomes by stabilizing hemodynamics, preventing recurrent arrhythmias, and preserving myocardial function.[3] The ILCOR CoSTR[4] and the 2023 AHA Focused Update[5] on this topic were reviewed, and an independent literature search undertaken.

Observational studies have demonstrated higher overall and favorable neurologic outcome among OHCA patients who receive invasive coronary angiography with PCI performed within 24 hours of admission, recognizing that selection bias and confounding by indication can magnify this effect. Evidence regarding the optimal timing of coronary angiography after OHCA comes from multiple RCTs enrolling 1590 comatose hemodynamically stable OHCA patients without STEMI, the majority having a shockable rhythm.[6–12] Therefore, the certainty of data is limited for types of cardiac arrest patients excluded from these trials. Randomized data are also lacking for patients with ST-segment elevation or cohorts permitted to cross over in RCTs because of the presence of CS, signs of significant myocardial damage, electrical instability, or ongoing ischemia. A key challenge is the competing risk of poor outcome due to hypoxic-ischemic brain injury in patients who had cardiac arrest compared to those who have acute coronary syndromes but did not have cardiac arrest. Poor outcome due to the brain injury may mitigate and confound the potential benefit of coronary revascularization in this population.[13]

Recommendation-Specific Supportive Text

1. The presence of STEMI or STEMI-equivalent pattern on ECG after cardiac arrest implies transmural myocardial ischemia and a high probability of acute coronary occlusion, which can result in worsening cardiovascular instability if not promptly revascularized.[14] Multiple observational studies have demonstrated improved neurologically favorable survival when early coronary angiography is performed followed by PCI in patients with cardiac arrest who have STEMI.[15] This recommendation mirrors global recommendations for all patients with STEMI. Randomized controlled trials examining the optimal timing of coronary angiography after OHCA systematically excluded patients with STEMI.
2. Evaluating for CAD prior to hospital discharge with invasive coronary angiography in cardiac arrest survivors with a presumed cardiac etiology is supported by other cardiology-focused guidelines and scientific statements.[3,16–18] Randomized controlled trials examining the timing of coronary angiography after OHCA performed invasive coronary angiography in all patients with neurological awakening.[6–12]
3. Cardiogenic shock (hemodynamic instability) or recurrent ventricular arrhythmias (electrical instability) after cardiac arrest can be caused by severe myocardial ischemia. Patients with these unstable cardiovascular conditions are at high risk of rearrest if myocardial ischemia goes untreated. Randomized controlled trials examining the timing of coronary angiography after OHCA in comatose patients allowed crossover to the emergent timing arm for shock, recurrent VF, or evidence of severe myocardial ischemia. Elevated serum troponin levels[19–29] and ischemic ECG abnormalities (other than STEMI)[6,30–34] are common after OHCA but have inadequate sensitivity or specificity for unstable CAD and do not predict the benefit of invasive coronary angiography. This makes the optimal definition of severe myocardial ischemia uncertain, although the TOMAHAWK (Angiography After Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation) trial

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used a serum troponin cut-off 70 times the upper reference limit. Patients with OHCA with refractory VF from a presumed cardiac etiology who receive ECPR have a high prevalence of unstable CAD, and early invasive coronary angiography was part of the ECPR bundle in RCTs.[2,35–37]

4. In multiple RCTs of stable comatose OHCA patients without STEMI, there was no evidence of improved overall survival or favorable neurologic outcome with early invasive coronary angiography (eg, within 2 hours) versus delayed or selective invasive coronary angiography (eg, after awakening), with some studies suggesting potential harm with early angiography.[38] In the delayed angiography group, up to 40% of patients did not receive invasive coronary angiography due to lack of awakening[12] and up to 17% crossed over to early intervention[8] due to hemodynamic or electrical instability or severe myocardial ischemia. Invasive coronary angiography can be safely deferred until after neurological awakening in comatose OHCA patients without any of the following: STEMI or STEMI-equivalent patterns, CS, recurrent ventricular arrhythmias, or evidence of significant myocardial ischemia. Cardiac arrest patients without coma were excluded from these RCTs.
5. There is substantial overlap between the OHCA and CS populations, as acute myocardial infarction is often the underlying pathophysiology in both.[3,39] Multivessel CAD is identified in up to 50% of patients receiving invasive coronary angiography after OHCA, as in patients with CS from acute myocardial infarction.[40,41] No RCTs have examined the optimal revascularization approach for patients with cardiac arrest and multivessel CAD, and RCTs examining multivessel revascularization in patients with STEMI have excluded patients with cardiac arrest.[42] The CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trial[41] randomized patients with CS from acute myocardial infarction (including 55% OHCA patients) who had multivessel CAD and underwent culprit vessel PCI to either immediate multivessel PCI or delayed selective multivessel PCI. Patients randomized to immediate multivessel PCI had higher mortality and more complications, with similar findings of harm with initial multivessel PCI in the subgroup of patients with cardiac arrest.[43] Thus, immediate revascularization of nonculprit coronary lesions is not recommended over initial culprit-only revascularization in patients with multivessel CAD and shock after cardiac arrest and is supported by the 2021 AHA/ACC/SCAI Guideline for coronary revascularization and 2025 AHA/ACC Guideline for acute coronary syndromes.[14,44]

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TEMPORARY MCS FOR ADULTS AFTER CARDIAC ARREST

Recommendations for Temporary MCS for Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	C-EO	1. In adult patients with cardiac arrest who have been placed on MCS, appropriate monitoring and management by a team with experience managing the device(s) and the potential associated complications is recommended.
2b	B-NR	2. In highly selected adult patients with refractory CS after cardiac arrest and ROSC, temporary MCS may be considered.
3: No Benefit	B-R	3. In adult patients with CS after cardiac arrest and ROSC, temporary MCS should not be routinely used.

Synopsis

Cardiogenic shock commonly occurs as either a cause or consequence of cardiac arrest.[1] Patients with CS are usually managed with vasopressors and inotropes, but treatment failures and drug toxicity are common with these therapies.[1] Temporary MCS devices have been developed to increase blood pressure and cardiac output in patients with CS as an alternative or adjunct to vasoactive drug therapy. These devices include the intra-aortic balloon pump, percutaneous ventricular assist devices (including the Impella and TandemHeart families of devices), and extracorporeal membrane oxygenator (ECMO). Temporary MCS devices can provide hemodynamic stabilization in refractory CS, allowing time for neuroprognostication and potential cardiac recovery. Balancing the aforementioned benefits with associated increased risk of bleeding and ischemic complications observed with percutaneous ventricular assist devices and ECMO is important. Temporary MCS is becoming more commonly used as a rescue strategy for patients with refractory CS despite initial vasoactive drug therapy. While few trials of temporary MCS have exclusively included cardiac arrest patients, many of the CS patients enrolled in clinical trials of temporary MCS had cardiac arrest. Accordingly, the evidence guiding the use of temporary MCS in CS more broadly may apply to patients with cardiac arrest in the absence of studies showing differential benefits in the cardiac arrest subgroup specifically.

Recommendation-Specific Supportive Text

1. Management of temporary MCS is nuanced and requires specific knowledge. Balancing hemodynamic needs with device management is often challenging because responses to interventions can be paradoxical or counterintuitive during MCS. Given these challenges, optimizing outcomes necessitates a team experienced in MCS management. Although specific team composition and training are not well defined, a volume-outcome relationship has been noted with the use of advanced temporary MCS devices whereby centers with higher volume have better patient survival, suggesting that greater familiarity with these devices may result in improved outcomes.[2,3]

2, 3. Temporary MCS devices, including intra-aortic balloon pump, percutaneous ventricular assist devices, and ECMO, can potentially improve hemodynamics for patients with CS refractory to vasopressor and inotrope therapy. No large-scale RCTs have specifically evaluated patient-centered outcomes with early routine use of MCS devices in cardiac arrest patients. One small (n=60) RCT showed no difference in mortality with early routine intra-aortic balloon pump in patients with acute coronary syndrome who had suffered an in-hospital cardiac arrest with ROSC.[4] Patients with cardiac arrest made up the majority (64%) of patients included in RCTs assessing MCS in CS, though the subgroup of patients with cardiac arrest ranged from <20% to >90% across studies.[4–18]

In a meta-analysis of 14 trials, there was no difference in survival for CS patients treated with routine MCS compared to standard of care (OR, 1.17; 95% CI, 0.97–1.42 [ILCOR meta-analysis]). A patient-level meta-analysis of 9 RCTs in acute myocardial infarction CS (n=1114) found no survival benefit for early routine use of percutaneous ventricular assist devices or ECMO in the 51.6% with prior cardiac arrest (HR, 0.91; 0.71–1.15).[19] Patient-level subgroup analysis of 816 resuscitated cardiac arrest patients from 11 RCTs (n=816) found no difference in survival with MCS (OR, 1.21; 95% CI, 0.91–1.60 [ILCOR meta-analysis]). The singular RCT that showed survival benefit with routine use of MCS in CS patients included 20% cardiac arrest survivors but systematically excluded OHCA patients who were comatose after ROSC.[16] Importantly, individual RCTs and meta-analyses demonstrate increased harm, including severe bleeding and ischemic vascular events, with the routine use of MCS.[13,15,16,18,19] Accordingly, routine

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use of MCS in cardiac arrest patients with CS is not likely to improve survival, however, selective use of MCS in cardiac arrest patients with refractory CS may be considered, particularly for those who are not comatose and have STEMI as represented in the DanGer Shock (Danish–German Cardiogenic Shock) trial.[16,20]

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ADVANCED NEUROMONITORING IN ADULTS AFTER CARDIAC ARREST

Recommendation for Advanced Neuromonitoring in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendation**
2b	**C-LD**	1. The usefulness of monitoring ICP, cerebral blood flow, brain tissue oxygenation, or jugular venous oxygen saturation in adults after cardiac arrest is not well established.

Synopsis

Hypoxic-ischemic brain injury causes imbalance in physiological processes involved in cerebral homeostasis.[1] These disruptions place patients at risk for secondary brain injury, which may contribute to mortality

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and unfavorable neurologic outcomes. Causes of secondary brain injury are heterogeneous and vary temporally and between patients but include inadequate cerebral perfusion, oxygenation, and mismatch in metabolic supply and demand.[2] Conventional patient monitoring by clinical examination and vital signs can be insensitive to detecting secondary brain injury.[3,4] Advanced neuromonitoring refers to placing probes into or adjacent to brain tissue through a cranial burr hole or through jugular vein cannulation. These probes permit direct and frequent measurement of ICP, cerebral blood flow, brain tissue oxygen saturation ($Pbto_2$), jugular venous oxygen saturation, and neurophysiology (electrocorticography).[5,6] They also allow for sampling of the interstitial space (microdialysis) and calculation of cerebral autoregulation indices, such as pressure reactivity index and optimal cerebral perfusion pressure. These measurements can provide additional information about cerebral physiology and facilitate targeted interventions. While these techniques have been used in other types of acute brain injury populations, there has been limited investigation in hypoxic-ischemic brain injury. Limitations of previous studies in cardiac arrest populations include their observational nature; highly selected subpopulations; variability in the timing, duration, and methods of monitoring; and thresholds used to prompt interventions.

Recommendation-Specific Supportive Text

1. There are no RCTs comparing invasive neuromonitoring to no invasive neuromonitoring after cardiac arrest. Eleven nonrandomized observational studies[7–17] evaluated ICP monitoring. Five studies found an association between ICP elevation or lower intracranial compliance with poor functional outcomes.[7,10,13,16,17] Three observational studies using intracranial ICP monitoring evaluated cerebral autoregulation using pressure reactivity index.[8,13,18] The pressure reactivity index is a measure of cerebral autoregulation derived from the correlation of ICP and MAP. Two of these studies measured deviations from the optimal cerebral perfusion pressure, which was associated with mortality and lower $Pbto_2$.[8,18] Of 5 nonrandomized studies, 2 showed that cerebral hypoxia measured using $Pbto_2$ or arterio-jugular differences of oxygen was more common in patients with poor functional outcomes.[8,13–16] One single-center prospective nonrandomized interventional study evaluated functional outcomes with care guided by monitoring of ICP, $Pbto_2$, and jugular venous oxygen saturation.[8] The invasive monitoring group had superior functional outcomes at 6 months compared to a historical matched comparison group. All findings for ICP, cerebral autoregulation, $Pbto_2$, and jugular venous oxygen saturation were inconsistent across studies, and there was overall high risk of bias.

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SEIZURES, MYOCLONUS, AND OTHER EPILEPTIFORM ACTIVITY

Diagnosis and Management of Seizure and Other Epileptiform Activity in Adults After Cardiac Arrest

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

Synopsis

Seizures and status epilepticus are common acute neurologic complications in the post–cardiac arrest period, occurring in 10% to 35% of patients who do not follow commands after ROSC.[1–6] Cerebral hyperexcitability after cardiac arrest may exacerbate a mismatch between neuronal bioenergetic supply and demand, thereby contributing to secondary brain injury.[5] Post–cardiac arrest hyperexcitability can manifest as a wide range of electroclinical findings, from seizures with overt clinical manifestations, such as convulsions to periodic or rhythmic discharges on EEG and other abnormal EEG patterns.[7] Clinical or electrographic findings can manifest with or without impairment of consciousness and may or may not reach the criteria for seizures or status epilepticus (Table 2).[8]

The indications for and intensity of antiseizure medications vary in clinical practice and across studies. Although the occurrence of status epilepticus in post–cardiac arrest patients has been associated with poor outcomes in observational studies,[2,9,10] some patients survive with recovery of functional independence. Myoclonus is covered in a separate section because only a subset of patients with post–cardiac arrest myoclonus meets criteria for electroclinical seizures or status epilepticus. Marked heterogeneity in the definitions of seizures and status epilepticus across studies challenges the interpretation of available data.

Recommendation-Specific Supportive Text

1. In patients who are unable to follow commands after cardiac arrest, EEG can detect nonconvulsive seizures and status epilepticus (Table 3).[11–13] This recommendation is informed by the high prevalence of nonconvulsive seizures and other epileptiform activity in cardiac arrest survivors.[5] However, there is no direct evidence that detection of nonconvulsive seizures with EEG improves outcomes. An ILCOR systematic review from 2023 did not specifically address the timing and method of EEG monitoring in this setting.[14]
2. There are no nonrandomized trials or RCTs comparing the effect of treating clinical seizures versus no seizure treatment.[14] There is no widely accepted definition for clinically apparent seizure or status epilepticus after cardiac arrest, and previous literature has used a variety of clinical and EEG classifications. It remains unclear which seizures or status epilepticus represent an epiphenomenon of severe brain injury or treatment-responsive targets to prevent secondary brain injury. Despite the lack of high-certainty evidence, untreated clinically apparent seizure activity is thought to be potentially harmful to the brain; therefore, treatment of seizures or status epilepticus is recommended.[15]
3. Seizures or status epilepticus that have no clearly apparent clinical correlate, (ie, electrographic or nonconvulsive seizures or status epilepticus), emerge in 1% to 20% of post–cardiac arrest patients.[16] The American Clinical Neurophysiology Society (ACNS) has developed specific criteria for electrographic or nonconvulsive seizures or status epilepticus for critically ill patients (Table 2), though prior studies have used varying definitions. Given the limited evidence to support withholding treatment of nonconvulsive seizures after arrest, a similar approach to nonconvulsive seizure treatment for other etiologies is reasonable. The TELSTAR (Treatment of Electroencephalographic Status Epilepticus after

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

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 is seen following therapeutic trial, that is diagnostic for 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 s 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 motor activity with an electrographic correlate 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 min in frequency, morphology, or location but not qualifying as evolution
Data from Hirsch LJ et al (2021).[8]

Cardiopulmonary Resuscitation) trial[17] is the first RCT of protocolized tiered treatment targeting suppression of electrographic seizures, status epilepticus, or interictal patterns detected on continuous EEG in adults after arrest compared with standard care (Table 2). The trial randomized 172 subjects and the use of antiseizure medication was allowed but discouraged in the standard care group. The rate of unfavorable neurological outcome (defined as Cerebral Performance Category score of 3–5) did not differ at 3 months, but only 10% of patients in both treatment groups had electrographic seizures (the rate of clinically apparent and electroclinical seizures were not reported). Although the trial was not powered for subgroup analyses, patients with electrographic seizures (ie, periodic discharge frequencies surpassing 2.5 Hz), evolving patterns, or those with nongeneralized periodic discharges between 0.5 and 2.5 Hz had better outcomes with protocolized, tiered antiseizure treatment than standard care alone.

4. 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 6–10 electrode montages). Seizures, epileptiform abnormalities, and clinical myoclonus may occur immediately after ROSC or emerge several days after initial resuscitation.[7,12,18] Continuous EEG after cardiac arrest, although more costly and labor intensive, increases sensitivity for seizures, status epilepticus, and epileptiform activity detection when compared with brief intermittent recordings given the variability in the timing these patterns occur and frequent lack of clinical correlation. However, use of continuous EEG was not associated with improvement in survival or functional outcome in observational cardiac arrest studies[19,20] or the CERTA (Continuous EEG Randomized Trial in Adults) trial,[21] a multicenter pragmatic study involving critically ill patients with impaired consciousness, of whom nearly one-third had been post–cardiac arrest patients.
5. Cardiac arrest as the etiology of seizures and status epilepticus has been an exclusion criterion in RCTs specific to status epilepticus[22,23]; consequently, therapeutic algorithms are extrapolated from other settings, including guidelines for generalized convulsive status epilepticus. The 2023 ILCOR CoSTR summary[14] recommended that seizures be treated when diagnosed in postarrest patients. No specific antiseizure medications were recommended.
6. The ACNS defines the ictal-interictal continuum as rhythmic or periodic patterns that may be consistent with possible nonconvulsive seizures or status epilepticus even without fulfilling strict electrographic criteria (Table 2).[8] Patients with patterns on the ictal-interictal continuum who exhibit both electrographic and clinical response to a therapeutic trial with a loading dose of a nonsedating antiseizure medication (ie, not benzodiazepines) are considered to have electroclinical status epilepticus; thus, therapeutic trials of antiseizure medication may be considered for interictal findings. Clinical response to a therapeutic trial may not be apparent on bedside examination in patients who are unresponsive to commands after ROSC, therefore, determination of an electroclinical response to a therapeutic trial may be challenging.
7. No new studies were identified in the updated ILCOR CoSTR summary from 2023.[14] Seizure

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prophylaxis did not improve outcomes after cardiac arrest in 2 prospective RCTs[24,25] and 1 nonrandomized prospective clinical trial with historical controls.[26] Prophylaxis was also not effective in preventing subsequent seizures in the post–cardiac arrest period.[24–26] However, these studies lacked systematic diagnosis of seizures with EEG monitoring, seizures reported were abstracted from clinical documentation, and the sample size was insufficiently powered for this outcome. Additionally, these studies were designed as therapeutic trials of neuroprotection with thiopental, magnesium and diazepam, or diazepam alone, with the primary outcome being functional neurologic outcome with the Cerebral Performance Category scale. Therefore, their study designs are inadequate to provide definitive evidence on the role of seizure prophylaxis in the prevention of acute symptomatic seizures and later development of epilepsy following cardiac arrest. Furthermore, the chosen therapeutic agents in these studies[24–26] are not commonly used as seizure prophylaxis in clinical practice in the current era, thus, precluding extrapolation of findings on seizure prophylaxis with other agents that might have a more favorable side effect profile with fewer sedating effects.

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Diagnosis and Management of Myoclonus in Adults After Cardiac Arrest

Recommendations for the Diagnosis and Management of Myoclonus in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	**C-LD**	1. We recommend promptly performing and interpreting EEG for the diagnosis of seizures in adult patients with myoclonus after ROSC.
3: No Benefit	**C-LD**	2. Treatment to suppress myoclonus without an EEG correlate is not recommended in adult survivors of cardiac arrest.

Synopsis

Myoclonus is a common clinical manifestation of hypoxic-ischemic brain injury, being observed in approximately 18% to 34% of post–cardiac arrest patients.[1–5] Myoclonus can present as diffuse or multifocal muscle jerks or more subtle focal motor movement involving the face and limbs.[6,7] Up to half of patients with myoclonus are found to have electrographic seizures or status epilepticus, and the clinical exam alone is insufficient to predict which patients are having electrographic seizures.[8–10] Myoclonus with a time-locked EEG correlate is a seizure (Table 2), although it is controversial whether this is an epiphenomenon of hypoxic-ischemic brain injury or if it is a seizure pattern that should be treated to prevent secondary brain injury.[8,10,11] Independent of the presence of a time-locked EEG correlate, myoclonus may interfere with supportive care and ventilatory mechanics.[12,13]

Post–cardiac arrest studies are limited by substantial heterogeneity in definitions and terminology used for describing and classifying myoclonus and its associated EEG findings, including the presence of electrographic seizures and status epilepticus or epileptiform discharges or other electrographic events time locked to the myoclonus[8,11,14–16] (Table 3).

Recommendation-Specific Supportive Text

1. There is no specific clinical exam pattern, timing of occurrence, or myoclonus pattern that is reliably associated with the presence or absence of seizures or status epilepticus on EEG after cardiac arrest.[4,6–8] Therefore, prompt EEG monitoring is necessary to diagnose whether myoclonus is associated with seizures, status epilepticus, or the presence of other EEG correlates (Table 3).[16] Back averaging of EEG and electromyography signals may be necessary to determine the precise relationship between EEG events (eg, spikes, bursts) and myoclonus.[8,17] Myoclonus can cause significant muscle artifact on EEG, which can be overcome with neuromuscular blockade under close monitoring.
2. There is no randomized or nonrandomized study evaluating the role of pharmacologic interventions for the management of myoclonus without an EEG correlate after cardiac arrest. Similarly, there is no evidence implicating myoclonus without an EEG correlate in the pathogenesis of secondary brain injury after cardiac arrest.[18] Myoclonus after cardiac arrest is often refractory to treatment, and multiple antiseizure medications or anesthetic agents may be needed for myoclonus control.[2,5,7,8,13,18–24] High risk of bias related to patient selection and confounding effects and inconsistent reporting of myoclonus and EEG characteristics in the literature preclude a specific treatment recommendation for myoclonus without an EEG correlate.[14] The risk of cardiovascular, neurological, and other medication side effects outweighs the unknown benefit of suppressing myoclonus without an EEG correlate on patient outcomes.

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Table 3. Commonly Used Terms and Definitions for Myoclonic Activity After Cardiac Arrest

Terminology	Definition	Note
Status myoclonus Clinical myoclonus without EEG evaluation	Repetitive myoclonic jerks that are diffuse or generalized, focal, or multifocal, occurring once every 10 s for at least 10 min or at least once every min for at least 30 min	Clinical diagnosis that is made without EEG evaluation Status myoclonus cannot be differentiated from myoclonic seizures without an EEG. This term is used only until the myoclonus is further characterized by EEG.
Electroclinical myoclonic seizure/status epilepticus Cortical myoclonus Myoclonus with EEG correlate	Clinical manifestation of myoclonic jerks with a consistent and unequivocal EEG correlate that is not confounded by muscle artifact on EEG	No definite distinguishable features on clinical exam May require back averaging EEG-EMG for confirmation Distinct electroclinical phenotypes have been identified, which may carry different prognostic implications.
Subcortical myoclonus Myoclonus without EEG correlate	Clinical manifestation of myoclonic jerks without EEG correlate	No definite distinguishable features on clinical exam Ascertaining lack of EEG correlate can be challenging in clinical practice and may be aided by use of neuromuscular blockade.

EEG indicates electroencephalography; and EMG, electromyography.

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NEUROPROGNOSTICATION

Introduction

Hypoxic-ischemic brain injury is the leading cause of morbidity and mortality in patients who achieve ROSC after OHCA and accounts for a significant portion of unfavorable outcomes after resuscitation from in-hospital cardiac arrest.[1,2] Most deaths attributable to brain injury after cardiac arrest are due to withdrawal of life support based on a predicted unfavorable neurological outcome. Prognostication is critically important as surrogates commonly make decisions relying on the perceived estimated likelihood of recovery that is shared by the treatment team. Accurate neuroprognostication is important to avoid inappropriate withdrawal of life support in patients who may otherwise achieve meaningful recovery and to avoid ineffective treatment when poor outcome is inevitable (Figure 2).[3]

Neuroprognostication frequently incorporates assessment of structural injury (eg, neuroimaging and biomarkers) or neurological function (eg, neurophysiologic tests and clinical examination). The ideal timing for neuroprognostic tests avoids the effects of confounding (eg, from temperature, medications, and systemic organ dysfunction). Multiple tests are incorporated to estimate the likelihood for recovery to a favorable or unfavorable state. Most neuroprognostic studies utilize dichotomized outcome scales, with a favorable functional outcome defined by the ability to achieve independence (ie, Glasgow-Pittsburgh Cerebral Performance Category scores of 1–2 or modified Rankin Scale scores of 0–3), although some studies have thresholds characterized by recovery of consciousness (ie, Cerebral Performance Category score of 1–3 or modified Rankin Scale score of 0–4). These studies do not capture granular details on the functional state of patients, nor do they consider their individual preferences or values, limiting their utility. Further guidance on best practices on the interpretation of outcomes with a patient-centered approach is included in "Part 3: Ethics."

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General Considerations for Neuroprognostication in Adult Patients After Cardiac Arrest

Recommendations for General Considerations for Neuroprognostication in Adult Patients After Cardiac Arrest		
COR	LOE	Recommendations
1	B-NR	1. In adult patients who remain comatose after cardiac arrest, we recommend that neuroprognostication involve a multimodal approach and not be based on any single finding.
1	B-NR	2. In adult patients who remain comatose after cardiac arrest, we recommend that neuroprognostic impressions be delayed until adequate time has passed to ensure avoidance of confounding by medication effect or a transiently poor examination in the early postinjury period.
1	C-EO	3. We recommend that teams caring for adult patients who remain comatose after cardiac arrest have early, regular, and transparent multidisciplinary discussions with surrogates about the anticipated time course for uncertainties around neuroprognostication.
2a	B-NR	4. In adult patients who remain comatose after cardiac arrest, it is reasonable to consolidate the interpretation of multimodal prognostic assessments at a minimum of 72 h after normothermia and discontinuation of sedatives.

Synopsis

Neuroprognostication relies on interpreting the results of tests and correlating those results with outcome. Given that a false positive test for unfavorable neurological outcome could lead to inappropriate withdrawal of life support from a patient who otherwise would have recovered, specificity is the most important test characteristic when predicting unfavorable outcome. In some instances, prognostication and withdrawal of life support may appropriately occur earlier because of nonneurologic disease, catastrophic brain herniation, patient's goals and wishes, or clearly nonsurvivable situations. Many of the tests considered are subject to error because of the effects of medications, organ dysfunction, and temperature. Importantly, many published neuroprognostic studies are impacted by self-fulfilling prophecy bias, given that practices of neuroprognostication are inherently part of PCAC, and in turn, outcomes are modulated by such practices. Furthermore, research studies have methodological limitations, including small sample sizes, single-center design, lack of blinding, failure (or inability) to account for unmeasured factors that impact the pace of recovery, and the use of outcome at hospital discharge rather than a time point associated with maximal recovery (typically 3–6 months after arrest).[3] Additionally, prognostic tests may yield discordant or inconclusive results, and in such instances, continued observation and serial assessment remains a treatment option.

Recommendation-Specific Supportive Text

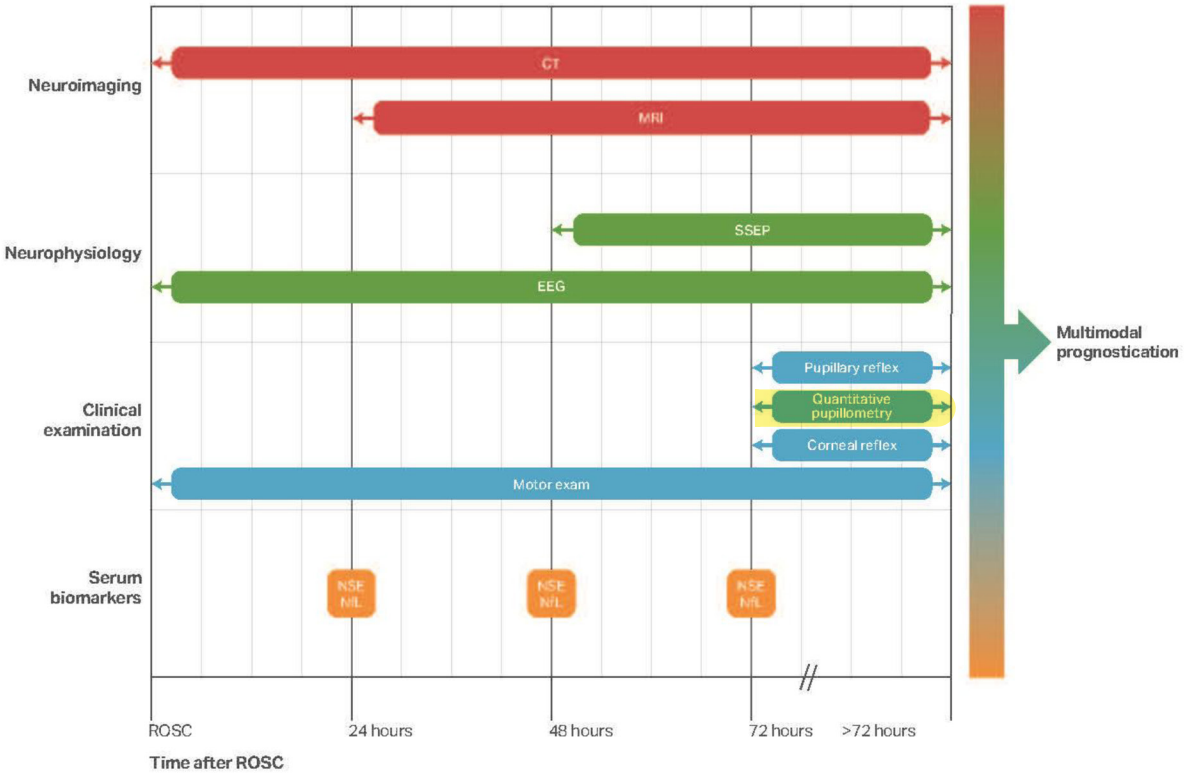
1. Any single method of neuroprognostication has an intrinsic error rate and may be subject to confounding, therefore, multiple modalities should be used to improve decision-making accuracy.[4–9] The overall certainty in the evidence of neuroprognostication studies is low due to inherent biases that limit the internal validity of studies and limited generalizability that challenge their external validity. Neuroprognostication approaches employing multimodal testing aim at mitigating error rates; concordant results increase certainty when predicting outcomes.[3,5,6,8,10–19]
2. Early withdrawal of life support based on presumed poor neurological prognosis remains frequent, despite the risk for unreliable outcome prediction within 72 hours after ROSC.[20,21] Sedatives and neuromuscular blockers may be metabolized more slowly in post–cardiac arrest patients, and injured brains may be more sensitive to the depressant effects of various medications. Residual sedation or paralysis can confound the accuracy of clinical examinations.[22]
3. Establishing clear and cohesive communication with families is a key aspect of PCAC. Communication should be implemented early and maintained longitudinally, addressing major needs, including the uncertainty of neurological prognosis.[23,24] Difficulties in family-team communication dynamics may contribute to premature withdrawal of life support.[25] Discordance in goals of care between clinicians and families/surrogates has been reported in more than 25% of critically ill patients.[26] Regular multidisciplinary meetings may help improve communication.
4. Operationally, the timing for prognostic impressions is typically at least 5 days after ROSC for patients treated with hypothermic temperature control (approximately 72 hours after normothermia) and is conducted under conditions that minimize the confounding effects of sedating medications. Each neuroprognostic test has a specific time window in which it has optimal test performance. Prognostic impressions comprise results of tests integrated into the multimodality assessment synthesized at least 72 hours after normothermia.[11,13,27–35]

Use of the Clinical Examination in Neuroprognostication

Synopsis

Historically, neuroprognostic studies evaluated findings from clinical examination that correlated with unfavorable neurological outcome. More recently, the focus of neuroprognostication after cardiac arrest has shifted to include prognostication for both favorable and unfavorable outcome. Given that a test may perform better in predicting unfavorable but not favorable outcome or vice versa, specific recommendations are made depending on the finding and the outcome (ie, favorable versus

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Neuroprognostic modality	Unfavorable outcome more likely	Favorable outcome more likely
Neuroimaging	• Reduced GWR on CT • Extensive areas of reduced ADC on MRI at 2-7 days after cardiac arrest • Extensive areas of restricted diffusion on MRI at 2-7 days after cardiac arrest	• Absence of restricted diffusion on MRI at 2-7 days after cardiac arrest
Neurophysiology	• Bilaterally absent N20 peaks on SSEP at 48 hours or more after cardiac arrest • Burst suppression at ≥72 hours after cardiac arrest in the absence of sedation • Status epilepticus ≥72 hours after cardiac arrest	• Continuous EEG background without discharges within 72 hours after cardiac arrest
Clinical examination	• Bilaterally absent pupillary light reflex at ≥72 hours after cardiac arrest • Bilaterally absent corneal reflexes at ≥72 hours after cardiac arrest • Decreased response on quantitative pupillometry at ≥72 hours after cardiac arrest	• Withdrawal or better motor response
Serum biomarkers	• High NSE within 72 hours after cardiac arrest • High NfL within 72 hours after cardiac arrest	• Normal NSE within 72 hours after cardiac arrest

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Figure 2. Recommended approach to multimodal neuroprognostication.
A multimodal approach to neuroprognostication is recommended, denoted by the multicolored arrow at the right of the figure. Neuroprognostic impressions are delayed until adequate time has passed to ensure avoidance of confounding by medications, temperature control, organ failure, or other sources. ADC indicates activated diffusion coefficient; CT, computed tomography; EEG, electroencephalogram; GWR, gray-white ratio; MRI, magnetic resonance imaging; NfL, neurofilament light chain; NSE, neuron-specific enolase; ROSC, return of spontaneous circulation; and SSEP, somatosensory evoked potential.

unfavorable outcome) with which it has correlated. Serial clinical examinations in comatose survivors of cardiac arrest assess the level of consciousness, pupillary light and corneal reflexes, and best motor response to noxious stimulation. The presence of myoclonus during the first week after cardiac arrest is also noted. Myoclonus

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describes repetitive jerk-like involuntary movements that can be generalized, focal, multifocal, synchronous, or asynchronous in their involvement of body parts and may or may not have an electroclinical correlate with discharges on EEG (refer to the Seizures, Myoclonus, and Other Epileptiform Activity section). Clinical examination findings that correlate with poor outcome are subject to confounding by temperature and medications.

Recent ILCOR systematic reviews included studies regardless of temperature control, and findings were correlated with neurological outcome at time points ranging from hospital discharge to 12 months after arrest.[10,36] A 2023 systematic review specifically evaluated the prognostic value of different test modalities for the prediction of favorable outcome.[37]

Clinical Examination for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest

Recommendations for Clinical Examination for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
2b	**B-NR**	1. When performed with other prognostic tests, it may be reasonable to consider bilaterally absent pupillary light reflex at ≥72 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose.
2b	**B-NR**	2. When performed with other prognostic tests, it may be reasonable to consider quantitative pupillometry at ≥72 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose.
2b	**B-NR**	3. When performed with other prognostic tests, it may be reasonable to consider bilaterally absent corneal reflexes at ≥72 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose.
2b	**B-NR**	4. The usefulness of undifferentiated myoclonus as a predictor of unfavorable neurological outcome in adult patients who remain comatose is uncertain, even when occurring within 72 h after cardiac arrest.
2b	**B-NR**	5. The usefulness of best motor response in the upper extremities of absent or extensor response as a predictor of unfavorable neurological outcome in adult patients who remain comatose after cardiac arrest is uncertain.

Recommendation-Specific Supportive Text

1. Twenty-seven retrospective studies demonstrated that absent pupillary light reflex evaluated immediately after ROSC and up to 7 days after arrest predicted unfavorable neurological outcome with specificity ranging from 48% to 100%[5–8,11,27,28,38–57]; these studies support the reliability of pupillary light reflex as a prognostic tool.[4,58,59] Studies with earlier time points for assessments of pupillary light reflex had lower specificity[43,46]; the highest specificity was seen at time points ≥72 hours after arrest[5,6,8,11,40,42] and when combined with absent corneal reflexes.[5,7,8,42] The false positive rates of bilaterally absent pupillary light reflex when assessed at least 72 hours after arrest in predicting unfavorable outcome were consistently low across studies. However, pupillary light reflex is vulnerable to the effect of medications and ambient light, subjective interpretation of the examiner, rigor of technique for assessment, individual factors, and self-fulfilling prophecy bias.
2. Quantitative pupillary light reflex of 0% is an objective finding that describes bilateral absence of pupillary light reflex as assessed by pupillometry.[49] The automated quantification of pupillary reactivity with pupillometry yields measurements of amplitude and velocity of constriction and dilatation. Four retrospective studies evaluated quantitative pupillary light response (ie, the percentage of reaction to light),[49,60–62] and 9 evaluated NPi (reactivity index from comparison with normal responses)[13,18,49,62–67] at time points ranging from immediately after ROSC[65] to 72 hours after arrest. Quantitative responses of 4% to 5% had higher sensitivity in predicting unfavorable neurologic outcome within 72 hours after arrest while maintaining 100% specificity. The NPi ≤2 threshold at 24 hours demonstrated 100% specificity for unfavorable neurological outcome in most studies.[13,18,49,66,67] NPi is nonspecific and may be affected by medications; thus, an absolute NPi cutoff that predicts unfavorable outcome remains unknown.[4,13,18,49,59,62–67]
3. Eighteen studies evaluated the bilateral absence of corneal reflexes at time points ranging from immediately after ROSC to 7 days after arrest with specificity ranging from 25% to 100%[5,7,8,27–29,35,40,42–45,48,50,53,54,68,69]; these studies support the reliability of corneal reflex as a prognostic tool. Studies with higher specificity evaluated corneal reflexes at time points ≥72 hours after arrest or in combination with bilaterally absent pupillary light reflexes.[5,7,8,42] Corneal reflexes are subject to confounding by medications and rigor of technique of the examiner, and few studies specifically evaluated the potential of residual medication effect or described the type of stimuli used for testing.
4. Marked heterogeneity in study definition of myoclonus after cardiac arrest challenge the interpretation of this finding as a neuroprognostic tool.[70] Eleven observational studies evaluated the presence of myoclonus (not otherwise specified) within 96 hours after arrest with specificities for unfavorable neurological outcome ranging from 77.8% to 100%,[11,13,27,29–35,68] yielding false positive rates up to 22.2% (and upper bound of 95% CI of 60%).[4] Six studies evaluated status myoclonus within 72 hours from ROSC with specificities for unfavorable outcome ranging from

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94% to 100%.[6,7,33,53,71,72] There were methodological limitations in all studies, including a lack of standard definitions, lack of blinding, incomplete data on EEG correlates, and the inability to differentiate between myoclonus subtypes. This imprecision may result in erroneous estimates of unfavorable outcome if undifferentiated myoclonus is used as a prognostic marker. Given these limitations in the interpretation of literature and the need for characterization of electroclinical subtypes of myoclonus after cardiac arrest, an expert consensus suggested avoiding using the term *status myoclonus*.[73]

5. Historically, the best motor examination in the upper extremities has been used as a prognostic tool, with extensor or absent motor responses being correlated with unfavorable outcome. Previous literature was limited by methodological concerns, including confounding for effects of hypothermic temperature control and medications, as well as self-fulfilling prophecy bias. The literature was so imprecise with higher-than-acceptable false positive rates (up to 75.1%)[4,7,58,59] that the finding of absent or extensor response as best motor response was considered potentially harmful when used alone for predicting a unfavorable neurological outcome.[74] Conversely, multimodal neuroprognostic studies using the Glasgow Coma Motor subscore as an entry point have demonstrated sensitivity ranging from 23% to 71% while maintaining high specificity.[5–9]

Clinical Examination for Neuroprognostication for Favorable Outcome

Recommendations for Clinical Examination for Neuroprognostication for Favorable Outcome		
COR	**LOE**	**Recommendations**
2b	**B-NR**	1. The usefulness of quantitative pupillometry to support the prognosis of favorable neurological outcome in adult patients who remain comatose after cardiac arrest is not well established.
2b	**B-NR**	2. It may be reasonable to consider withdrawal motor response or better to support the prognosis of favorable neurological outcome in adult patients who remain comatose after cardiac arrest.
3: No Benefit	**B-NR**	3. The finding of preserved pupillary light reflexes is not useful to support the prognosis of favorable neurological outcome in adult patients who remain comatose after cardiac arrest.
3: No Benefit	**B-NR**	4. The finding of preserved corneal reflexes is not useful to support the prognosis of favorable neurological outcome in adult patients who remain comatose after cardiac arrest.

Recommendation-Specific Supportive Text

1. Two retrospective studies evaluated the predictive performance of present pupillary light reflex to support a prognosis for favorable neurological outcome, when evaluated alone[12] or in combination with present corneal reflexes,[16] from admission[16] to up to 3 days following normothermia and discontinuation of sedatives.[12] Sensitivity when testing after mitigation of confounders reached 97.3%; however, specificities only surpassed 80% when both corneal and pupillary reflexes were present early after ROSC.[12]
2. Four observational studies evaluated the prediction performance of best motor responses (Glasgow Coma Motor subscores) from admission to 96 hours after arrest to support a prognosis of favorable neurological outcome.[7,12,16,75] Sensitivity ranged from 11.6% to 79.26% with specificity ranging from 71.7% to 97.7%; higher specificities were seen with higher motor scores (withdrawal or localizing responses, Glasgow Coma Motor subscores of 4 or 5, respectively).[37] This recommendation is supported by a 2022 ILCOR systematic review.[36]
3. Two retrospective studies evaluated the prediction performance of pupillometry when assessed at admission to up to 72 hours after arrest to support a prognosis for favorable neurological outcome.[12,13] In a post hoc analysis of the largest (n=456) neuroprognostic study evaluating the usefulness of pupillometry in cardiac arrest, the mean lowest NPi measured within 3 days after arrest in patients with a favorable outcome was 4.1.[13] The ideal thresholds and timing of testing for pupillometry derived metrics that predict favorable outcome is unknown.
4. Two retrospective studies evaluated the prediction performance of the presence of corneal reflexes to support a prognosis for favorable neurological outcome, when evaluated alone[12] or in combination with present pupillary light reflexes,[16] from admission[16] to up to 3 days following normothermia and discontinuation of sedatives.[12] Sensitivity when testing after mitigation of confounders reached 93.6%; however, specificities only surpassed 80% when both corneal and pupillary reflexes were present <72 hours after ROSC.[12]

Serum Biomarkers for Neuroprognostication of Favorable and Unfavorable Outcome in Adults After Cardiac Arrest

Recommendations for Serum Biomarkers for Neuroprognostication of Favorable and Unfavorable Outcome in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
2b	**B-NR**	1. When performed in combination with other prognostic tests, it may be reasonable to consider high serum values of NSE or NfL within 72 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.

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Recommendations for Serum Biomarkers for Neuroprognostication of Favorable and Unfavorable Outcome in Adults After Cardiac Arrest (Continued)		
COR	**LOE**	**Recommendations**
2b	**B-NR**	2. When evaluated with other prognostic tests, it may be reasonable to consider normal levels of NSE within 72 h after cardiac arrest to support the prognosis of favorable neurological outcome in adult patients who remain comatose after ROSC.
2b	**B-NR**	3. The usefulness of other serum biomarkers for neuroprognostication in adult patients who remain comatose after ROSC is uncertain.

Synopsis

Serum biomarkers are blood-based tests that measure the concentration of proteins normally found in the central nervous system. These proteins are absorbed into blood in the setting of neurological injury, and their serum levels reflect the degree of brain injury. Limitations to their prognostic utility include variability in testing methods on the basis of site and laboratory, between-laboratory inconsistency in levels, susceptibility to additional uncertainty due to hemolysis, and potential extracerebral sources of the proteins. The 2020 and 2022 ILCOR systematic reviews evaluated studies that obtained serum biomarkers within the first 7 days after arrest and correlated serum biomarker concentrations with favorable and unfavorable neurological outcomes.[4,37] Other testing of serum biomarkers, including testing levels over serial time points after arrest, was not evaluated. The 2 most studied biomarkers were NSE and S100 calcium-binding protein B (S100B). Additional evidence for NfL in predicting favorable neurological outcomes and levels of other blood biomarkers for predicting favorable neurological outcomes has accumulated since these reviews. Prospective validation of different biomarkers and thresholds for both favorable and unfavorable neurological outcome in cohorts more broadly representative of resuscitated cardiac arrest patients is of high clinical importance.

Recommendation-Specific Supportive Text

1. For prediction of unfavorable outcome, 17 observational studies evaluated NSE collected within 72 hours after cardiac arrest,[4,13,18,72,76–86] and threshold levels for unfavorable outcome ranged from 17 to 106 µg/L with specificity for poor outcome of 44% to 100%. The evidence is limited because of a lack of blinding, laboratory inconsistencies, a broad range of thresholds needed to achieve 100% specificity, and imprecision. Data from only 2 observational studies assessing NfL for unfavorable outcome prediction were included in the 2020 ILCOR systematic review.[87,88] In the interim, 9 additional observational studies evaluated NfL within 72 hours after arrest for predicting unfavorable outcome.[81,82,89–95] Multiple studies directly compared NfL to NSE for prognostication of unfavorable outcome and found both improved sensitivity with NfL while maintaining high specificity. Many of the included studies are secondary analyses of RCTs. Strengths of these studies include multiple sites, blinding of clinical staff, and standardized, blinded outcome assessment, but the trial populations may not reflect the overall post–cardiac arrest population. SIMOA (Quanterix) was the most used assay. Values may differ among commercially available assays.[96] Studies reported multiple thresholds and collected samples at different times. In the postarrest period, the optimal threshold and timing for both NSE and NfL levels are unknown, but very high levels may inform multimodal prognostication.
2. For predicting favorable outcome, the 2022 systematic review identified normal levels of NSE (<17 µg/L) between 24 and 72 hours as a predictor of favorable neurological outcome.[37] Specificity was >80% in the included studies. The biomarkers S100B, NfL, ubiquitin carboxyl-terminal hydrolase-L1 (UCH-L1), glial fibrillary acidic protein (GFAP), and tau were also included. NfL and GFAP had the highest specificity for favorable outcome but had relatively fewer studies compared with NSE. Interval searches identified 5 studies of NSE,[8,16,76,97,98] 1 of NfL,[90] and 1 of both GFAP and tau[99] for predicting favorable neurological outcome. Specificity for favorable neurological outcome was >80% for each biomarker. Different threshold values and sample timing were reported between studies. While the evidence for favorable outcome prediction with biomarkers is less established than for prediction of unfavorable outcome, sustained low levels of biomarkers, in particular, NSE, may be an encouraging finding. Specificity may be lower when predicting favorable neurological outcome due to competing risks of nonneurological organ dysfunction or failure.
3. In addition to 2 prospective and 2 retrospective studies identified in the 2020 ILCOR systematic review,[4] 3 observational studies evaluated S100B levels within the first 72 hours after arrest.[84,85,93] The maximal level that correlated with unfavorable outcome ranged broadly depending on the study and the timing when it was measured after arrest. Interval studies do not clarify the optimal timing or threshold value to inform prognostication. Only 1 study of GFAP[100] and tau[101] were identified. Seven observational studies investigated other biomarkers, including UCH-L1, GFAP, and serum and cerebrospinal fluid tau.[89,93,95,99,102–104] In studies that included multiple biomarkers, performance was not consistently better than NSE. Given the low number of studies, the certainty of evidence was low and these biomarkers could not be recommended for clinical practice.

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Use of Electrophysiological Tests for Neuroprognostication

Synopsis

Electroencephalography is widely used in clinical practice to evaluate cortical brain activity and diagnose seizures. Its use as a neuroprognostic tool for predicting both unfavorable and favorable neurological outcome is promising, but the literature is limited by several factors, including lack of standardized terminology and definitions, relatively small sample sizes, lack of blinding, subjectivity in the interpretation, and lack of accounting for effects of medications. There is also inconsistency in definitions used to describe specific findings and patterns. The EEG patterns that were evaluated in the 2020 ILCOR systematic review for predicting unfavorable neurological outcome include unreactive EEG, epileptiform discharges, seizures, status epilepticus, burst suppression, and "highly malignant" EEG.[4] Unfortunately, studies define "highly malignant" EEG differently or imprecisely, limiting use of this finding. Use of standardized terminology from the ACNS avoids this heterogeneity and limits potential for misclassification. Several EEG patterns were observed in a 2022 systematic review for predicting favorable neurological outcome.[37] While studies had several operational definitions, most classifications assessed EEG continuity, voltage, and absence of epileptiform discharges.

Somatosensory-evoked potentials (SSEPs) evaluate the integrity of the dorsal column–lemniscal sensory pathway and are subject to less interference from medications than other modalities. In the context of neuroprognostication after cardiac arrest, SSEPs are obtained by stimulating the median nerve and evaluating for the presence of cortical N20 potentials, which are generated in the primary somatosensory cortex and demonstrate integrity of the thalamocortical pathway involved in cortical arousal and consciousness. The reliability of this modality is limited by technical challenges, including operator skill, interrater agreement, and impairment of signal to noise ratio from muscle and environmental contamination. Recommended technical standards are available.[105]

Electrophysiology for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest

Recommendations for Electrophysiology for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
2b	**B-NR**	1. When evaluated with other prognostic tests, the prognostic value of seizures in adult patients who remain comatose after ROSC is uncertain.
2b	**B-NR**	2. When evaluated with other prognostic tests, it may be reasonable to consider status epilepticus continuing ≥72 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.
2b	**B-NR**	3. When evaluated with other prognostic tests, it may be reasonable to consider burst suppression on EEG in the absence of sedating medications at ≥72 h after arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.
2b	**B-NR**	4. When evaluated with other prognostic tests, the usefulness of rhythmic or periodic discharges to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC is uncertain.
2b	**B-NR**	5. When evaluated with other prognostic tests, it may be reasonable to consider bilaterally absent cortical N20 waves on SSEPs at ≥48 h after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.
3: No Benefit	**B-NR**	6. We recommend that the absence of EEG reactivity within 72 h after cardiac arrest not be used to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.

Recommendation-Specific Supportive Text

1. No additional studies have been identified since the publication of the 2020 ILCOR systematic review.[4] The 2020 systematic review included observational studies focused on electrographic seizures, though some studies also included convulsive seizures and the definitions for seizures were nonstandardized across studies. The specificity of unequivocal seizures meeting ACNS critical care EEG criteria was 100%; however, the sensitivity of this finding was poor (0.3%–26.8%), and other studies that were not included in the review found patients with postarrest seizures who had favorable outcomes.[31,106,107] Additional methodological concerns include selection bias for which patients underwent EEG monitoring and inconsistent definitions of seizure. Further, critical care EEG terminology has been updated since the publication of these studies.[108] The term *seizure* encompasses a broad spectrum of pathologies that likely have different prognoses, ranging from a single brief electrographic seizure to refractory status epilepticus, and this imprecision justifies the more limited recommendation.
2. In the 2020 ILCOR systematic review, the specificity of status epilepticus for unfavorable outcome ranged from 82.6% to 100%.[4] No additional studies were identified that reported sensitivity or specificity of this finding. One retrospective study

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reported electrographic characteristics of patients with definitive or possible status epilepticus.[109] Of the 64 subjects included, 5 survived 30 days after arrest and 1 had a favorable outcome. The most common cause of death in decedents was withdrawal of life-sustaining therapies, which occurred a median of 8 days (IQR, 7–11) after arrest. Interestingly, although status epilepticus is a severe form of seizure the specificity of status epilepticus for unfavorable outcome was less than reported in the studies examining the seizures overall (as above). Additional concerns within the studies include the inconsistent definition of *status epilepticus*, lack of blinding, and the use of status epilepticus to justify withdrawal of life-sustaining therapies leading to potential self-fulfilling prophecies. The 72-hour timing is based on most studies reporting presence of status epilepticus within this period and case reports of good outcome when status epilepticus is successfully treated within this period.

3. The term *highly malignant EEG* was inconsistently applied in studies included in the 2020 ILCOR systematic review.[4] Twelve studies evaluated burst suppression or suppression on EEG monitoring.[6,8,9,40,69,72,81,110–114] Across these studies, *highly malignant EEG* was classified as burst suppression or suppression according to the ACNS critical care EEG terminology.[108,115] Specificity ranged from 90.7% to 100%, and sensitivity was 15% to 51%. The potential for self-fulfilling prophecies, interrater disagreement, and lack of control for medication effects limited the ability to make a stronger recommendation, despite the overall high specificity.[112] Further, in a preplanned analysis of the TTM2 trial, specificity of burst suppression or suppression for unfavorable outcome was lower (93%) compared to studies with specific centralized or expert EEG review.[114] Additional studies identifying subtypes of burst suppression, such as synchronous or identical bursts, are needed.[116] Burst suppression can be caused by medications, so it is particularly important that clinicians have knowledge about the potential effects of medication on this prognostic tool.
4. The 2020 ILCOR systematic review considered discharges as either rhythmic/periodic or nonrhythmic/periodic.[4] Sensitivity and specificity of rhythmic/periodic patterns for unfavorable outcome ranged from 0.5% to 50.8% and 77.7% to 100%, respectively, with wide confidence intervals. As the time from the cardiac arrest to test increased, the specificity of rhythmic/periodic discharges for unfavorable outcome improved. Nonrhythmic/periodic patterns had a similar range of sensitivity (0.5%–38.5%) and specificity (84.6%–100%). One observational study reported outcomes in patients with stimulus-induced rhythmic or periodic patterns recorded >36 hours after arrest.[117] Of the 142 included patients, 20 (14%) had stimulus-induced rhythmic or periodic patterns recorded on EEG monitoring. The rate of unfavorable outcome was not different between patients with (n=13, 65%) or without stimulus induced rhythmic or periodic patterns (n=88, 72%) (P=0.596). The literature of both rhythmic/periodic and nonrhythmic/periodic discharges are limited by lack of accounting for effects of medications and variable timing of EEG monitoring. Low specificity currently limits the use of these findings to support an unfavorable prognosis.
5. Bilateral absence of N20 peaks following median nerve stimulation is the most studied and well-accepted neuroprognostic predictor for SSEP testing. Twenty observational studies[5–8,11–13,27,35,38,39,41–43,47,49,50,55,57,69,72,118–130] evaluated bilateral absent N20 peaks assessed up to 6 days after arrest with specificity ranging from 50% to 100%. Six studies had specificity below 100%,[11,27,47,50,118,123] and additional methodological limitations included lack of blinding and potential for self-fulfilling prophecy bias. Newer studies evaluated the unilateral absence of N20 combined with amplitude thresholds, which may increase sensitivity for detection of unfavorable outcome.[6,57,131,132] While studies evaluated SSEPs obtained at any time starting immediately after ROSC, there is a high likelihood of potential confounding factors early after cardiac arrest, leading to the recommendation that SSEPs should only be obtained >48 hours after arrest.
6. A preplanned analysis of the TTM2 trial data reported the prognostic value of unreactive EEG between 24 hours to 14 days.[114] Specificity for unfavorable neurological outcome was 60% with a sensitivity of 79%. The study relied on local EEG reviewers to assess reactivity rather than a centralized expert review. Specificity was lower than in studies included in the 2020 ILCOR review, which ranged from 41.7% to 100% but was below 90% in most studies.[4] One study assessed EEG reactivity during hypothermia and normothermia intending to assess agreement for reactivity between raters and sensitivity for unfavorable outcome for reactivity to different stimulations.[35] Percent agreement ranged from 58% to 70%, and sensitivity ranged from 52% to 86% depending on stimulation type and whether assessment occurred during hypothermia or normothermia. Thus, the overall certainty of the evidence was rated as very low. There is interest in automated reactivity assessment and stimulation paradigms.

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Electrophysiology for Neuroprognostication of Favorable Outcome in Adults After Cardiac Arrest

Recommendations for Electrophysiology for Neuroprognostication of Favorable Outcome in Adults After Cardiac Arrest		
COR	LOE	Recommendations
2b	B-NR	1. When evaluated with other prognostic tests, it may be reasonable to consider a continuous EEG background without discharges within 72 h after cardiac arrest to support the prognosis of favorable neurological outcome in adult patients who remain comatose after ROSC.
2b	B-NR	2. The usefulness of the amplitude of the N20 wave on SSEP following medium nerve stimulation to support the prognosis of favorable neurological outcome in adult patients who remain comatose after ROSC is not well established.

Recommendation-Specific Supportive Text

1. The 2022 systematic review for prediction of favorable outcome found a continuous EEG background without discharges within 72 hours after cardiac arrest to predict a favorable neurological outcome.[37] Specificity ranged from 51% to 100%, with most studies reporting a specificity >80%. Specificity was higher in earlier (12 and 24 hours) compared to later time points (48 and 72 hours). One additional observational study evaluated continuous normal voltage background without discharges on EEG 24 hours after cardiac arrest.[16] Sensitivity and specificity for favorable neurological outcome at 6 months after arrest were 64% and 89%, respectively. When compared to unfavorable outcome, the specificity for predicting favorable outcome is overall less given the competing risk of nonneurological mortality and morbidity.
2. Quantitative characteristics of the N20 signal are of interest as prognostic indicators, and there are several methods for calculating the amplitude of the N20 wave. The threshold of >4 μV when measured as the peak-to-trough difference between the peak of the N20 wave and the trough of the subsequent P25 wave has achieved specificity above 90% with sensitivity above 40% in most studies using this finding to predict favorable neurological outcome.[16,36,37,72] One study found that patients sedated with midazolam had lower amplitudes (measured as N20/P25 peak-to-peak amplitude) when compared to propofol.[14] The ideal amplitude thresholds, measurement methods, and timing of N20 wave amplitude testing for SSEP that predict favorable outcome is unknown.

Use of Neuroimaging for Neuroprognostication

Synopsis

Neuroimaging may be helpful to detect and quantify structural brain injury after cardiac arrest. The most common modalities are CT and magnetic resonance imaging (MRI). The use of quantitative analysis modalities assessing the burden of hypoxic-ischemic brain injury in clinical practice is limited by the availability of quantitative methods outside research settings, while qualitative imaging results are often subjective and have lower sensitivity.[133,134] On CT, cytotoxic brain edema can be quantified as the gray-white ratio (GWR), defined as the ratio between the density (measured as Hounsfield units) of gray matter and white matter. Normal brain has a GWR of approximately 1.3. In the setting of cerebral edema, GWR declines, either due to decreased density of gray matter (representing cytotoxic edema) or decreased attenuation of white matter. On MRI, cytotoxic brain edema can be measured as restricted diffusion on diffusion-weighted imaging (DWI) and can be quantified by the apparent diffusion coefficient (ADC). The ADC is a sensitive measure of injury, with normal values ranging between 650 and 1000 × 10^{-6} mm^2/s and values decreasing with injury. Brain injury findings from CT and MRI evolve over the first several days after arrest, so the timing of the imaging study of interest is particularly important as it relates to prognosis.

Neuroimaging for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest

Recommendations for Neuroimaging for Neuroprognostication of Unfavorable Outcome in Adults After Cardiac Arrest		
COR	LOE	Recommendations
2b	B-NR	1. When performed with other prognostic tests, it may be reasonable to consider reduced GWR on brain CT after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.
2b	B-NR	2. When performed with other prognostic tests, it may be reasonable to consider extensive areas of restricted diffusion on brain MRI at 2 to 7 d after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.
2b	B-NR	3. When performed with other prognostic tests, it may be reasonable to consider extensive areas of reduced ADC on brain MRI at 2 to 7 d after cardiac arrest to support the prognosis of unfavorable neurological outcome in adult patients who remain comatose after ROSC.

Recommendation-Specific Supportive Text

1. Forty-one observational studies[6,17,55,56,68,121,125,133–166] evaluated GWR—the most commonly studied method for quantification of hypoxic-ischemic brain injury on brain CT.[167] Whole-brain GWR (GWR average) and GWR in specific regions were evaluated with high specificity in predicting unfavorable neurological outcome; lower prediction performance was seen when using thalamus as a region of interest and with higher cutoffs for GWR.

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Thirty-four of the studies evaluated CT obtained within 24 hours after arrest,[6,17,55,56,68,121,133–139,141–143,145,147–153,155,156,158–161,163–166] and 6 studies included brain CTs obtained up to 10 days after arrest.[125,140,146,154,157,162] In retrospective studies, the predictive performance improved when images were obtained at 24 to 72 hours[134,140,151,155] and up to 10 days from ROSC.[154,162] There were methodological limitations, including selection bias, risk of multiple comparisons, and heterogeneity of measurement techniques, such as anatomic sites, equipment, and calculation methods. Thus, specific methods for calculation of and thresholds for GWR and ideal timing for CT acquisition that predict unfavorable prognosis with highest specificity remain unknown. Fewer studies have evaluated CT metrics as predictors of death by neurological criteria[148,150]; external validation and reproducibility of methods are lacking.

2. Ten observational studies[16,55,69,110,168–173] investigated DWI changes on MRI qualitatively within 2 to 7 days after arrest for unfavorable outcome prediction. The studies evaluated MRI qualitatively. And definitions of relevant findings differed between studies, such as use of "high signal intensity" and "positive findings." In some studies, only specific brain regions were examined, with or without using a standardized scoring system. Moreover, studies are limited by subjective thresholds and lack of blinding. The specificity ranged from 55.7% to 100%. In the context of multimodal prognostication, an extensive burden of reduced DWI on MRI may be correlated with unfavorable prognosis, but a broader recommendation could not be supported. The imprecise definition and short-term outcome in some studies led to significant uncertainty about how to use qualitative DWI MRI to predict unfavorable prognosis.
3. Ten observational studies investigated quantitative ADC on MRI within 2 to 7 days after arrest for unfavorable prognosis prediction.[17,69,158,164,170,171,174–177] The studies used custom-made computational tools to quantitatively determine the whole brain or region of interest volume below a specific ADC threshold for poor outcome prediction. The ADC thresholds used, ADC calculation methods used, and regions included for analyses varied among studies, with cutoffs for unfavorable outcome with 100% specificity using 650×10^{-6} mm^2/s or 450×10^{-6} mm^2/s varying from 20.5% to 42.2% and 1.3% to 5.2%, respectively. There is no standardization of quantitative measurements of ADC in cardiac arrest, and such analyses require expertise in advanced computational methods; hence, there are concerns about feasibility and reliability. In the context of multimodal prognostication, an extensive burden of decreased ADC on MRI may be correlated with unfavorable prognosis. A specific ADC threshold for global or regional brain injury that predicts unfavorable prognosis is not known.

Neuroimaging for Neuroprognostication of Favorable Outcome in Adults After Cardiac Arrest

Recommendations for Neuroimaging for Neuroprognostication of Favorable Outcome in Adults After Cardiac Arrest		
COR	**LOE**	**Recommendations**
2b	B-NR	1. The usefulness of GWR on brain CT after cardiac arrest to support the prognosis of favorable neurological outcome in adult patients who remain comatose after ROSC is not well established.
2b	B-NR	2. When performed with other prognostic tests, it may be reasonable to consider the absence of restricted diffusion on brain MRI at 2 to 7 d after cardiac arrest to support the prognosis of favorable neurological outcome in adult patients who remain comatose after ROSC.

Recommendation-Specific Supportive Text

1. Three observational studies evaluated the role of GWR on brain CTs performed within 6 hours up to 36 hours after arrest to identify patients with favorable outcomes.[56,142,158] In the largest cohort, patients who regained consciousness before hospital discharge had a median GWR 1.38. The ideal thresholds and methods of calculation for GWR and timing for CT acquisition that predict favorable prognosis are unknown.[36,37]
2. Six studies investigated the absence of qualitative DWI abnormalities within 2 to 7 days from arrest as a predictor of favorable outcome.[16,45,168–171] These studies had a sensitivity for favorable outcome prediction of 51% to 100%, but there was heterogeneity of DWI assessment methods and which regions were evaluated. In the context of multimodal prognostication, the absence of injury using DWI on MRI may be correlated with a favorable prognosis, but imprecise definitions and criteria for brain MRI assessment led to uncertainty about how to use DWI MRI to predict favorable prognosis.

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ORGAN DONATION AFTER CARDIAC ARREST IN ADULTS

Recommendations for Organ Donation After Cardiac Arrest in Adults		
COR	**LOE**	**Recommendations**
1	B-NR	1. Organ donation should be considered in all adult patients resuscitated from cardiac arrest who meet neurological criteria for death (ie, brain death).
1	B-NR	2. Organ donation should be considered in all adult 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.
2b	C-LD	5. It may be reasonable to consider utilization of organs from adult patients resuscitated with ECPR who remain supported on ECMO and who meet neurological criteria for death (ie, brain death) or for whom withdrawal of life-sustaining therapies is planned.

Synopsis

Organ transplantation wait times in the United States are increasing as patients in need of transplant outpace available organs.[1] Thousands die annually waiting for transplantation.[1] Patients with cardiac arrest make up an important pool of potential donors because cardiac arrest is common and a substantial proportion of those who cannot recover are still able to donate.[2–7] 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.

The role of extracorporeal membrane support in organ donors is complex and evolving. Patients with cardiac arrest may receive extracorporeal membrane support either through ECPR or through having it placed in the postarrest period. Those patients who remain on extracorporeal membrane support and die by brain death or have a planned withdrawal of life-sustaining therapies represent a unique population of potential organ donors.

Recommendation-Specific Supportive Text

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[8–14]; this holds true for donation after brain death and controlled DCD.

3. Laws and regulations governing the determination of death and organ donation vary not only between countries[15,16] but also by state despite efforts to standardize death determined by neurological criteria worldwide.[15]

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4. A 2023 ILCOR CoSTR scientific statement focuses on the importance of increasing organ availability after cardiac arrest.[7] It recognizes organ donation as an important outcome of cardiac arrest and emphasizes the importance of research and clinical protocols incorporating this principle. Organ donation after cardiac arrest directly benefits recipient patients.
5. A 2024 meta-analysis[17] based mostly on retrospective observational studies, case reports, and one retrospective analysis of a prospective trial[18] demonstrated that organs donated from patients who were already on extracorporeal membrane support were viable for transplantation. In a subset of patients receiving ECPR, graft survival was high, reaching 89%. The most common organ donated was kidney, followed by liver and heart. The included studies indicate that patients who received ECPR are a potential source of donor organs and that organs donated from patients who received ECPR can have good graft survival.

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RECOVERY AND SURVIVORSHIP AFTER CARDIAC ARREST

Recommendations for Recovery and Survivorship After Cardiac Arrest		
COR	**LOE**	**Recommendations**
1	B-R	1. It is recommended that cardiac arrest survivors and their caregivers have structured assessment and treatment/referral for emotional distress after medical stabilization and before hospital discharge.
1	C-LD	2. It is recommended that cardiac arrest survivors have multimodal rehabilitation assessment and treatment for cognitive, physical, neurological, and cardiopulmonary impairments before hospital discharge.
1	C-LD	3. It is recommended that cardiac arrest survivors and their caregivers have multidisciplinary discharge planning, to include medical and rehabilitative treatment recommendations and return to activity/work expectations.
2b	B-R	4. Interventions to address health care professional burnout may be beneficial.
2b	C-LD	5. Debriefings and referral for follow-up for emotional support for lay rescuers, emergency medical services professionals, and hospital-based health care professionals after a cardiac arrest event may be beneficial.

Synopsis

Survivors of cardiac arrest experience emotional, social, physical, neurological, and cognitive sequalae, which can manifest during or after hospitalization.[1,2] Broadly defined, survivorship is the journey from stabilization through rehabilitation, recovery, and societal reintegration.[1] Improving cardiac arrest survivorship involves families, health

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care partners, and communities. Caregivers of cardiac arrest survivors also experience emotional and social challenges as they navigate survivorship issues.[1,2]

Optimizing survivorship for survivors and their caregivers involves in-hospital screening, treatment, referral, and postdischarge surveillance of postarrest sequalae.[1] Survivorship plans given at discharge can provide direction by including a summary of the inpatient course, individualized medical and rehabilitative treatment recommendations, and postdischarge recovery expectations.[1] All those impacted by cardiac arrest can be powerful advocates for informing community responses to cardiac arrest, tailored interventions, and relevant patient-/family-centered outcomes.[1]

Finally, lay rescuers, emergency medical services professionals, and hospital-based health care professionals who care for cardiac arrest patients often experience distress.[3,4] Debriefings after witnessing cardiac arrest events, identifying the natural stressors associated with caring for such patients, and offering well-being interventions or referrals for follow-up mental health services may provide opportunities to mitigate distress and burnout.

Recommendation-Specific Supportive Text

1. Approximately one fourth of cardiac arrest survivors and their caregivers experience emotional distress (including anxiety, depression, and posttraumatic stress).[1,5–8] Fatigue is also common and may be related to distress and physical and cognitive symptoms.[2,9–11] Often, these symptoms begin to manifest during hospitalization and can linger from months to years.[7,9,10]
   One RCT compared a psychosocial intervention between 2 groups; both groups included survivor-caregiver pairs, but in one group, only the survivors received the psychosocial intervention and in the other group, both the survivors and caregivers received the psychosocial intervention.[12,13] There were improvements in emotional distress for the survivors in both groups; however, those in the survivor-caregiver intervention group had the greatest benefit. Caregivers in the survivor-caregiver intervention group had more improvements in caregiver burden compared with the caregivers in the survivor-only intervention group.[12,13] Two other RCTs in survivors showed improvements in emotional distress in those receiving psychosocial intervention compared with control.[14–16] The evaluation before discharge is important to facilitate care coordination and referral.
2. Cognitive impairments, particularly in memory, attention, and executive function, are common in cardiac arrest survivors.[17–19] Physical, neurological, and cardiopulmonary impairments are also prevalent.[10,20–23]
   One RCT found improved quality of life in survivors enrolled in an early, cognitive-focused screening, self-management, and referral program compared to treatment as usual.[24] Three other preliminary trials demonstrated feasibility of a residential physical rehabilitation intervention, cardiac rehabilitation, and a telephone-based occupational therapy intervention in cardiac arrest survivors, with preliminary benefits in physical, cardiopulmonary, and quality of life outcomes.[25–27] The evaluation prior to discharge is important to facilitate care coordination and referral.
3. Community reintegration and return to work or other daily activities may be slow and depend on availability of social support and degree of postarrest sequelae.[27–31] Survivors and caregivers need direction on managing their postarrest challenges (eg, guidance on possibility of experiencing psychological, cognitive, physical, neurological, and cardiopulmonary symptoms and which professionals to seek out should they arise) and returning to daily activities.[1,2]
4. Burnout among health care professionals is common,[32] is not unique to those who provide care for patients with cardiac arrest, and is often characterized by emotional exhaustion, depersonalization/cynicism, and reduced sense of personal accomplishment.[33] Burnout negatively impacts health care professionals' productivity (eg, absenteeism, turnover) and patient care (eg, reduced patient satisfaction and increased clinician errors).[34,35]
   Seven RCTs targeting burnout in health care professionals all led to some improvement in at least one dimension of burnout or mental health outcome. Intervention mechanisms varied considerably, including yoga, mindfulness, gratitude journaling, various other positive psychology exercises, and individualized professional coaching. Benefits included improved well-being, work engagement, quality of life, perceived stress, and depressive and anxiety symptoms.[36–42]
   Although these results are promising, variability in intervention methods and outcome measures, considerable attrition, and high risk of bias inherent in behavioral trials limit the degree to which any single well-being intervention method can be recommended.
5. Rescuers and hospital-based health care professionals may experience emotional distress caring for a cardiac arrest patient.[3,4,43,44] Team debriefings may allow for quality improvement as well as recognition of the natural stressors associated with caring for a cardiac arrest patient. In one qualitative study of lay rescuers and one nonrandomized study of emergency department professionals, participants reported benefitting emotionally from

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debriefings[45,46]; however, a scoping review found that nurses may prefer to not discuss distress during debriefings and rather to pursue support later.[43]

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Disclosures

Appendix 1. Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Karen G. Hirsch	Stanford University	NIH*	None	None	None	None	None	None
Jon C. Rittenberger	Guthrie Medical Center	None	None	None	Cipriani & Warner: Defense Expert†	None	UpToDate*	None
Edilberto Amorim	University of California, San Francisco, Weill Institute for Neurosciences	NINDS†; American Heart Association†; Hellman Foundation†; Zoll Foundation†; CURE Epilepsy†; Regents of the University of California†; Department of Defense†; Cures Within Reach†; Department of Defense†; NIH†	None	None	None	None	None	None
Patrick J. Coppler	University of Pittsburgh	NIH*	None	None	None	None	None	None
Ian R. Drennan	University of Toronto Ornge Critical Care and Transport Medicine Sunnybrook Health Sciences (Canada)	ZOLL†	None	ZOLL†	None	None	None	None
Andrea Elliott	Regents of the University of Minnesota	None	None	None	None	None	None	None
Alexandra June Gordon	Stanford University	None	None	None	None	None	None	None
Jacob C. Jentzer	Mayo Clinic	None	None	None	None	None	None	None
Nicholas J. Johnson	University of Washington/Harborview Medical Center	NIH†; American Heart Association†	None	None	None	None	Neuroptics, Inc*	None

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Appendix 1. Continued

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Ari Moskowitz	Montefiore Medical Center	NIH/NHLBI†; American Heart Association†	None	None	Expert Witness*	None	Aquestive Therapeutics*	None
Bryn E. Mumma	University of California Davis	None	None	None	None	None	None	None
Alexander M. Presciutti	Massachusetts General Hospital	National Center for Complementary and Integrative Health†; Neurocritical Care Society*	None	None	None	None	Cardiac arrest survivor alliance*	None
Amber J. Rodriguez	American Heart Association National Center	None	None	None	None	None	None	None
Albert Yen	University of California	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.

‡Author chose not to endorse the final Post-Cardiac Arrest Care chapter or be listed with the writing group.

Appendix 2. Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Jestin N. Carlson	Allegheny Health Network	None	None	None	None	None	None	None
Romergryko G. Geocadin	Johns Hopkins University School of Medicine	NIH (Preclinical and clinical research on cardiac arrest brain injury)†	None	None	Medicolegal Consulting†	None	None	None
Teresa L. May	MaineHealth	NINDS (PRECICEAP co-I)*	None	None	None	None	None	None
Mary Ann Peberdy	Virginia Commonwealth University	American Heart Association (drone delivery of AEDs)*	None	None	None	None	None	None
Janice Zimmerman	The Methodist Hospital Physician Organization	None	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.

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