European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2025: Post-resuscitation Care

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[h1]Abstract

The European Resuscitation Council (ERC) and the European Society of Intensive Care Medicine (ESICM) have collaborated to produce these post-resuscitation care guidelines for adults, which are based on the International Consensus on Cardiopulmonary Resuscitation Science with Treatment Recommendations (CoSTR) pubished by the International Liaison Committee on Resuscitation (ILCOR). The topics covered include the post-cardiac arrest syndrome, diagnosis of cause of cardiac arrest, control of oxygenation and ventilation, coronary reperfusion, haemodynamic monitoring and management, control of seizures, temperature control, general intensive care management, prognostication, long-term outcome, rehabilitation, and organ donation. The post-resuscitation care of children is described in the ERC guidelines 2025 Paediatric Life Support.

Key words

Post-cardiac arrest, diagnosis, complications, temperature control, prognostication, rehabilitation, withdrawal of life sustaining treatment.

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109 **Abbreviations**

ACNS	American Clinical Neurophysiology Society
ACS	Acute coronary syndrome
ADC	Apparent diffusion coefficient
AF	Atrial fibrillation
AHA	American Heart Association
AKI	Acute kidney injury
ALS	Advanced Life Support
AMI	Acute myocardial infarction
ANZCOR	Australian and New Zealand Committee on Resuscitation
ARDS	Acute respiratory distress syndrome
ATP	Adenosine triphosphate
ACVC	Association for Acute Cardiovascular Care of the European Society of Cardiology
BIS	Bi-spectral index
BOX	Blood Pressure and Oxygenation Targets After OHCA
BS	Burst suppression
CAC	Cardiac arrest centre
CAD	obstructive coronary artery disease
CAG	Coronary angiography
CBF	Cerebral blood flow
CIDS	Canadian implantable defibrillator study
CORTICA	Corticosteroids in in-hospital cardiac arrest
COSCA	Core Outcome Set for Cardiac Arrest
CoSTR	Consensus on Cardiopulmonary Resuscitation Science with Treatment Recommendations
CPC	Cerebral Performance Category
CPR	Cardiopulmonary resuscitation
CR	Corneal reflex
CT	Computed tomography
DBD	Organ donation after brain death
DCD	Donation After Circulatory Determination of Death

DVT	Deep venous thrombosis
DWI	Diffusion-weighted imaging
ECG	Electrocardiogram
ECPR	Extracorporeal cardiopulmonary resuscitation
EEG	Electrographic seizure
EHRA	European Heart Rhythm Association
ESAIC	European Society of Anaesthesiology and Intensive Care
ESC	European Society of Cardiology
ESE	Electrographic status epilepticus
ESICM	European Society of Intensive Care Medicine
EUSEM	European Society for Emergency Medicine
FPR	False positive rate
FSS	Fatigue Severity Scale
GFAP	Glial fibrillary acidic protein
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
GWR	Grey White Matter ratio
HADS	Hospital Anxiety and Depression Scale
HIBI	Hypoxic ischaemic brain injury
HSFC	Heart and Stroke Foundation of Canada
IAHF	Inter-American Heart Foundation
ICD	Implantable cardioverter defibrillator
ICP	Intracranial pressure
ICU	Intensive care unit
ILCOR	International Liaison Committee on Resuscitation
LBBB	Left bundle branch block
LMWH	Low molecular weight heparin
MAP	Mean arterial pressure
MCS	Mechanical circulatory support
MFIS	Modified Fatigue Impact Scale
MRI	Magnetic resonance imaging
NSE	Neuron specific enolase
OHCA	Out-of-hospital cardiac arrest

PCAS	Post-Cardiac Arrest Syndrome
PCI	Percutaneous coronary intervention
PLR	Pupillary light reflex
PPCI	Primary percutaneous coronary intervention
RASS	Richmond Agitation Sedation Scale
RCA	Resuscitation Council of Asia
RCSA	Resuscitation Council of Southern Africa
ROC	Receiver operating characteristic
ROSC	Return of spontaneous circulation
SBP	Systolic blood pressure
SCA	Sudden cardiac arrest
SCD	Sudden cardiac death
SDMT	Symbol Digit Modalities Test
SGA	Supraglottic airway
SSEP	Somatosensory evoked potential
STEMI	ST elevation myocardial infarction
STEPCARE	Sedation, TEmperature and Pressure after Cardiac Arrest and REsuscitation
TBI	Traumatic brain injury
TCD	Transcranial Doppler
VF	Ventricular fibrillation
VT	Ventricular tachycardia
WLST	Withdraw of life-sustaining therapy

[h1]Introduction and scope

In 2015 the European Resuscitation Council (ERC) and the European Society of Intensive Care Medicine (ESICM) collaborated to produce their first combined post-resuscitation care guidelines, which were co-published in *Resuscitation* and *Intensive Care Medicine*.[1,2] These 2025 guidelines represent the third collaboration between the ERC and ESICM and reflect the science published since the previous guidelines published in 2021.[3,4] The topics covered include the post-cardiac arrest syndrome, control of oxygenation and ventilation, haemodynamic targets, coronary reperfusion, targeted temperature management, control of seizures, prognostication, long-term outcome and rehabilitation.

[h1]Methods

[h2]The international consensus on cardiopulmonary resuscitation science evidence review process

The International Liaison Committee on Resuscitation (ILCOR, www.ilcor.org) includes representatives from the American Heart Association (AHA), the European Resuscitation Council (ERC), the Heart and Stroke Foundation of Canada (HSFC), the Australian and New Zealand Committee on Resuscitation (ANZCOR), the Resuscitation Council of Southern Africa (RCSA), the Inter-American Heart Foundation (IAHF), the Resuscitation Council of Asia (RCA), and the Indian Resuscitation Council Federation (IRCF). From 2000 to 2015, researchers from the ILCOR member councils evaluated resuscitation science in 5-yearly cycles. After the publication of the 2015 International Consensus on Cardiopulmonary Resuscitation Science with Treatment Recommendations (CoSTR),[5] ILCOR committed to a continuous evidence-evaluation process, with topics prioritised for review by the task forces and with the CoSTR updates published annually. For the 2025 CoSTR, the six ILCOR task forces performed three types of evidence evaluation: the systematic review, the scoping review, and the evidence update.[6] Only systematic reviews (these used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology) could result in new or modified treatment recommendations.[7] The data analysis from each systematic review was presented to the task force, and the task force drafted the summary CoSTR. Each treatment recommendation indicated the strength of the recommendation and the certainty of the evidence. Draft 2025 CoSTRs were posted on the ILCOR website (ilcor.org) for a 2-week comment period, after which final wording of science statements and treatment recommendations were completed by the task forces and published in *Resuscitation* and *Circulation* as the 2025 CoSTR.[6]

[h2] The European Resuscitation Council (ERC) and European Society for Intensive Care Medicine (ESICM) Process for Developing Post-Resuscitation Care Guidelines

Fourteen individuals were selected for the ERC-ESICM Post-Resuscitation Care Writing Group based on their expertise, ERC and ESICM representation, and diversity (gender, physician, non-physician, survivor, seniority (senior and mid-career), and geography (Northern and Southern Europe)). These ERC-ESICM guidelines on post-resuscitation care for adults are based mainly on the advanced life support section of the 2025 CoSTR document and represent consensus among the writing group, which included representatives of the ERC and the ESICM.[8] Where treatment recommendations are

provided by ILCOR, these have been adopted by the ERC and ESICM. In the absence of an ILCOR recommendation or good practice statement, ERC-ESICM guidance was based on review and discussion of the evidence by the working group until consensus was achieved, and more direct language is used. The writing group chairs ensured that everyone on the working group had the opportunity to present and debate their views and ensured that discussions were open and constructive. All discussions took place during 14 videoconferences that were held between April 2024 and March 2025. Consensus was achieved by all 14 writing group members on all the treatment recommendations using an open process.

These guidelines were drafted and agreed by the Post-Resuscitation Care Writing Group members and the Guideline Steering Committee before posting on the ERC website for public comment between XX and XX 2025. The opportunity to comment on the guidelines was advertised through social media (Facebook, X formally known as Twitter) and the ERC network of 33 national resuscitation councils. XX individuals from XX countries made XX comments. A total of [INSERT NUMBER] individuals from [INSERT COUNTRIES] submitted [INSERT NUMBER] comments, leading to [INSERT CHANGES] in the final version. The guidelines were presented to and approved by the ERC General Assembly on DATE.

[h1]Summary of the Key Changes

A summary of the main changes from the 2021 ERC-ESICM Post-resuscitation care guidelines is set out in Table 1.

Table 1. Comparison of ERC-ESICM Post-Resuscitation Care Guidelines (2021 vs 2025)

Diagnosis of Cause and Complications of Cardiac Arrest	Suggested coronary angiography first in patients with myocardial ischemia. CT brain and chest scan were considered if coronary angiography did not find causative lesions.	Coronary angiography remains first if ST-elevation is present; otherwise, whole-body CT scan (including head, neck, chest, abdomen, pelvis, and CT pulmonary angiography) takes priority.
Airway and Oxygenation Management	Recommendation to start with 100% oxygen immediately after ROSC, then titrate to 94-98%	Maintains recommendation and adds explicit guidance highlighting inaccuracies in

	SpO_2 or PaO_2 10–13 kPa (75-100 mmHg).	pulse oximetry in patients with darker skin tones.
Ventilation Management	Recommended normocapnia ($PaCO_2$ 4.7–6.0 kPa (35-45 mmHg)).	Maintains recommendation with additional caution in patients with hypothermia, noting risk of hypocapnia.
Coronary Reperfusion Strategy	Immediate coronary angiography strongly considered in OHCA without ST-elevation if high likelihood of coronary occlusion.	Suggests delaying cardiac catheterisation if clinical context does not clearly indicate a high likelihood of acute coronary occlusion in OHCA patients without ST-elevation.
Hemodynamic Management	Emphasised targeting MAP >65 mmHg guided by adequate urine output and lactate normalization.	Specifies MAP target of >60–65 mmHg.
Post-ROSC arrhythmias	Not included in any detail	Section added on recurrent and refractory arrhythmias post-ROSC
Seizure Management	Recommended EEG monitoring.	Explicitly states patients with myoclonus but benign EEG backgrounds should undergo wake-up trials days after arrest.
Temperature Management	Recommended targeted temperature management at 32-36°C for at least 24 hours and fever avoidance (>37.7°C) for at least 72 hours post-ROSC.	Preferred terminology is temperature control. Recommends actively preventing fever ≤37.5°C for at least 72 hours post-ROSC.
General Intensive Care Management	Recommended prophylactic stress ulcer prophylaxis and thromboembolism prophylaxis.	Maintains previous recommendations. Emphasises using short-acting

		sedatives to facilitate neurological assessment, discourages routine neuromuscular blocking drugs unless severe acute respiratory distress syndrome.
Neurological Prognostication	Emphasised multimodal neurological assessment at ≥72 hours.	Maintains recommendation with specified indicators of favourable neurological outcome and suggested timing for brain CT and SSEP recording added to the algorithm.
Rehabilitation and Follow-up	Recommended functional assessment before discharge and follow-up within 3 months post discharge including screening of cognitive, emotional problems and fatigue. Brain injury and cardiac rehabilitation when indicated.	Maintains recommendations and adds structured guidance on rehabilitation in the ICU including early mobilisation, delirium management, ICU diaries, and to address physical limitations during follow-up. Stronger focus on the involvement of co-survivors.
Organ Donation	Recommended considering organ donation post-resuscitation.	Maintains recommendation and adds recommendations for cardiac arrest registries to report organ donation activities.
Investigating Unexplained Cardiac Arrest	Not included.	New recommendations for comprehensive diagnostic work-up (including genetic testing, cardiac MRI, sodium channel blocker tests, exercise

	testing) and emphasises long-term follow-up.

[h1]Concise guidelines for clinical practice

This section includes only a summary of the main recommendations. The evidence underpinning each recommendation is detailed in the section on 'evidence informing the guidelines'.

[h2]Immediate post-resuscitation care

- Post-resuscitation care is started immediately after sustained return of spontaneous circulation (ROSC), regardless of location (Figure 1).

[h2]Diagnosis of cause and complications of cardiac arrest

- Early identification of a non-coronary cause can be achieved by performing transthoracic echocardiography and a whole body computed tomography (CT) scan (including head, neck, chest, abdomen, pelvis, and CT pulmonary angiography) at hospital admission, before or after coronary angiography if indicated.
- In patients with persistent ST-elevation on the electrocardiogram (ECG) (or equivalent), undertake coronary angiography first. Perform a head-to-pelvis CT scan (including CT pulmonary angiography) if coronary angiography fails to identify causative lesions.
- If there are signs or symptoms pre-arrest suggesting a non-coronary cause (e.g. headache, seizures or neurological deficits, shortness of breath or documented hypoxaemia in patients with known respiratory disease, abdominal pain), perform a whole body CT-scan (including CT pulmonary angiography).

[h2]Airway and breathing

[h3]Airway management after return of spontaneous circulation

- Airway and ventilation support should continue after ROSC is achieved.
- Patients who have had a brief period of cardiac arrest and an immediate return of normal cerebral function and are breathing normally, may not require airway or ventilatory support but should be given supplemental oxygen via a facemask if their arterial blood oxygen saturation is less than 94%.

- Patients who remain comatose following ROSC, or who have another clinical indication for sedation and mechanical ventilation, should have their trachea intubated if this has not been done already during CPR.
- Tracheal intubation (with or without drugs) should be performed only by experienced operators who have a high success rate.
- Correct placement of the tracheal tube must be confirmed with waveform capnography.
- In the absence of personnel experienced in tracheal intubation, it is reasonable to retain or insert a supraglottic airway (SGA) or maintain the airway with basic techniques until personnel skilled in drug-assisted tracheal intubation are available.
- Post ROSC patients may require drug assisted tracheal intubation – the same level of care should be provided as for any other critically ill patient with a physiologically or anatomically challenging airway in terms of skills of the provider, monitoring, and choice of drugs for induction, and maintenance of sedation

[h3]Control of oxygenation

- Immediately after ROSC, use 100% (or the maximum available) inspired oxygen until the arterial oxygen saturation (SpO_2) can be measured and titrated reliably with pulse oximetry or the partial pressure of arterial oxygen (PaO_2) can be measured.
- As soon as SpO_2 can be measured reliably or arterial blood gas values are obtained, titrate the inspired oxygen to achieve an arterial oxygen saturation of 94-98% or arterial partial pressure of oxygen (PaO_2) of 10–13 kPa (75–100 mmHg). Be aware that pulse oximetry can overestimate the true oxygen saturation in people with darker skin tones.
- Avoid hypoxaemia (PaO_2 < 8 kPa or 60 mmHg) following ROSC.
- Avoid hyperoxaemia77 following ROSC.

[h3] Control of ventilation

- Obtain arterial blood gases and use end tidal CO_2 in mechanically ventilated patients.
- Target normocapnia (a partial pressure of carbon dioxide of 35-45 mm Hg or approximately 4.7-6.0 kPa) in adults with ROSC after cardiac arrest.
- In patients with accidental hypothermia or treated with hypothermia monitor $PaCO_2$ frequently as hypocapnia may occur.
- In hypothermic patents use consistently either temperature or non-temperature corrected blood gas values.

- Use a lung protective ventilation strategy aiming for a tidal volume of 6–8 mL kg^{-1} ideal body weight.

[h2]Circulation

[h3]Coronary reperfusion

- Emergent cardiac catheterisation laboratory evaluation (and primary percutaneous coronary intervention (PPCI) if required) should be performed in adult patients with ROSC after cardiac arrest of suspected cardiac origin with persistent ST-elevation on the electrocardiogram (ECG).
- In patients with ROSC after out-of-hospital cardiac arrest (OHCA) without ST-elevation on the ECG, cardiac catheterisation laboratory evaluation should be delayed unless the clinical context suggests a high likelihood of acute coronary occlusion.

[h3] Haemodynamic monitoring and management

- All patients should be monitored with an arterial line for continuous blood pressure measurements, and it is reasonable to monitor cardiac output in haemodynamically unstable patients.
- Perform echocardiograpy as soon as possible in all patients to detect any underlying cardiac pathology and quantify the degree of myocardial dysfunction.
- Avoid hypotension and target a mean arterial pressure (MAP) >60–65 mmHg after cardiac arrest (Figure 2).
- Maintain perfusion with fluids, noradrenaline and/or dobutamine, depending on individual patient need for intravascular volume, vasoconstriction or inotropy.
- Do not give steroids routinely after cardiac arrest.
- Avoid hypokalaemia and hyperkalaemia, which are associated with ventricular arrhythmias.
- In select patient populations (e.g. Glasgow Coma Scale score ≥8 on hospital arrival, with ST-elevation myocardial infarction (STEMI) and <10 minutes cardiac arrest) consider mechanical circulatory support (such as intra-aortic balloon pump, left-ventricular assist device or arterio-venous extra corporal membrane oxygenation) for persisting cardiogenic shock from left ventricular failure if treatment with fluid resuscitation, inotropes, and vasoactive drugs is insufficient. Left-ventricular assist devices or arterio-venous extra corporal membrane oxygenation should also be considered in haemodynamically unstable patients with acute coronary syndromes (ACS) and recurrent ventricular tachycardia (VT) or ventricular fibrillation (VF) despite optimal therapy.

[h3] Post-ROSC arrhythmias

- In patients with arrhythmia immediately after ROSC, follow the ALS guideline for peri-arrest arrhythmia.
- In patients with arrhythmia after ROSC, treat any potential underlying causes, such as coronary occlusion or electrolyte disorders.
- In patients with no arrhythmia after ROSC, do not routinely give anti-arrhythmic drug prophylaxis.

[h2]Disability (optimising neurological recovery)

[h3]Control of seizures

- Use electroencephalography (EEG) to diagnose electrographic seizures in patients with clinical convulsions and to monitor treatment effects.
- Use levetiracetam or sodium valproate as first-line antiepileptic drugs in addition to sedative drugs to treat seizures after cardiac arrest.
- Do not use seizure prophylaxis in post-cardiac arrest patients.
- Attempt a wake-up trial in patients with myoclonus and benign EEG background (days after arrest).

[h3] Temperature control

- Actively prevent fever by targeting a temperature ≤37.5 °C for patients who remain comatose after ROSC from cardiac arrest.
- Comatose patients with mild hypothermia (32–36°C) after ROSC should not be actively warmed to achieve normothermia.
- We recommend against the routine use of prehospital cooling with rapid infusion of large volumes of cold intravenous fluid immediately after ROSC.
- Use surface or endovascular temperature control techniques when temperature control is used in comatose patients after ROSC.
- When a cooling device is used, we suggest using a temperature control device that includes a feedback system based on continuous temperature monitoring to maintain the target temperature.
- Prevent active fever for 36 to 72 hours in post-cardiac arrest patients who remain comatose.

[h3] Other therapies to improve neurological outcome

- There is insufficient evidence to recommend the use of any specific drug therapy for comatose survivors of cardiac arrest.

[h2] General intensive care management

- Do not use prophylactic antibiotics routinely in patients following ROSC. However, it is reasonable to have a low threshold for giving antibiotics when there is any clinical suspicion of pneumonia.
- Use short acting sedative agents when treating post-cardiac arrest patients receiving mechanical ventilation – this may enable earlier clinical examination that is less confounded by sedation when assessing neurological recovery.
- We do not recommend systematic use of neuromuscular blocking drugs in comatose post-cardiac arrest patients.
- In patients with critical hypoxaemia and ARDS following cardiac arrest, the use of a neuromuscular blocker may be considered.
- Patients should be nursed 30° head-up.
- It is reasonable to start gastric feeding at low rates (trophic feeding) and increase as tolerated.
- Given the high incidence of upper gastrointestinal ulceration in post-cardiac arrest patients and the use of anticoagulant and antiplatelet drugs both pre and post arrest, use stress ulcer prophylaxis in post-cardiac arrest patients, especially in those with coagulopathy.
- Anticoagulation of post-cardiac arrest patients should be individualised and be based on general ICU recommendations.
- Use standard glucose management protocols for adults with ROSC after cardiac arrest.

[h2] Predicting neurological outcome

[h3] General guidelines

- In patients who are comatose after resuscitation from cardiac arrest, neurological prognostication should be performed using clinical examination, electrophysiology, biomarkers, and imaging, to both inform the patient's relatives and to help clinicians to target treatments based on the patient's chances of achieving a neurologically meaningful recovery (Figure 3).
- No single predictor is 100% accurate. Use multimodal neuroprognostication strategies.
- When predicting poor neurological outcome, a high specificity and precision are desirable, to avoid falsely pessimistic predictions. When predicting good outcome, the aim is to identify those

patients with a better potential for recovery. Since the consequence of a false prediction in this setting is less severe, the predictive performance of the test is not as critical. Both predicting good and poor outcome are important, to reduce prognostic uncertainty.

- The clinical neurological examination is central to prognostication. To avoid falsely pessimistic predictions, clinicians should exclude potential residual effects of sedatives and other drugs that may confound the results of the tests.
- Index tests for neurological prognostication are aimed at assessing the severity of hypoxic-ischaemic brain injury. Neurological prognosis is one of several aspects to consider in discussions about an individual's potential for recovery.

[h3]Clinical examination

- Clinical examination is prone to interference from sedatives, opioids or muscle relaxants. Potential confounding from residual sedation should always be considered and excluded.
- Consider neurological prognostication in patients who are not awake and obeying commands (Glasgow coma scale motor score <6) at 72 h or later after ROSC
- In unconscious patients at 72 h or later after ROSC, the following tests may predict a poor neurological outcome:
    - The bilateral absence of the pupillary light reflex.
    - The bilateral absence of corneal reflex
    - The presence of myoclonus within 96 h and, in particular, status myoclonus within 72 h.
- We also suggest recording the EEG in the presence of myoclonic jerks to detect any associated epileptiform activity or to identify EEG signs, such as background reactivity or continuity, suggesting a potential for neurological recovery.

[h3]Neurophysiology

- Perform EEG to predict outcome and detect seizure activity in comatose patients. Routine EEG or continuous EEG monitoring may be used.
- Suppressed background with or without periodic discharges and burst suppression on EEG ('highly malignant' patterns) are accurate indicators of a poor prognosis. We suggest using these EEG patterns after 24 h from ROSC.
- The bilateral absence of somatosensory evoked cortical N20 potentials indicates poor prognosis after cardiac arrest.

- Always consider the EEG and somatosensory evoked potentials (SSEPs) results in the context of clinical examination findings and other tests. Always consider using a neuromuscular blocking drug when performing SSEP.

[h3]Biomarkers

- Use serial measurements of neuron specific enolase (NSE) to predict outcome after cardiac arrest. Increasing values between 24 and 48 h or 72 h in combination with high values at 48 and 72 h indicate a poor prognosis.

[h3]Imaging

- Use brain imaging studies to predict poor neurological outcome after cardiac arrest. Ensure that the images are evaluated by someone with specific experience in these studies.
- Use presence of generalised brain oedema, manifested by a marked reduction of the grey matter/white matter ratio on brain CT, or extensive diffusion restriction on brain MRI to predict poor neurological outcome after cardiac arrest.
- Repeat the brain CT if the patient is unconscious at the time of prognostication (72 h–96 h after ROSC) and the first brain CT does not show signs of HIBI.

[h3] Multimodal prognostication

- Once major confounders have been excluded, start the prognostication assessment with an accurate clinical examination (Figure 4).
- In an unconscious patient at ≥72 h from ROSC, in the absence of confounders, poor outcome is likely when two or more of the following predictors are present: no pupillary and corneal reflexes at ≥72 h, bilaterally absent N20 somatosensory evoked potential (SSEP) wave at ≥24 h, highly malignant EEG at >24 h, neuron specific enolase (NSE) >60 µg L^{-1} at 48 h and/or 72 h, status myoclonus ≤72 h, or a diffuse and extensive anoxic injury on brain CT/MRI. Most of these signs can be recorded before 72 h from ROSC, however, conclusions on prognosis will be made only at the time of clinical prognostic assessment at ≥72 h.

[h2] Withdrawal of life-sustaining therapy

- Separate discussions around withdrawal of life-sustaining therapy and the assessment of prognosis for neurological recovery; withdrawal of life-sustaining therapy decisions should

consider aspects other than brain injury such as age, co-morbidity, general organ function and the patients' preferences.

- Allocate sufficient time for communication around the level-of-treatment decision within the team and with the relatives.
- After a decision on withdrawal of life-sustaining therapy, use a structured approach to shift from curative to end-of-life palliative care and consider organ donation.

[h2] Rehabilitation and follow-up after cardiac arrest

- Implement early mobilisation, delirium management and ICU diaries during hospitalisation
- Provide information for patients and co-survivors
- Perform functional assessments of physical and non-physical impairments before discharge to identify rehabilitation needs and refer to early rehabilitation if indicated.
- Provide cardiac rehabilitation as indicated by the cause of the cardiac arrest.
- Organise a follow-up of cardiac arrest survivors within three months after hospital discharge; screening for cognitive, physical, emotional problems, fatigue, and impact on life roles
- Invite co-survivors to the follow-up; ask about emotional problems and impact on life roles
- Undertake specialist referral and further rehabilitation as indicated.

[h2]Organ donation

- We recommend that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated for organ donation.
- In comatose ventilated patients who do not fulfil neurological criteria for death, if a decision to start end-of-life care and withdrawal of life support is made, organ donation should be considered for when circulatory arrest occurs.
- All decisions concerning organ donation must follow local legal and ethical requirements.
- Cardiac arrest registries should report if organ donation after initial resuscitation from cardiac arrest occurred.

[h2] Investigating unexplained cardiac arrest

- Diagnostic testing of patients with unexplained cardiac arrest includes blood sample collection for toxicology and genetic testing, data retrieval from cardiac implantable electronic devices and wearable monitors, repeated 12 lead ECG and continuous cardiac monitoring, cardiac MRI, sodium channel blocker tests, and exercise testing.

- A confirmed diagnosis of a heritable condition should prompt targeted genetic testing.
- Long-term follow-up of unexplained cardiac arrest patients is recommended because of the high risk of recurrence of arrhythmia.

[h2]Cardiac arrest centres

- Adult patients with non-traumatic OHCA should be considered for transport to a cardiac arrest centre according to local protocols.
- Adult patients with non-traumatic OHCA should be cared for at a cardiac arrest centre whenever possible.
- Health care networks should establish local protocols to develop and maintain a cardiac arrest network.

[H1] Evidence informing the guidelines

[h2]Post-cardiac arrest syndrome

In the post-resuscitation phase, several pathophysiological mechanisms are involved in the primary ischaemic and secondary reperfusion injury.[9] The cessation of cerebral blood flow (CBF) in the no-flow phase prevents aerobic metabolism, which results in rapid depletion of adenosine triphosphate (ATP), failure of energy-dependent Na+/K+ ion exchange pumps, accumulation of intracellular calcium, and cessation of neuronal activity.[10]

Following the return of spontaneous circulation (ROSC) and restoration of CBF, reperfusion of the ischemic cerebrovascular bed causes further accumulation of intracellular calcium as a result of glutamate release, and activation of proteases and phospholipases. This causes cellular energy failure and further neuronal damage.[11] The inflammatory and coagulative cascades are activated in the post cardiac arrest syndrome, resulting in the release of cytokines which further amplify the inflammatory response and contribute to multiorgan failure.[12] In the post cardiac arrest phase, secondary brain injury may be caused by haemodynamic instability (in particular hypotension from vasodilation), derangements in arterial blood gases (hypo/hyperoxaemia, hypo/hypercapnia), hypo/hyper glycaemia, fever, with consequent altered CBF autoregulation, seizures, cerebral oedema.

The severity of the post-cardiac arrest syndrome is associated with the duration of no flow and low flow.[13] Any primary hypoxic-ischemic brain injury (HIBI) can be exacerbated directly by secondary ischaemia-reperfusion of the brain and indirectly by the extracerebral complications of generalised ischaemia-reperfusion such as respiratory failure, haemodynamic instability and multiorgan failure.[14,15]

A scientific statement by the ILCOR categorised HIBI into four distinct but overlapping phases: ischemic depolarization, reperfusion repolarization, dysregulation, and recovery and repair.[16] This document aimed also to explore the reasons of failure in translating preclinical data to clinical practice suggesting the presence of important limitations of the experimental models, but also the heterogeneity of the patients included and their post resuscitation care, suggesting a more tailored approach and the selection of specific patients which could benefit of specific treatments.

Post-resuscitation care management aims to mitigate the severity of HIBI [17] which is the most common cause of in hospital death.[16] A wide variety of drugs have been studied for their ability to improve the functional outcome of comatose cardiac arrest survivors but to date none has convincingly shown therapeutic benefit.[18] Withdrawal of life sustaining treatment (WLST) following multimodal neurological prognostication of a poor outcome accounts for most of the later deaths.[19]

[h2]Diagnosis of cause and complications of cardiac arrest

Cardiac causes, particularly ischaemic heart disease, are the most common cause of OHCA in the general adult population.[20] However, about one third of these events are due to extracardiac causes that can be identified by transthoracic echocardiography and early CT imaging, sometimes making specific therapeutic intervention possible.[21,22] Extra-cardiac causes are diverse and include acute respiratory disease, massive pulmonary embolism, intracranial haemorrhage, thromboembolic stroke and aortic dissection. Neurological causes of OHCA are relatively rare but they are strongly associated with an unfavourable neurological outcome, making early brain imaging valuable for the management of these patients.[23,24]

Early CT-scan also helps to identify traumatic complications related to CPR (such as liver and spleen lacerations or perforation of digestive tract). Many cardiac arrest patients present with resuscitation-related injuries, most commonly thoracic complications such as rib fractures, pulmonary contusion or pneumothorax, but sometimes also pelvic or abdominal complications.[25,26]

The ERC and ESICM guidelines 2021 suggested that CT brain and CT pulmonary angiogram should be considered in post-cardiac arrest patients when there is no evidence of cardiac causes.[3] Recently, several observational studies have shown that this strategy enables diagnosis or identification of a complication in 5 to 22% of cases.[27-30] In a prospective pre-/post-analysis, a standard of care strategy (i.e., CT scan at the discretion of the treating physician) was compared with a strategy of a systematic whole body CT-scan within 6 hours of hospital arrival.[27] The systematic strategy identified the cause of CA more frequently than the standard of care strategy (92 vs 75%, $p < 0.001$), with a significantly shorter time to diagnosis (3 hours vs 14 hours, $p < 0.0001$) and without an increase in the rate of complications attributable to the systematic CT-scan, such as contrast-associated renal dysfunction or transport complications (i.e. accidental extubation or line dislodgement).

[h2]Airway and breathing

[h3]Airway management after return of spontaneous circulation

Patients can have their trachea intubated before, during or following cardiac arrest depending on the setting or particular circumstances.[31] Following most cardiac arrests tracheal intubation will occur during resuscitation or if the patient remains comatose after ROSC.[32]

Tracheal intubation following ROSC in comatose patients will facilitate post-resuscitation care that includes controlled oxygenation and ventilation, protection of the lungs from aspiration of stomach

contents, and interventions to control of seizures, temperature, and brain injury – see below for further details.

Post ROSC patients are haemodynamically unstable and, depending on their level of consciousness, may require drug assisted tracheal intubation. The same level of care should be provided as for any other critically ill patient with a physiologically or anatomically challenging airway in terms of skills of the provider, monitoring, and choice of drugs for induction, and maintenance of sedation.[33-36] There are no recommendations for a specific drug combination,[37] but use of a low dose of a sedative with the aim of avoiding profound hypotension, an analgesic and a rapid onset neuromuscular blocking drug is probably optimal. Successful tracheal intubation and ventilation must be confirmed by the presence of a sustained end-tidal carbon dioxide waveform on waveform capnography.[38]

[h3]Control of oxygenation

These guidelines are informed by the ILCOR systematic review on oxygenation and ventilation targets after cardiac arrest which identified 15 studies from 12 RCTs.[8,39] The ILCOR treatment recommendations in relation to oxygenation have been adopted by ERC/ESICM:

- We recommend the use of 100% inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably in adults with ROSC after cardiac arrest in the pre-hospital setting (strong recommendation, moderate certainty evidence) and in-hospital setting (strong recommendation, low certainty evidence).
- We recommend avoiding hypoxemia in adults with ROSC after cardiac arrest in any setting (strong recommendation, very low certainty evidence).
- We suggest avoiding hyperoxemia in adults with ROSC after cardiac arrest in any setting (weak recommendation, low certainty evidence).
- Following reliable measurement of arterial oxygen levels, we suggest targeting an oxygen saturation of 94-98% or a partial pressure of arterial oxygen of 75-100 mm Hg (approximately 10-13 kPa) in adults with ROSC after cardiac arrest in any setting (good practice statement).
- 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 (good practice statement).

This guidance is based on aiming for 'normal' values of oxygenation (normoxia) given that there is evidence of harm from hypoxaemia and potential for harm from hyperoxaemia.[40]

Randomised trials in the prehospital[41] and hospital settings,[42] which compared an oxygen saturation of 90-94% with 98-100% and a PaO_2 of 68–75 mmHg (9-10 kPa) with 98–113 mmHg

(13-15 kPa) did not identify an optimal arterial oxygen saturation or partial pressure of oxygen but support normoxaemia being safe and hence the recommendations for an oxygen saturation of 94-98% or a PaO_2 target of 75-100 mm Hg (10-13 kPa). The results of the largest RCT in the prehospital setting found there were more desaturation events in the lower target group (90-94%) compared with 98-100% and suggest that early titration to a lower oxygen target is harmful.[41] There is also general consensus that hypoxaemia is harmful and interventions to mitigate this risk such as the use of a high inspired oxygen until blood oxygen values can be reliably measured with a pulse oximeter or blood gases are therefore recommended. A recent secondary analysis of the Targeted Temperature Management-2 (TTM2) trial showed an association between early severe hyperoxaemia (PaO_2 > 245 mmHg [~ 33kPa]) following intensive care admission and a poor functional outcome in patients with OHCA.[43,44] Avoiding hyperoxemia is based on very low-to-moderate certainty evidence that shows either harm or no benefit (in RCTs) from hyperoxaemia. The relationship between arterial oxygen values and mortality in critically ill patients is depicted by a U-shaped curve[45] but most RCTs evaluating the impact of hyperoxaemia have studied oxygen values on the flat central part of the curve thus missing the more extreme values that have been associated with increased mortality.[46]

Recent evidence shows that pulse oximeters can overestimate the true oxygen saturation in people with darker skin tones.[47]

There are currently two large RCTs of oxygen targets in critically-ill patients which include predefined subgroups of patients admitted to intensive care after cardiac arrest.[48,49] There is also a large study looking specifically at early restricted oxygen therapy after cardiac arrest.[50]

In most post-cardiac arrest patients, controlled oxygenation will require tracheal intubation and mechanical ventilation for at least 24-72 h. The exception being the completely conscious patient with a patent airway who should be treated with an oxygen mask or non-invasive ventilation targeting a peripheral oxygen saturation (SpO_2) of 94-98%.

[H3] Control of ventilation

These guidelines are informed by the same ILCOR systematic reviews noted in the section on oxygenation. Three RCTs addressed control of ventilation.[8,39]

After ROSC, blood carbon dioxide values ($PaCO_2$) are commonly increased because of intra-arrest hypoventilation and poor tissue perfusion,[51] causing a mixed respiratory acidosis and metabolic acidosis.[52] Carbon dioxide is a well-known regulator of blood vessel tone and cerebral blood flow.[53] Increased $PaCO_2$ (hypercapnia) increases cerebral blood flow, cerebral blood volume and

intracerebral pressure. Hypocapnia causes vasoconstriction that may decrease blood flow and cause cerebral ischaemia.[54]

The evidence for a specific $PaCO_2$ target after ROSC is inconsistent and RCTs have not shown any benefit for any specific target. The largest RCT found no differences in outcomes from targeting normocapnia (35 to 45 mmHg) or mild hypercapnia (50-55 mmHg).[55] Several studies show that end-tidal CO_2 values on waveform capnography do not closely match $PaCO_2$ values and this makes targeting specific $PaCO_2$ targets difficult when arterial blood gas measurement is not feasible. In hypothermic patients $PaCO_2$ management including measurement is particularly challenging and these patients are prone to hypocapnia.[56,57] There is currently no evidence to support a particular strategy for measuring $PaCO_2$ during hypothermia, we have therefore recommended using a consistent approach with either temperature or non-temperature correction according to local protocols.[58]

The main method for controlling $PaCO_2$ in a mechanically ventilated patient is by adjusting the minute volume by changing the ventilation frequency or tidal volume. In general, limiting the tidal volume and using a lung protective ventilation strategy is the standard of care, especially in patients with acute respiratory distress syndrome (ARDS).[59-61] Acute respiratory distress syndrome is not uncommon in cardiac arrest patients and is associated with worse outcomes.[60,62,63] Low lung compliance predicts poor functional outcome in OHCA patients.[64] Although ventilation with lower tidal volumes is not standard practice in neurointensive care,[65] an analysis of 1848 patients recruited to the TTM2 trial showed that they were ventilated with a median tidal volume of 7 mL kg^{-1} predicted body weight.[66]

The recommendation for tidal volume is based on current guidance for lung protective ventilation in the ICU [67] and limited observational data from post cardiac arrest patients.[68] One observational study suggests that using a tidal volume of 6–8 mL kg^{-1} to ventilate the lungs of out-of-hospital cardiac arrest patients in the ICU may be associated with improved outcome.[68] This study also showed that by using higher ventilation frequency normocapnia may be achieved.[68] In contrast, another observational study showed no association between tidal volume and neurological outcome after in-hospital cardiac arrest.[69] In studies of patients with brain injury after trauma or stroke protective ventilation (tidal volume < 8 mL kg^{-1} and PEEP ≥ 5 cm H_20) is not associated with mortality and lower incidence of ARDS, but is associated with improved oxygenation and is generally considered safe.[70] Patients should be nursed 30° head-up to decrease the risk of aspiration pneumonia[71] – this may also decrease intracranial pressure (ICP).

[h2]Circulation

[h3]Coronary reperfusion

Among the many causes of OHCA, acute coronary syndrome remains the most common cause in adults who survive to ICU admission with sustained ROSC.[20,72] Immediate coronary reperfusion using a strategy of primary PCI of the culprit coronary lesion has been used for more than 30 years. This invasive strategy is supported by many observational studies that reported a significant association between early PCI with survival and favourable neurological outcome after OHCA. While the benefit of early PCI for OHCA caused by a recent coronary occlusion is generally accepted, the main challenge is to identify the best candidates for coronary angiography among all resuscitated patients.

[h4]Percutaneous coronary intervention following ROSC with ST-elevation

In patients with ST segment elevation or left bundle branch block on the post-ROSC electrocardiogram (ECG), more than 80% will have an acute coronary lesion.[73] A systematic review completed for the 2021 ILCOR CoSTR identified five observational studies.[74] An ILCOR evidence update in 2025 identified no additional studies involving participants with ST-elevation. Unadjusted data from the five observational studies indicated benefit at various time points for survival and survival with favourable neurologic outcome; however, none of these studies confirmed such benefit when reporting adjusted data.[74] Nevertheless, given the strong evidence for benefit of early PCI for STEMI (without cardiac arrest), the ERC-ESICM treatment recommendation from 2021 was to recommend that emergent cardiac catheterisation laboratory evaluation (and immediate PCI if required) should be performed in adult patients with ROSC after cardiac arrest of suspected cardiac origin with ST-elevation on the ECG.[3] The 2023 European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes also state that 'a primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG with persistent ST-segment elevation (or equivalents as defined in the ESC Guidelines).[75]

[h4]Percutaneous coronary intervention following ROSC without ST-elevation

In OHCA patients without ST segment elevation, several large observational series showed that absence of ST segment elevation does not completely exclude the presence of a recent coronary occlusion.[76,77] However, the proportion of patients with recent acute coronary occlusion is small and several studies have shown a lack of benefit with systematic early coronary angiography in this population. Large, randomised trials (COACT, TOMAHAWK) have shown that immediate routine

early coronary angiography is not superior to a delayed invasive strategy in OHCA with an initial shockable rhythm and without ST-segment elevation or equivalent and without cardiogenic shock.[78,79] Smaller trials (EMERGE, PEARL, and COUPe) have also reached the same conclusion,[80-82] and a meta-analysis of these five RCTs confirmed the absence of benefit in the general population and in the different subgroups (age, initial cardiac rhythm, history of coronary artery disease, presumed ischemic event as the cause of arrest, time to ROSC).[83] The 2025 ILCOR treatment recommendation is unchanged from 2020 and states: 'when early coronary angiography is considered for comatose post-arrest patients without ST elevation, we suggest that either an early or delayed approach for angiography is reasonable (weak recommendation, low-certainty evidence)'.[8] The 2023 ESC guidelines for the management of acute coronary syndromes in patients without persistent ST-segment elevation favour a delayed approach and state that 'routine immediate angiography after resuscitated cardiac arrest is not recommended in haemodynamically stable patients without persistent ST-segment elevation (or equivalents)'.[75] Delaying coronary angiography may buy time for initial management in ICU, enabling early initiation of post-resuscitation care and prognostication. This 'wait and see' management may also avoid performing coronary angiography in patients with the lowest probability of an acute coronary lesion.

When an ischaemic cause is considered likely, a similar approach as for patients with STEMI should be followed. The decision for early coronary angiography should be based on careful assessment of the patients for the presence of haemodynamic or electrical instability and ongoing myocardial ischaemia taking into account multiple factors including previous medical history, prearrest warning symptoms, initial cardiac rhythm for cardiac arrest, ECG pattern post ROSC, and echocardiography, as well as comorbidities.

Brain injury caused by cardiac arrest should be considered in the decision. Ideally, coronary interventions would be undertaken only in those patients without permanent severe neurological injury. Patients with irreversible hypoxic–ischaemic brain injury are unlikely to benefit from PCI, even if a culprit coronary lesion is successfully treated.[84] However, the absence of a universally acceptable prognostic tool in the first hours after ROSC makes it impossible to identify such patients with high sensitivity and specificity prehospital or at the time of hospital admission.

[h3] Haemodynamic monitoring and management

[h4] Haemodynamic monitoring

Post-resuscitation myocardial dysfunction and low cardiac index may occur in up to 60% of post-cardiac arrest patients[85,86] and may be even more common in patients with an acute myocardial

infarction (AMI) as the cause of the arrest.[87] Early echocardiography can identify underlying cardiac pathology, quantify the degree of myocardial dysfunction and help guide haemodynamic management. Serial echocardiography or invasive monitoring with a pulmonary artery catheter quantifies myocardial dysfunction and indicates trends.[88-90] Impaired cardiac function is most common during the first 24-48 h after which it gradually resolves.[85,86] Whether low cardiac output (or index) is associated with poor outcome is currently unclear. A sub-study of the TTM2 trial showed that low cardiac index may not be associated with outcome if lactate clearance is maintained.[91] These findings were independent of target temperature. In a substudy of the Blood Pressure and Oxygenation Targets After OHCA (BOX) trial, in a multivariable analysis, a low cardiac index at admission was not associated with increased mortality.[92] Both non-invasive and invasive monitoring with echocardiography, arterial lines and measurement of cardiac output are commonly used in intensive care and it is reasonable to use these to guide treatment in cardiac arrest patients.

[h4] Haemodynamic management

[h5] Mean arterial pressure and cerebral perfusion

Guidelines on post-cardiac arrest care published in 2021 recommended targeting a mean arterial pressure (MAP) higher than 65 mmHg during the first 72 hours.[3] This was based mainly on observational data and three pilot trials.[93-95] A systematic review completed in 2023 and adoloped by ILCOR in 2024 included 4 studies with more than 1000 patients and compared a standard MAP target of higher 60–65 mmHg with targets higher than 71 mmHg.[96] The studies did not mandate the use of any specific drug or protocol to achieve the set targets, but noradrenaline was the most commonly used vasopressor. A higher MAP target was not associated with higher survival, better functional outcome or less acute kidney injury, but was also not associated with significant risks such as recurrent cardiac arrest or cardiac arrhythmias. ILCOR made a treatment recommendation to target a MAP higher than 60–65 mmHg but noted that the evidence is weak and that no studies have compared a MAP of 60–65 mmHg with lower MAP targets. In making these recommendations, ILCOR noted also that many observational studies have documented higher mortality in patients with MAP values below 60–65 mmHg. Furthermore, a MAP target of higher than 65 mmHg is common in many other critically ill patients, such as those with septic shock.

A recent scientific statement from the American Heart Association and the Neurocritical Care Society recommends targeting a MAP higher than 80 mmHg in post cardiac arrest patients. This was based mainly on the physiological rationale that cerebral blood flow is inadequate after cardiac arrest. If the ICP is elevated the cerebral perfusion pressure is likely to be compromised by a MAP of 60–65

mmHg because the MAP is one of the main determinants of cerebral blood flow (CBF).[97] Although a high MAP is generally required in non-anoxic brain injured patients because of cerebral swelling and increased intracranial pressure (ICP),[98] few data on ICP values are available in cardiac arrest survivors. In many post-cardiac arrest patients, CBF autoregulation is impaired or the lower limit is right-shifted.[99,100] This means that at lower MAP values, in some patients CBF may be MAP-dependent with an increased risk of cerebral hypoperfusion (i.e. hypotension) or hyperaemia and intracranial hypertension (i.e. hypertension).

The use of cerebral oxygen saturation or ICP monitoring to determine the presence of autoregulation and to determine an optimal MAP may enable a more individualised approach.[101] In a retrospective study, the estimated optimal MAP (i.e. MAP target at which the autoregulation is more effective) was 85 mmHg in post-cardiac arrest patients with preserved autoregulation and 100 mmHg when the autoregulation was impaired.[99] Another small observational study calculated a median optimal MAP of 89 mmHg in the same setting.[102] However, there are no prospective studies evaluating whether an autoregulation-driven MAP target may influence neurological injury and/or outcome. A more recent study has shown that after cardiac arrest, in particular in cases of non-cardiac origin, episodes of elevated ICP and/or brain hypoxia are frequent and a higher MAP is necessary to improve brain oxygenation.[102] Preliminary evidence based on measurement of brain tissue oxygenation ($PbtO_2$) has shown that in resuscitated comatose patients impairment of oxygen diffusion to the brain may cause persisting brain hypoxia despite optimisation of oxygen delivery to the brain.[103] The implementation and the safety of these invasive monitoring tools in cardiac arrest patients need to be further evaluated. While these are all observational findings, they indicate optimal MAP targets may need to be individualised and support further research into identification of optimal MAP targets for individual cardiac arrest survivors receiving intensive care.

In the post cardiac arrest patient, transcranial Doppler (TCD) can give information about cerebral haemodynamics and, in the future, may have a role in optimising haemodynamics in these patients.[104] Changes in cerebral blood flow can be seen using TCD and this may be a target for treatment.[105-107] However, the technique and interpretations of the images is operator dependent and requires an acoustic window in the patient's skull. Moreover, cerebral haemodynamics are continuously changing and serial measurements are possible only intermittently, and the monitoring is labour-intensive. No study to date has used any of these approaches to modify MAP targets in individual patients. In general, based on the evidence summarised by ILCOR[39] including the recent systematic review including more than 1000 patients,[96] the ERC/ESICM suggests avoiding hypotension and targeting a MAP>60–65 mmHg after cardiac arrest. A higher MAP target might be

appropriate in selected patients, particularly in patients with chronic hypertension and in those with persistent and documented peripheral hypoperfusion despite a MAP between 60 and 65 mmHg (oliguria, persistent high lactate value).

[h5] Heart rate

Tachycardia was associated with poor outcome in one retrospective study.[108] During hypothermic temperature control the normal physiological response is bradycardia. In animal models this has been shown to reduce the diastolic dysfunction that is usually present early after cardiac arrest.[109] Bradycardia was previously considered to be a side effect of hypothermia, especially below a rate of 40 min^{-1}; however, bradycardia has been shown to be associated with a good outcome.[110,111] Similar association between bradycardia and improved long-term outcome has been shown in patients not treated with hypothermic temperature control.[112] However, there are few studies on the association between heart rate and outcome conducted in patients treated with normothermia or with avoidance of fever only. Although bradycardia generally reduces cardiac output, this is well tolerated in this post-arrest setting. ERC/ESICIM recommends that bradycardia (heart rate < 30–40 min^{-1}) be left untreated provided there are no signs of hypoperfusion (i.e. increasing lactate, reduced urinary output etc.).

[h4] Fluid resuscitation, vasoactive and inotropic drugs

There is little evidence suggesting that the strategy for fluid therapy in post-cardiac arrest patients should differ from any other intensive care unit patients. In the initial phases, many of the patients are in cardiogenic shock but over the next hours to days the inflammatory response that accompanies the post-cardiac arrest syndrome may result in a distributive shock with accompanying hypovolaemia.[113] In less controlled prehospital environments, the rapid infusion of large volumes of cold fluid immediately after the return of spontaneous circulation is harmful.[114] Patients who are hypovolaemic (based on clinical judgement and echocardiography) will benefit from judicious fluid administration using crystalloids (either balanced solutions or normal saline). A systematic review and meta-analysis suggested that the estimated effect of using balanced crystalloids compared with saline in critically ill adults ranges from a 9% relative reduction to a 1% relative increase in the risk of death; thus, there is a high probability that using balanced crystalloids may reduce mortality.[115] However, for patients with traumatic brain injury, the effect estimate ranged from a 2% relative reduction to a 60% relative increase in risk of death.[115] Recent ESICM guidelines suggest using balanced crystalloids rather than isotonic saline for volume expansion in adult critically ill patients;[116]

however, in keeping with the findings of the systematic review,[115] these ESICM guidelines also suggest using isotonic saline rather than balanced crystalloids for volume expansion in adult critically ill patients with traumatic brain injury. No studies compared outcomes for balanced crystalloid versus isotonic saline in post-cardiac arrest patients.

The adequacy of haemodynamic optimisation that includes the use of intravenous fluids may be judged by improvement of blood pressure, adequate urinary output (>0.5 ml/kg/h) and decreasing lactate values. Several studies have documented that acute kidney injury (AKI) is common in patients after cardiac arrest with an incidence ranging from 34 to 52%.[117-121] Most cases of AKI are mild but in a sub study of the BOX trial, 77/759 (10.1%) patients required continuous kidney replacement therapy.[118] A lower mean arterial pressure (<70 mmHg) after cardiac arrest is associated with a higher incidence of AKI[122] but there is no evidence suggesting that more liberal fluid management would decrease the prevalence of AKI.[123] Recent randomised controlled trials evaluating mean arterial blood pressure targets in post-cardiac arrest care have implemented fluid therapy with meticulous monitoring. The ERC/ESICM suggests use of controlled and carefully supervised administration of fluids, including measurement of filling pressures and cardiac output in selected patients (e.g. those with myocardial dysfunction), which may help to optimise clinical outcomes.[124,125]

The ILCOR Advanced Life Support Task Force has concluded that 'there is insufficient evidence to recommend a specific vasopressor to treat low blood pressure in patients after cardiac arrest'.[8] A recent ILCOR systematic review identified only one small randomised controlled trial that included 40 patients who experienced non-traumatic cardiac arrest and had a post-ROSC mean arterial pressure (MAP) below 65 mmHg. These patients were randomised to receive either noradrenaline or adrenaline. The study reported identical 30-day mortality rates of 90% in both groups.[126] Observational studies comparing adrenaline and noradrenaline have yielded inconsistent results. [127-130] While some studies associate adrenaline use with higher hospital mortality, increased rates of cardiac re-arrest, and worse neurological outcomes,[127-129] other research has not demonstrated significant differences in survival to hospital discharge, favourable neurological outcomes, or cardiac rearrest rates.[130] Observational data suggest that the combination of dopamine with either noradrenaline or adrenaline may be associated with higher mortality or an increased risk of poor neurological outcomes compared with dopamine monotherapy.[124,131] These findings should be interpreted with caution. Despite adjustments for confounding variables, residual confounding remains a significant limitation. The results are particularly prone to confounding by indication because adrenaline and vasopressor combinations are often reserved for the most critically ill and

unstable patients. In the out-of-hospital settings, adrenaline tends to be more readily available than noradrenaline and is more likely to be used in the peri-arrest conditions.

Indirect evidence is available from studies conducted on patients with cardiogenic shock and acute myocardial infarction. In one study involving 57 patients randomised to receive either noradrenaline or adrenaline as the first-line vasopressor, the trial was prematurely discontinued because refractory shock was more common in the adrenaline-treated group.[132] Another study, which included 280 critically ill patients with hypotension, found no significant differences in clinical outcomes between the noradrenaline and adrenaline groups. However, there were more treatment withdrawals in the adrenaline group.[133] In an RCT comparing dopamine with noradrenaline in the treatment of shock, among those in cardiogenic shock dopamine was associated with an increased rate of death at 28 days (P = 0.03).[134]

Despite the scarcity of high-certainty evidence, noradrenaline is considered a reasonable first-line vasopressor for managing hypotension in patients following cardiac arrest.[135] It is the most commonly used first-line vasopressor in cases of hypotensive shock and is generally well-tolerated in post-ROSC cardiac arrest patients. Randomised trials evaluating the use of noradrenaline to achieve higher MAP targets in comatose post-ROSC patients reported no clinically significant arrhythmias requiring urgent intervention or recurrent shock, even when higher doses of noradrenaline were administered compared with lower MAP groups.[93,94,125] Noradrenaline is recommended as the first-line vasopressor for managing common comorbidities in post-ROSC cardiac arrest patients, such as cardiogenic shock due to acute heart failure, acute coronary syndromes, and sepsis.[136-139] However, in settings where noradrenaline is not available (e.g., pre-hospital), the use of adrenaline as an infusion or as small boluses may be an accepted approach. If central venous access has not been established, a dilute solution of noradrenaline (e.g., 8–40 microgram/mL) can be safely infused through a peripheral intravenous cannula.[140,141]

Echocardiography is the primary bedside imaging modality for diagnosing and monitoring acute cardiovascular conditions. It is non-invasive, rapid, and provides accurate cardiac morphology and hemodynamic assessment. Echocardiography is also valuable in guiding therapeutic procedures and can be repeated as needed, making it essential in emergency care. In shock patients, it helps in the differential diagnosis by identifying cardiac and non-cardiac causes, distinguishing various forms of cardiogenic shock, and guiding appropriate therapy.[142]

Post-resuscitation myocardial dysfunction (as confirmed by echocardiography and/or hemodynamic investigations) frequently requires inotropic support. Experimental evidence highlights dobutamine as the most established treatment in this context;[143] however, in the BOX trial the higher doses of

noradrenaline received by the high MAP target group were associated with a higher cardiac index than the lower MAP group.[144] In patients with cardiogenic shock, dobutamine is used to mitigate peripheral vasoconstriction and decrease afterload. However, its inotropic benefits are often limited in such scenarios. According to the ESC guidelines for managing cardiogenic shock, inotropic agents should be considered for patients with a systolic blood pressure below 90 mmHg and signs of hypoperfusion who do not respond to standard treatments, such as fluid resuscitation, to improve peripheral perfusion and preserve end-organ function.[138] In post-cardiac arrest patients, the systemic inflammatory response syndrome is a frequent complication, often resulting in vasoplegia and severe vasodilation.[86] In these situations, inotropic support should be initiated only after mean arterial pressure has been optimised using fluids and vasopressors. The NEUROPROTECT trial investigated the use of dobutamine to enhance cardiac index in patients within the higher MAP target group.[93] While this approach did not decrease neurological injury, it also did not worsen myocardial injury. Similarly, the BOX trial used dopamine at a maximum dose of 10 µg/kg/min alongside fluid resuscitation and noradrenaline infusion to achieve the desired MAP.[125]

[h4] Steroids

A recent ILCOR evidence update on the use of steroids in post-cardiac arrest patients included three RCTs that evaluated the role of steroids in comatose survivors of in-hospital cardiac arrest.[145-148] The first RCT demonstrated improved survival to hospital discharge when methylprednisolone, vasopressin, and adrenaline, compared with adrenaline and placebo alone, were administered during cardiac arrest, followed by hydrocortisone post-ROSC for patients in shock (19% vs. 4%; RR 4.87; 95% CI 1.17–13.79).[147] The second RCT showed improved survival to hospital discharge with favourable neurological outcomes when methylprednisolone, vasopressin, and adrenaline, compared with adrenaline and placebo alone, were administered during cardiac arrest, combined with hydrocortisone post-ROSC (13.9% vs. 5.1%; RR 2.94; 95% CI 1.16–6.50).[146] In contrast, the third RCT, which restricted the use of steroids to the post-resuscitation phase, found no benefit from steroid administration after ROSC.[148] A systematic review and individual patient data meta-analysis pooled data from these studies (n=869 patients).[149] While the analysis showed higher rates of ROSC with steroid use, it found no significant difference in survival to discharge or survival to discharge with favourable neurological outcomes. Data from one RCT showed no differences in health-related quality of life at 90 days, as measured by the EQ-5D-5L visual analogue scale and health utility index.[148]

Following the ILCOR meta-analysis, a new RCT—the CORTICA trial—compared low-dose steroids with placebo in patients with in-hospital cardiac arrest.[150] The trial included 184 patients and reported no significant differences in predefined outcomes, including haemodynamics, end-organ failure-free days, risk of poor in-hospital or functional outcomes, and adverse events.

Based on the combined evidence from the three RCTs in the meta-analysis, ILCOR made a weak recommendation against the routine use of vasopressin and corticosteroids in conjunction with standard care for adult in-hospital cardiac arrest.[145] This recommendation reflects the low confidence in the effect estimates for critical outcomes (low to moderate certainty of evidence). The neutral findings of the CORTICA trial,[150] which showed no significant benefit of low-dose steroids, further supports the ERC/ESICM recommendation against the the routine use of vasopressin and corticosteroids.

Three ongoing RCTs are anticipated to provide additional evidence for the use of vasopressin and steroids in patients experiencing in-hospital cardiac arrest (VAST-A, NCT05139849). For patients with out of hospital cardiac arrest the ongoing HYVAPRESS (NCT04591990) trial is investigating the effect of steroids and vasopressin, and the DANOCHA (NCT05895838) trial is evaluating the effect of steroids.

[h4] Potassium

Hyperkalaemia occurs frequently immediately after cardiac arrest – data from 4 RCTs indicate that almost 20% of patients admitted to ICU after cardiac arrest had hyperkalemia.[151] However, the release of endogenous catecholamines, along with the correction of metabolic and respiratory acidosis, promotes the intracellular movement of potassium, which may lead to hypokalaemia. Post-cardiac arrest hyperkalaemia is associated with poorer clinical outcomes.[151,152]

Based on observational data, ILCOR suggests that intravenous insulin combined with glucose can be used in cases where cardiac arrest is suspected to be caused by acute hyperkalaemia (weak recommendation, with very low certainty of evidence).[8,153] In such patients, ILCOR concluded that there is insufficient evidence to support or oppose the use of intravenous sodium bicarbonate or calcium (weak recommendation, very low certainty of evidence).

Hypokalaemia and hyperkalaemia may increase the risk of ventricular arrhythmias.[154] Observational studies suggest maintaining serum potassium values between 4.0 and 4.5 mmol/L through potassium supplementation, which is recommended as a best practice.[155]

[h4] Mechanical circulatory support

Managing post-ROSC patients with refractory shock that persists despite fluid resuscitation and vasoactive drugs presents a significant clinical challenge. In such cases, mechanical circulatory support (MCS – such as intra-aortic balloon pump, left-ventricular assist device or arterio-venous extra corporal membrane oxygenation) might be considered the next therapeutic step.[138]

A pooled analysis of up to 14 randomised trials[8] showed no significant difference in survival outcomes (ranging from 30 days to 1 year) between the early routine use of temporary MCS devices and standard care in patients with cardiogenic shock, regardless of whether a cardiac arrest had occurred.[156-169] For patients who experienced cardiac arrest, the evidence was mostly indirect, being based on randomised trials involving cardiogenic shock patients, many of whom had experienced cardiac arrest.

While the overall findings do not support the routine use of MCS devices, certain subgroups may benefit. An individual data meta-analysis of nine RCTs evaluating temporary MCS in infarct-related cardiogenic shock showed that the use of MCS devices in these patients did not lower 6-month mortality, regardless of the device type, and was associated with increased major bleeding and vascular complications.[170] However, in the subgroup of patients with cardiogenic shock and ST-elevation who were not at risk of hypoxic brain injury, MCS use led to a reduction in mortality. Therefore, MCS should be reserved for select patient populations, such as patients with a Glasgow Coma Scale score ≥8 on hospital arrival, with ST-elevation myocardial infarction (STEMI) and a short duration of cardiac arrest (<10 minutes). For patients at high risk of brain injury, the potential benefits of these devices may be diminished.

Given the current evidence, making definitive recommendations for selecting post-ROSC cardiogenic shock patients for MCS is challenging. Based on the findings, ILCOR made a weak recommendation against the routine use of these devices in cardiogenic shock patients following cardiac arrest and ROSC, citing low certainty of evidence.[8] However, MCS may be considered for carefully selected patients in appropriate settings where the devices can be effectively used (weak recommendation, low certainty of evidence). When these devices are used, it is advised to closely monitor for potential adverse events and complications to ensure timely identification and management (good practice statement).[8] The ERC/ESICM has adopted these ILCOR recommendations.

[h3] Post-ROSC arrhythmias

Recurrent arrhythmias following ROSC pose significant clinical challenges, impacting both short-term management and long-term prognosis in cardiac arrest survivors.[171] Myocardial ischemia and post-arrest myocardial dysfunction are the primary causes of electrical instability. However, other

contributing factors in the acute phase include electrolyte imbalances, elevated catecholamine values, the use of vasopressors and inotropes, as well as pre-existing structural heart disease or channelopathies.[127] Arrhythmias may range from isolated extrasystoles and short runs of supraventricular and ventricular tachycardia to life-threatening tachyarrhythmias and bradyarrhythmias.[171]

Comprehensive information on the management of these arrhythmias, both immediately before and after cardiac arrest, in accordance with guidelines from relevant scientific associations, is provided in the ERC Guidelines 2025 Adult Advanced Life Support (ALS).[172] In a post hoc analysis of a prospective randomised trial, the cumulative incidence of atrial fibrillation was reported to be 15% on the first day and 11% on the second day following OHCA.[173] Atrial fibrillation was independently associated with increased mortality, predominantly driven by cardiovascular complications and multiple organ failure, highlighting a vulnerable subset of patients requiring close monitoring. Data from a multicentre database encompassing 9,295 patients revealed that a new diagnosis of atrial fibrillation within the first two weeks post-ROSC was strongly associated with elevated risks of stroke and mortality.[174] However, the optimal management strategy to improve outcomes in such cases remains unclear.

Recurrence of ventricular arrhythmias is common during the ICU stay of cardiac arrest survivors. In a retrospective study involving consecutive OHCA patients with VF or pulseless VT as initial rhythms, obstructive coronary artery disease, and successful primary PCI, early recurrence of ventricular arrhythmias was documented in more than 9.8% of cases, primarily within the first 24 hours.[175] Furthermore, in a post hoc analysis of a randomised trial of hypothermic temperature control, VF/VT occurred in 16.2% of patients between days 1 and 3, with no significant differences observed between core temperatures of 33°C and 36°C.[176] The recurrence of life-threatening ventricular arrhythmias after ROSC may signal unrecognised underlying causes of cardiac arrest, such as hypoxaemia, hypovolemia, hypothermia, hypo/hyperkalaemia, acidaemia, toxins, cardiac tamponade, tension pneumothorax, coronary thrombosis, or pulmonary embolism.[177] Prompt recognition and treatment of these conditions are crucial to preventing recurrent cardiac arrest.[177]

Refractory arrhythmias often result from a complex interplay between myocardial substrate abnormalities (e.g., arrhythmia syndromes or myocardial scarring from structural heart disease), arrhythmia triggers, and autonomic imbalance. This necessitates a stepwise approach to management, including assessing the arrhythmia's severity, identifying triggers, evaluating the cardiac substrate, determining hemodynamic impact, and risk stratifying the patient.[178]

Medical management should proceed according to ALS guidelines for refractory arrhythmias. In some cases of electrical storm, measures such as sedation, stellate ganglion blockade, mechanical circulatory support, or urgent catheter ablation should be considered if initial interventions fail to resolve or prevent arrhythmias.[179] During the first hours and days, the benefit of prophylactic antiarrhythmic treatment has not been established. Antiarrhythmic medications should be reserved for the control recurrent ventricular arrhythmias. Long-term management for many of these patients involves the implantation of an implantable cardioverter-defibrillator (ICD).[180]

[h3] Implantable cardioverter defibrillators

An implantable cardioverter defibrillator (ICD) is a device designed to manage and treat certain life-threatening arrhythmias. The European Society of Cardiology has established guidelines specifying the indications for ICD therapy.[180] Indications for ICD implantation can be classified into two categories: primary prevention and secondary prevention. Primary prevention applies to patients who have not yet experienced a life-threatening arrhythmia but are at high risk of developing one. This group includes individuals with cardiomyopathies, inherited arrhythmic syndromes, congenital heart disease, or primary arrhythmias occurring in structurally normal hearts.[181,182] Secondary prevention is intended for patients who have already survived a serious arrhythmic event and remain at high risk of recurrence.

Careful patient selection is crucial to identify those most likely to benefit from ICD implantation, especially individuals whose survival may be prolonged by preventing sudden cardiac death caused by arrhythmias.

For post-resuscitation patients, ICDs are often necessary for secondary prevention. A meta-analysis[183] of three major early ICD trials comparing ICD therapy with medical treatment for secondary prevention of sudden cardiac death documented a 28% reduction in mortality (HR 0.72; 95% CI 0.6–0.87; P = 0.0006).[184-186] This benefit was primarily attributed to a significant decrease in arrhythmic deaths (HR 0.5; 95% CI 0.37–0.67; P < 0.0001) among ICD-treated patients.

The ESC currently recommends ICD implantation in patients with documented ventricular fibrillation (VF) or hemodynamically unstable ventricular tachycardia (VT) where reversible causes have been excluded.[180]

[h2]Disability (optimising neurological recovery)

[h3]Control of seizures

Some of the evidence informing this guideline is set out in a systematic review that informed the

2024 ILCOR CoSTR summary.[39] The 2024 ILCOR updated treatment recommendations have been adopted by ERC/ESICM:

- We suggest against the use of prophylactic antiseizure medication in post–cardiac arrest adults (weak recommendation, very low–certainty evidence).
- We suggest treatment of clinically apparent and EEG seizures in post–cardiac arrest adults (good practice statement).
- We suggest treatment of rhythmic and periodic EEG patterns that are on the ictal-interictal continuum in comatose post–cardiac arrest adults (weak recommendation, low-certainty evidence).

Seizures are reported in 20-30% of cardiac arrest patients in the ICU and are usually a sign of a severe hypoxic-ischaemic brain injury. Seizures may be observed as clinical convulsions (clinical seizure) and/or in the EEG (electrographic seizure). Standardised criteria for possible and definite electrographic seizure activity have been published.[187] Myoclonus is sudden, brief, shock-like involuntary muscle contractions and is by far the most common type of clinical seizure in post-arrest patients.[188,189] It is often generalised but may be focal (periodic eye-opening, swallowing, diaphragmic contractions etc) or multi-focal.[190] It typically develops during the first 1-2 days after the arrest and is often transient during the first days-week. It is associated with a poor prognosis[191] but some patients survive with a good outcome.[192,193] Most post-hypoxic myoclonus has a cortical origin [194] and the EEG shows time-locked discharges or burst-suppression in a substantial proportion of patients.[192]

Focal or generalised tonic-clonic seizures also occur after cardiac arrest, and it is not uncommon that an individual patient has several seizure sub-types.[188]

Lance-Adams syndrome is a less frequent form of myoclonus usually developing in a patient who has regained consciousness.[195,196] It is more common after hypoxic cardiac arrest and mainly affects the limbs where it is induced by purposeful actions or sensory stimulation. It may be disabling and often becomes chronic.[193,197]

Studies using continuous EEG-monitoring reveal that electrographic epileptiform (rhythmic and periodic) activity and clinical convulsions are equally common and that there is a substantial overlap.[198] The evaluation of electrographic seizures is often confounded by the concomitant effects of brain injury, metabolic factors and sedation, making possible clinical correlates and effects of treatment harder to evaluate. Definitions of electrographic status epilepticus have been published by the American Clinical Neurophysiology Society (ACNS).[187] Whether patients with rhythmic and periodic EEG patterns in the ictal-interictal continuum are classified as electrographic status

epilepticus or not is influenced by the timing of EEG, treatment with sedative drugs and the local EEG-interpreter.

There is currently no evidence supporting prophylactic treatment with antiepileptic drugs in the post-arrest setting. Previous studies on the effects of bolus-doses of thiopental[199] and diazepam/magnesium[200] after resuscitation showed no benefit in terms of survival or neurological function but these studies were designed to investigate neuroprotection, not seizure suppression.

There is limited evidence that conventional antiseizure drugs (mainly valproate and levetiracetam) suppress epileptic activity in the EEG of post cardiac arrest patients.[201] These drugs are known to supress myoclonus of other origins.[202] Phenytoin and the pro-drug fosphenytoin are still used for the treatment of status epilepticus. In post-cardiac arrest patients, however, their negative inotropic and vasodilating effects makes them less suitable.[203]

Seizures may increase the cerebral metabolic rate and have the potential to exacerbate brain injury caused by cardiac arrest: treat seizures with levetiracetam and/or sodium valproate or a combination. Consider possible drug interactions. After the first event, start maintenance therapy. Consider increased dose of propofol or benzodiazepines to suppress myoclonus and electrographic seizures. Thiopental or phenobarbital may be considered in selected patients. Clonazepam may suppress myoclonus but may cause sedation.

Sedative drugs have potent seizure-suppressing effects and are recommended as third-line treatment of status epilepticus. Propofol and benzodiazepines are used routinely during the first days after cardiac arrest while the patient is mechanically ventilated. Depending on the dosing, these drugs will suppress clinical myoclonus and epileptiform activity in the EEG.[204,205] The seizures may be unmasked during sedation holds.

Treatment of detected clinical seizures has not been studied in an RCT.[39] However, in one multi-centre RCT, patients were treated with antiepileptic drugs and sedative agents in a stepwise goal-directed manner to suppress abundant rhythmic and periodic activity detected in the EEG.[206] The outcome was equally poor in most (90%) patients in both intervention and control group.

In several case series, 4–44% of patients with post-anoxic status epilepticus had a good outcome.[207-210] These patients were usually treated with multiple anti-epileptic drugs and had a delayed awakening, often beyond 1-2 weeks. Whether antiseizure medications or prolongation of intensive care contributed to good outcome in these patients cannot be confirmed in these case series.

The EEG is an important tool to detect corresponding electrographic seizure activity in a patient with observed clinical convulsions and to monitor treatment effects. Shivering is a common seizure mimic during hypothermic temperature control. Active treatment of status epilepticus usually necessitates

repeated routine EEGs or continuous EEG-monitoring. The relative benefit of continuous EEG compared with routine EEG has not been shown. Continuous EEG monitoring is labour intensive and likely to add significant cost to patient care. The net cost-effectiveness of this approach is controversial and may depend substantially on the setting.[211,212]

Since post-anoxic seizures and status epilepticus are manifestations of hypoxic-ischaemic brain injury, an assessment of the prognosis and potential for an eventual good outcome are central components of a treatment strategy. The EEG-background pattern is important but may sometimes be difficult to assess if there are concomitant abundant discharges. A continuous, normal voltage and reactive EEG background are benign features whereas a burst-suppression pattern or a suppressed background without reactivity are features related to worse prognosis.[192,210] Early onset (<24 h) of electrographic seizures, before the recovery of a continuous background is associated with worse prognosis.[213-215] In these patients, the EEG is often affected by the ongoing treatment. It is therefore suggested that additional information is obtained on the severity of brain injury from methods not significantly affected by sedative drugs, such as somatosensory evoked potentials, serum NSE and neuroradiological investigations (preferably MRI).

Treatment with sedatives and conventional antiepileptic drugs in high doses may delay awakening, prolong the need for mechanical ventilation, and increase critical care length of stay.[216] Consider that generalised myoclonus in combination with epileptiform discharges may be early signs of Lance-Adams syndrome which is compatible with awakening and a good outcome.[192,195] In such cases, aggressive treatment with high doses of sedatives and anti-epileptic drugs may confound the clinical examination and lead to overly pessimistic prognostication. The preferable approach is to treat the patient holistically instead of focusing purely on the EEG.

[h3] Temperature control

A comprehensive systematic review of temperature control in comatose post–cardiac arrest patients was conducted by the ALS Task Force of ILCOR in 2021[217] and updated in 2023.[39,218] The systematic review covered six aspects of temperature management: (1) use of hypothermic temperature control, (2) timing, (3) specific temperature, (4) duration of temperature control, (5) method of temperature control, and (6) rate of rewarming. Only controlled trials were included in these reviews. The 2021 and 2023 systematic reviews identified 38 trials.

The term targeted temperature management was updated by the ALS Task Force and the following definitions have been adopted:

- Hypothermic temperature control – active temperature control with the target temperature below the normal range
- Normothermic temperature control – active temperature control with the target temperature in the normal range
- Fever prevention temperature control – monitoring temperature and actively preventing and treating temperature above the normal range
- No temperature control – no protocolised active temperature control strategy

Comparisons in the systematic reviews included temperature control versus no temperature control, timing of temperature control, specific temperature targets, durations of temperature control, methods of temperature control, and rates of rewarming. Overall, there was no difference between hypothermic temperature control and normothermic temperature control or between other specific temperatures studied or different durations or methods of temperature control.

The ILCOR ALS Task Force made the following treatment recommendations and good practice statements, and these have been adopted unchanged for these 2025 ERC- ESICM Guidelines.

- We suggest actively preventing fever by targeting a temperature ≤37.5 °C for patients who remain comatose after ROSC from cardiac arrest (weak recommendation, low-certainty evidence).
- Whether subpopulations of cardiac arrest patients may benefit from targeting hypothermia at 32°C to 34 °C remains uncertain.
- Comatose patients with mild hypothermia after ROSC should not be actively warmed to achieve normothermia (good practice statement).
- We recommend against the routine use of prehospital cooling with rapid infusion of large volumes of cold intravenous fluid immediately after ROSC (strong recommendation, moderate-certainty evidence).
- We suggest surface or endovascular temperature control techniques when temperature control is used in comatose patients after ROSC (weak recommendation, low-certainty evidence).
- When a cooling device is used, we suggest using a temperature control device that includes a feedback system based on continuous temperature monitoring to maintain the target temperature (good practice statement).
- We suggest active prevention of fever for 36 to 72 hours in post-cardiac arrest patients who remain comatose (good practice statement).

[h4] Hypothermia compared with normothermia or prevention of fever

Although the ILCOR systematic reviews found no difference in overall outcomes between patients treated with hypothermia and normothermia or fever prevention the authors of a Cochrane systematic review concluded that hypothermic temperature control may improve neurological outcomes after cardiac arrest.[219] The conflicting results of these systematic reviews have been reflected in differing opinions on whether there is a role for hypothermic temperature control in comatose post-cardiac arrest patients.[220,221] Differences in opinion led the ILCOR ALS Task Force to suggest that there may be subpopulations that might benefit from hypothermic temperature control. A single trial suggested benefit in those with a nonshockable initial rhythm;[222] however, a recent individual patient meta-analysis of this trial and the TTM-2 trial participants with an initial non-shockable rhythm concluded that hypothermic temperature control did not improve survival or functional outcome.[223]

Many animal models have suggested a benefit for hypothermic temperature control after resuscitation from cardiac arrest but in these cases target temperature has generally been achieved in less than 1 hour.[224] The failure to translate these findings into positive outcomes in clinical trials may reflect the 5-6 hours generally taken to achieve target temperature in the clinical setting.[16] Extracorporeal cardiopulmonary resuscitation (ECPR) may enable more rapid cooling and achievement of target temperature. There are no randomised controlled trials evaluating hypothermic temperature control in patients receiving ECPR; despite this, many centres have adopted hypothermic temperature targets in these patients.

[h4] Prehospital Cooling

There is no evidence that any method of prehospital cooling improves outcomes. One study indicates that rapid infusion of large amounts of cold fluid immediately after achieving ROSC in the prehospital setting is harmful.[225]

[h4] Temperature control devices

Fever control with or without a device is currently being evaluated in the STEPCARE Trial (https://stepcare.org). Until the results of this trial are known, it is considered good practise to monitor temperature continually and use a feedback-controlled system whenever a temperature control device is used to maintain a stable temperature. Two systematic reviews conflict on whether surface or endovascular cooling is preferable. One showed that intravascular cooling is associated with improved neurological outcome,[226] while the other found no association with survival or neurological outcomes.[227] A systematic review and network meta-analysis focusing on temperature

feedback during hypothermic temperature control included 14 studies (4062 patients) and concluded that intravascular temperature control had the highest probability of being beneficial.[228] In a randomised clinical trial of fever prevention in patients with acute vascular brain injury, use of an automated surface temperature management device did not improve functional outcome in comparison with standardised tiered fever treatment for a temperature ≥ 38°C.[229]

[h4] Duration of Temperature Control

Three trials have investigated the impact of duration of temperature control on outcome. One trial showed no difference between 24 and 48 hours of hypothermia,[230] another found no difference between 12 to 24 and 36 hours of hypothermia,[231] and a third compared temperature control for 36 hours versus 72 hours and also found no difference in outcomes.[232] Based on these data, the ILCOR ALS Task Force was unable to reach consensus on a treatment recommendation on duration of temperature control or fever prevention. The good practice statement includes a range of duration (36 to 72 hours) that is supported by the few data and by expert opinion.

[h3]Other therapies to improve neurological outcome

Many therapies have shown encouraging neuroprotective effects in experimental models. However, there are many limitations to animal models and the positive results of these preclinical clinical studies have failed to translate into clinical practice.[16] The ILCOR ALS Task Force adoloped a published systematic review on drug therapy for comatose survivors of cardiac arrest.[8,18] The adoloped ILCOR systematic review included 44 RCTs (5640 patients),[126,146-148,150,199,200,206,233-267] which were grouped into 3 themes: supportive drug therapy (5 studies), neuroprotective agent (18 studies), and anti-inflammatory/antioxidant (16 studies). The supportive therapies included antiplatelet drugs, sedation, and neuromuscular blockade, and none of these resulted in a difference in mortality at 30 days or hospital discharge.[235,249,250,253,261] The neuroprotective therapies that were investigated included thiopental,[199] amantadine,[238] nimodipine,[245,260] lidoflazine,[236] inhaled xenon,[248] nitric oxide,[240] hydrogen,[263] the exenatide (glucagon-like peptide-1 agonist),[266] epoetin alfa,[237] sodium nitrite,[240] magnesium,[264] MLC901 (nine herbal components),[256] and penehyclidine hydrochloride.[265] None of these studies documented significant effects on functional outcome and there were increased rates of serious adverse events in the intervention arms of the studies of thiopental (hypotension), lidoflazine (hypotension), and epoetin alfa (thrombosis).[199,236,237] Anti-inflammatory and antioxidant therapies investigated included steroids,[148,150,255] vasopressin in conjunction with steroids,[146] thiamine,[234,241,257] coenzyme Q10,[239,246,268] vitamin C,[258] tocilizumab

(interleukin-6 inhibitor),[252] iloprost,[251] urinastatin (neutrophil elastase inhibitor),[244] and the traditional Chinese medicine Shenfu.[267] None of these therapies reduced 30-day mortality. Medical gases, noble gases and gaseous molecules have also been evaluated at neuroprotectants. The combination of xenon and induced mild hypothermia, which is beneficial and superior to induced mild hypothermia alone in experimental settings,[269] has been studied in several clinical trials without convincing effects.[233,270] Volatile anaesthetics have demonstrated positive effects on cardiac and cerebral recovery in experimental settings[271] and clinical feasibility studies,[272,273] but outcome data are scarce and uncertain.[274-276]

The 2025 ILCOR treatment recommendation in respect of neuroprotective therapies after cardiac arrest is that there is insufficient evidence to recommend the use of any specific drug therapy for comatose survivors of cardiac arrest (weak recommendation, low- to very low–certainty evidence),[8] and the ERC/ESICM supports this

[h2]General intensive care management

Most of the guidelines for the general ICU management of post-cardiac arrest patients are based on expert opinion. Most aspects of post-cardiac arrest care follow general ICU practices. Some differences and nuances are inherent. Few aspects of general intensive care have been studied separately in the cardiac arrest population, but cardiac arrest patients have been included in trials on general intensive care practices. Specific features of the post cardiac arrest patients include the risk of brain injury and need to apply neurocritical care principles, the high occurrence of myocardial dysfunction, the use of anticoagulants and anti-platelet drugs and the high risk of aspiration pneumonitis among others. The typical length of stay in cardiac arrest patients will vary from three days to several weeks because of differences in time to awakening.[277] This will influence certain aspects of care such as the initiation of and management of nutrition.

[h3] Prophylactic antibiotics

Many post-cardiac arrest patients are at high risk of developing aspiration and ventilator-associated pneumonia [278,279] and in some centres it is routine practice to give prophylactic antibiotics to all comatose post-cardiac arrest patients.[255] An RCT examining the prophylactic use of antibiotics in OHCA patients showed a decrease in ventilator associated pneumonia but did not find any other differences in other clinical outcomes.[243] A systematic review underpins an ILCOR treatment recommendation which suggests against the use of prophylactic antibiotics in patients following ROSC (weak recommendation, low certainty of evidence) and this is supported by the

ERC/ESICM.[60,280] Despite this recommendation it is reasonable to have a low threshold for giving antibiotics when there is any clinical suspicion of pneumonia.

[3] Sedation and analgesia

Many post-cardiac arrest patients will require sedation and pain management, particularly those who are treated with active temperature control.[281] During hypothermic temperature control, shivering is common – this can be managed with opioids and sedation. The role of sedation in patients not treated with hypothermic temperature control remains controversial, and practice varies from deep to light sedation targets. While we await the results from the ongoing Sedation, TEmperature, and Pressure after Cardiac Arrest and REsuscitation (STEPCARE) trial comparing a deep sedation target with minimal sedation,[282] it is reasonable to treat pain, discomfort and shivering in patients not treated with hypothermic temperature control. It is best practice to monitor level of sedation with a tool such as the Richmond Agitation Sedation Scale (RASS).[283]

One RCT has compared the use of propofol and fentanyl with midazolam and fentanyl.[235] In a trial of 59 patients, the use of propofol and remifentanil resulted in shorter time to awakening but was associated with more frequent need of noradrenaline[235] Similar findings have been shown in observational studies[284] Volatile anaesthetics have been proposed as alternative sedatives because they are cleared more rapidly. A systematic review and meta-analysis included 3 observational studies compared volatile anaesthetics with conventional sedatives in post-cardiac arrest patients.[274] Those patients sedated with volatile anaesthetics received a shorter duration of mechanical ventilation, but there was no difference in any other outcomes. In a recent propensity-matched control study sedation of post-cardiac arrest patients with isoflurane was associated with a reduced incidence of delirium and shorter duration of mechanical ventilation compared with those given intravenous sedation.[276] However, results of a recent trial on 687 adults with ARDS, in most cases due to COVID-19, showed that inhaled sedation with sevoflurane resulted in fewer ventilator-free days at day 28 and higher 90-day mortality (53% vs. 44%; relative risk 1.31 [95% confidence intervals 1.05 – 1.62])) than sedation with propofol Moreover, patients randomised to inhaled sedation with sevoflurane had higher rates of acute kidney injury.[285] We suggest using short-acting intravenous sedative agents when treating post-cardiac arrest patients receiving mechanical ventilation – this may enable earlier clinical examination that is less confounded by sedation when assessing neurological recovery.

[3] Neuromuscular blocking drugs

A systematic review and meta-analysis of the use of neuromuscular blockers in post-cardiac arrest patients included 12 studies (3 RCTs and 9 observational studies) and over 11,000 patients.[286] Use of prophylactic (continuous) neuromuscular blockade was associated with reduced mortality compared with those patients managed without neuromuscular blocking drugs (OR 0.74; 95% CI 0.64–0.86; p < 0.0001). There was no difference in outcomes between those managed with continuous neuromuscular blocking drugs and those managed with bolus doses. There are major limitations to this systematic review: most of the included studies were retrospective and therefore potentially confounded; observational studies were combined with RCTs; most of the patients in these studies are likely to have been treated with hypothermic temperature control and any beneficial effects of neuromuscular blocking drugs may not be seen in patients treated with normothermic temperature control. In patients with ARDS and critical hypoxaemia, an RCT[287] and a meta-analysis[288] have shown reduced mortality with the use of neuromuscular blockers, but a more recent RCT showed no survival benefit.[289] Thus, in patients with critical hypoxaemia and ARDS following cardiac arrest, the use of a neuromuscular blocker may be considered, given some evidence for their use in ARDS. In other patients (without ARDS), ERC/ESICM does not recommend systematic use of neuromuscular blocking drugs.

[h3] Nutrition

Patients require a nasogastric tube to decompress any abdominal distension. There are no RCTs evaluating nutrition in post-cardiac arrest patients but 5 observational studies have indicated that enteral feeding is tolerated after OHCA.[290-294] In observational studies, early enteral nutrition (started in less than 48 hours from cardiac arrest) appears to be safe and associated with a higher proportion of patients with a good 3-month neurological outcome,[291] improved survival,[292] and a lower 7-day bacteraemia rate.[293] In contrast, in another observational study among patients treated with extracorporeal CPR and hypothermia, delayed enteral nutrition (> 48 hours) was associated with improved neurologically favourable survival compared with early enteral feeding.[294] It is reasonable to start gastric feeding at low rates (trophic feeding) and increase as tolerated. Low calorie, low protein intake during the acute phase of illness or during haemodynamically instability is associated with fewer complications compared with standard intakes of energy and protein.[295]

[h3] Gastric ulcer prophylaxis

Routine use of ulcer prophylaxis in intensive care patients does not decrease mortality.[296,297] However, a meta-analysis showed that in high-risk patients, the use of ulcer prophylaxis decreased

gastrointestinal bleeding[298] and a recent randomised trial in 4821 patients undergoing invasive mechanical ventilation showed a significant reduction in the risk of clinically significant upper gastrointestinal bleeding with pantoprazole 40 mg daily compared with placebo. The incidence of ventilator-associated pneumonia or Clostridium difficile infection was similar in the two study groups.[299] There has been no subgroup study of post-cardiac arrest patients. In one observational retrospective study, non-occlusive mesenteric ischaemia occurred in 2.5–6% of patients admitted to a cardiac arrest centre.[300] However, in a prospective study, among 214 post-cardiac arrest patients who were still intubated after 2-4 days and systematically underwent upper gastrointestinal endoscopy 121 (57%) had an upper gastrointestinal ischaemic lesion and these were severe (ulceration or necrosis) in half the cases.[301] Given the high incidence of upper gastrointestinal ulceration in post-cardiac arrest patients and the use of anticoagulant and antiplatelet drugs both pre and post arrest,[302] we suggest the use of stress ulcer prophylaxis in post-cardiac arrest patients, especially in those with coagulopathy.[303]

[3] Anticoagulation

Unless patients receive anticoagulation because of a myocardial infarction or ischaemia, deep venous thrombosis (DVT) prophylaxis is recommended in critically ill patients.[304,305] A systematic review that included 13 RCTs and 9619 critically ill patients showed that low molecular weight heparin (LMWH) reduced the rate of DVT compared with unfractionated heparin.[306] The use of antiplatelet drugs does not prevent DVTs.[307] Out-of-hospital cardiac arrest patients are at risk for developing DVTs especially if treated with hypothermic temperature control.[308] Deep venous thrombosis may be more common in those treated with an invasive temperature control device, likely related to catheter placement in the femoral vein.[309] No specific evidence exists on DVT prophylaxis in cardiac arrest patients. Thus, treatment should be individualised and be based on general ICU recommendations.[304]

[h3] Glucose control

Hyperglycaemia is common after OHCA.[152] Hyperglycaemia is best managed with continuous infusion of insulin. An evidence update on glucose control after resuscitation found no new studies that examined active glucose management in the post-cardiac arrest period and the 2014 ILCOR treatment recommendation remains valid and supported by the ERC/ESICM: we suggest no modification of standard glucose management protocols for adults with ROSC after cardiac arrest (weak recommendation, moderate-quality evidence).[8]

The 2024 Guidelines of the American Diabetes Association recommend a target glucose range of 7.8–10.0 mmol L^{-1} (140–180 mg dL^{-1}) for most critically ill patients.[310] The American Diabetes Association also recommends that more stringent goals, such as 6.1–7.8 mmol/L (110–140 mg/dL), may be appropriate for selected patients, as long as this can be achieved without significant hypoglycaemia. However, very tight glucose control does not appear to convey benefit[311] and may be associated with hypoglycaemia (< 4.0 mmol L^{-1} (< 70 mg dL^{-1})),[312] which is harmful in critically ill patients.[313] In general, glucose containing solutions are not recommended in patients with brain injury,[314] but they may be needed to treat hypoglycaemia.[313]

[h2]Predicting neurological outcome

About two-thirds of in-hospital deaths in patients who are admitted to an intensive care unit in a coma following resuscitation from OHCA are caused by hypoxic-ischaemic brain injury (HIBI).[315,316] In a minority of cases, these deaths occur as a direct consequence of HIBI, which results in an irreversible loss of all brain function, i.e., brain death.[317] However, most neurological deaths following cardiac arrest result from active withdrawal of life-sustaining treatment (WLST) in patients where the severity of HIBI indicates that survival with a poor neurological outcome is very likely.[318,319] Accurate prognostication is therefore essential to avoid an inappropriate withdrawal of life-sustaining treatment in patients who still have a chance of a neurologically meaningful recovery and to avoid futile treatment in patients with a severe and irreversible brain injury.

[h3] Outcomes measures in neuroprognostication studies

Neurological outcome after cardiac arrest is commonly reported as good or poor and is measured by ordinal hierarchal functional outcome scales, where a poor functional outcome refers to a patient being either dead or having a dependency in basic activities of daily living. Neurological outcome after cardiac arrest is most commonly reported using Cerebral Performance Categories (CPC).[320] The CPC is expressed as a five-point scale: CPC 1 (no or minimal neurological disability); CPC 2 (minor neurological disability); CPC 3 (severe neurological disability); CPC 4 (persistent vegetative state); and CPC 5 (death). Although CPC is the most commonly used scale, the preferred measure for functional outcome in cardiac arrest is the modified Rankin Score (mRS), which includes seven scores, from 0 (no symptoms) to 6 (dead).[321] In 2018, a statement from ILCOR[322] suggested using mRS rather than CPC for measuring functional recovery after cardiac arrest, because mRS is more suitable than CPC for discriminating between mild and moderate disability[323,324] and may have better

interrater reliability.[325] However, for both of these scales interrater reliability is generally acceptable in the separation of good and poor outcome.

For both clarity and statistical purposes in studies on neuroprognostication after cardiac arrest the outcome is dichotomised as 'good' or 'poor'. However, there is no universal consensus on what represents a poor functional outcome. Up to 2006, most neuroprognostication studies reported CPC 4 or 5 (vegetative state or death) as a poor outcome, and CPC from 1 to 3 (from absent to severe neurological disability) as a good outcome, while after that date an increasing number of studies included CPC 3 (severe neurological disability) among poor neurological outcomes.[326] In a 2020 systematic review, among 94 total studies on neurological prognostication after cardiac arrest, 90 (96%) defined poor neurological outcome as CPC 3-5 and only four defined poor outcome as CPC 4-5.[327]

In prognostic accuracy studies, a predictor (index test) is assessed for its ability to predict an outcome. When test results are expressed in binary format (i.e., positive vs. negative), the accuracy is expressed using sensitivity and specificity, which measure the test's ability to identify individuals who will develop or will not develop the target condition, respectively. Sensitivity is the fraction of subjects who will develop the target condition and have a positive test result. For this reason, sensitivity is also known as the true positive rate. A highly sensitive test will be positive in most of the patients who will develop the target condition. Specificity is the fraction of subjects who will not develop the target condition and have a negative test result. For this reason, specificity is also known as the true negative rate. A very specific test will be negative in most of the patients who will not develop the target condition. Importantly, the remaining patients who will not develop the target condition will have, by definition, a *positive* test result. These are the false positives, and their fraction of the total patients who will not develop the condition is the false positive rate. Specificity and false positive rate complement each other: Specificity = 1 - false positive rate.

Since most neuroprognostic tests predict poor functional outcome, having a very high specificity (i.e., a very low rate of falsely pessimistic predictions) is desirable. Ideally, an index test should be 100% specific, i.e., its false positive rate should be zero. There is no universal consensus on how low the false positive rate of an index test should be for neuroprognostication after cardiac arrest. In a survey of 640 healthcare providers, the majority (51%) considered an acceptable false positive rate for withdrawal of life-sustaining treatment from patients who might otherwise have recovered to be ≤0.1%.[328] Along with the absolute specificity value, the precision of its estimate is essential. A very specific test predicting poor outcome is of little clinical use when its precision is low (i.e., when the confidence intervals [CI] around the point estimate of its specificity are wide), because this indicates

a high degree of uncertainty around the estimated specificity. In the 2014 ERC-ESICM Advisory Statement on neuroprognostication after cardiac arrest, the single most robust predictors were identified as those in which the upper boundary of the 95% confidence interval of the false positive rate was below 5%.[329] To increase the safety of neuroprognostication, from 2021, ERC and ESICM have recommended using a combination of at least two concordant unfavourable predictors for predicting poor neurological outcome in patients who are comatose after cardiac arrest. In two multicentre validation studies of the 2021 ERC-ESICM neuroprognostication strategy, one conducted mostly in Central and Nothern Europe[330] and the second conducted in South Korea where withdrawal of life-sustaining treatment was not practised,[331] the ERC-ESICM neuroprognostication algorithm predicted poor outcome with 0% false positive rate and 95% confidence intervals of 0-1.2% and 0-3.4%, respectively.

For some neuroprognostic tests used after cardiac arrest, such as blood values of biomarkers of neurological injury or the grey matter to white matter density ratio on brain CT, the results are expressed as continuous variables. In this case, sensitivity and specificity will depend on the value of the variable that is chosen as a threshold to separate positive from negative test results, and the values of sensitivity and specificity that are obtained by varying the positivity threshold across all its possible values are expressed by a receiver operating characteristic (ROC) curve. The problem with dichotomising continuous predictive variables to obtain a binary test result is the difficulty in finding a consistent threshold for 100% specificity. Very high test results can be caused by outliers, which can distort the data and reduce test sensitivity.

[h3] Main sources of bias in neuroprognostication

One of the major biases in neuroprognostication after cardiac arrest is self-fulfilling prophecy. This occurs when the treating team is aware of the result of the prognostic test and uses it for decisions that affect the patient's outcome, e.g., withdrawal of life-sustaining treatment (WLST). This leads to an overestimation of test performance and potentially to an inappropriate WLST. In a systematic review on neuroprognostication after cardiac arrest published in 2013, 64/73 (88%) studies were at risk of self-fulfilling prophecy bias.[332,333]

Ideally, the index tests should be investigated blindly to avoid self-fulfilling prophecy bias. However, this is difficult to achieve in practice. Concealing clinical examination results from the treating team is almost impossible, while concealing EEG or brain imaging results would be unethical, since they may reveal the presence of potentially treatable complications (e.g., seizures or intracranial hypertension, respectively). Nevertheless, some predictors, such as biomarkers, have been

evaluated blindly.[334-336] A special condition limiting the risk of self-fulfilling prophecy bias is the absence of an active WLST policy. This has been described in some studies conducted in countries or communities where treatment limitations are not accepted due to cultural, legal or religious reasons.[337,338]

Other strategies to reduce the risk of falsely pessimistic predictions include avoiding confounding from treatments (e.g., sedatives or other drugs) affecting the results of some predictors, such as clinical examination or EEG; avoiding basing decisions on life-sustaining treatments on the results of a single index test, but instead using a multimodal approach (see Figure 4 – Multimodal prognostication algorithm); and always interpreting the results of the index tests within the clinical context.

A specific source of bias in neuroprognostic studies after cardiac arrest is the presence of a time lag between the recording of the index test, which is usually done very early after the arrest, and the assessment of the target condition, i.e., neurological outcome. Since recovery from hypoxic-ischaemic brain injury following cardiac arrest requires time, the minimum recommended timing for its assessment is 30 days or later from the event or neurological discharge.[322] However, further neurological recovery can occur later. Consequently, an early prediction of outcome, which is confirmed by CPC or mRS measured at hospital discharge, may occasionally prove false when the outcome is reassessed later.[339] For that reason, guidelines suggest reassessing neurological outcome at three or six months after the event.[340] Most studies in the systematic review informing these guidelines report neurological outcomes at least six months after cardiac arrest.[327]

Another bias, which is partly related to the time delay between index test assessment and outcome, is the interference from extracerebral causes of death after cardiac arrest. These include cardiovascular instability, which is the second most common cause of in-hospital death after cardiac arrest,[316] and multiple organ failure due to global ischaemia-reperfusion injury.[121,341] Although the incidence of these complications is maximal early after arrest, death from extracerebral organ failure may occur after neurological recovery.[277] The prevalence of death after awakening was 16% in the ICU in a single-centre study,[342] and 4.2% during hospital stay in a recent multicentre European study including 4646 patients.[343] In that study, death occurred at a median time of 9 (3-18) days after awakening, and it was more common after IHCA than after OHCA.

The present guidelines apply only to neurological prognostication. Besides hypoxic-ischaemic brain injury, other, albeit less common, causes of death in resuscitated comatose patients include cardiovascular instability,[316] and multiple organ failure.[121,341] These factors may result in treatment limitations independently from the patient's neurological status or cause non-neurological death

even after the neurological recovery has occurred.[340,343,344] In clinical practice, a comprehensive prognostic approach in resuscitated comatose patients should inevitably consider the role of extracerebral factors as well as patient characteristics such as age, comorbidities, and functional status.

[h3] Clinical examination

These guidelines are supported by evidence from a systematic review on prognostication and 2025 ILCOR CoSTRs.[60,327] The relevant treatment recommendations in the 2025 ILCOR CoSTR are:

- We suggest using pupillary light reflex at 72 h or later after ROSC for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very-low-certainty evidence).
- We suggest using bilateral absence of corneal reflex at 72 h or later after ROSC for predicting poor neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).
- We suggest using the presence of myoclonus or status myoclonus within 7 days after ROSC, in combination with other tests, for predicting poor neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence). We also suggest recording EEG in the presence of myoclonic jerks to detect any associated epileptiform activity /weak recommendation, very low-certainty evidence)

[h4] Ocular reflexes

Ocular reflexes currently used for neurological prognostication after cardiac arrest include pupillary and corneal reflexes. The pupillary light reflex comprises a temporary reduction of pupil size induced by a light stimulus. Standard pupillary light reflex is evaluated visually and elicited generally using a penlight. In recent years, a quantitative evaluation of pupillary light reflex using portable pupillometers has become available in the ICU. A bilaterally absent standard pupillary light reflex has low specificity for predicting poor outcome in the first hours after ROSC, but its accuracy progressively increases, and it achieves 0% false positive rate 100% specificity after 96 h from ROSC with 20-25% sensitivity.[327] This is presumably due to the process of brain recovery after anoxic-ischaemic injury, but it may be due partly to interference from sedatives used in the early post-resuscitation phase to maintain TTM. Standard pupillary light reflex is inexpensive and easy to use, but it is subjective and prone to interrater variability.[345]

Quantitative evaluation of pupillary light reflex (automated pupillometry) provides an objective and quantifiable measurement of the pupillary response. The most common pupillometry measures are the percentage reduction of pupillary size, generally indicated as q-pupillary light reflex[346] and the neurological pupil index.[346-348] The neurological pupil index is calculated from several dynamic parameters of the pupillary response (including constriction and dilation velocity, size, and percentage size reduction after stimulation) using a proprietary algorithm. A neurological pupil index value ≥3 is considered normal. Limited evidence showed that, unlike neurological pupil index , neurological pupil index can predict unfavourable outcome with no false positive results from 24 h or less to 72 h from ROSC.[327] In one study, this was because of the pupillometer's ability to detect a response even when the pupil size was very small, presumably from sedation.[349] Pupillometry results are expressed as a continuous measure, and the threshold for a 0% false positive rate varied among studies. In three studies in a recent evidence review, this neurological pupil index threshold varied between <2.0 and 3.14.[346-348] Another limitation of automated pupillometry is its cost.

The corneal reflex is elicited by touching the cornea's outer margin (limbus) with a cotton wisp. Alternatively, an air or water squirt can be used to minimise the risk of corneal abrasion.[350] An eye blink represents the corresponding response. In patients who are comatose after cardiac arrest, an absent corneal reflex predicts poor neurological outcome after 72 h from ROSC with 0% false positive rate (95% confidence interval 0-3.4%) and 25-40% sensitivity in most studies.[327] Like pupillary light reflex, corneal reflex is prone to interference from sedation. In addition, it may be affected by muscle relaxants. A 2020 survey showed that the modalities with which corneal reflex is assessed in comatose patients are inconsistent.[351]

[h4] Motor response

An absent or extensor motor response to pain (motor component [M] 1 or 2 of the Glasgow Coma Score) is associated with poor neurological outcome after cardiac arrest.[327] However, its specificity is low, almost never achieving 100%, even after 96 h from ROSC. Like corneal reflex, the motor response is based on striate muscle contraction, which can be affected by muscle relaxants.

[h4] Myoclonus and status myoclonus

Myoclonus consists of sudden, brief, involuntary jerks caused by muscular contractions or inhibitions. Their distribution can be focal, multifocal, or generalised.[352] The presence of myoclonus within 96 h from ROSC in patients who are comatose after cardiac arrest is associated with poor neurological outcome in most cases.[327,353,354] However, a false positive rate of up to 22% has been

described.[355] Most prognostication studies did not provide a definition or description of myoclonus. In some patients with favourable outcome, myoclonus may persist after recovery of consciousness in a chronic form of action myoclonus (i.e., triggered by spontaneous movements) known as Lance-Adams syndrome.[193,356]

Clinical myoclonus can inconsistently be associated with electrographic seizures; therefore, EEG recording can be helpful. Some studies have identified specific EEG features associated with benign myoclonus, such as a reactive[189,195] and/or continuous EEG background.[189,192] The presence of diffuse and continuous myoclonic jerks is usually described as status myoclonus. However, a consensus definition of status myoclonus is lacking. The 2014 ERC-ESICM Advisory Statement on neurological prognostication after cardiac arrest suggested that in comatose survivors of cardiac arrest, status myoclonus should be defined as a continuous and generalised myoclonus persisting for 30 min or more.[329] Evidence from two studies that did not distinguish electrographic features of status myoclonus[327] showed that status myoclonus within 24 h[357] or seven days from ROSC[188,357] is almost invariably associated with poor neurological outcome (specificity 99%-100%).

The advantages of predictors based on clinical examination include minimal equipment and costs (except pupillometry) and availability at the bedside. Their major limitations include interference from sedatives, opioids, and – except for the pupillary light reflex – from muscle relaxants. In addition, their assessment is prone to subjectivity. Automated assessment, like pupillometry for pupillary light reflex, may at least address these limitations. Finally, clinical examination results cannot be concealed from the treating team, potentially causing a self-fulfilling prophecy bias.

[h3]Neurophysiology

These guidelines are supported by evidence derived from a systematic review on prognostication and the subsequent updates incorporated in the 2025 ILCOR CoSTRs.[327,358] The relevant ILCOR treatment recommendations (which have been adopted by the ERC/ESICM) are:

- We recommend that neuroprognostication always be undertaken using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).
- We suggest using a bilaterally absent N20 wave of somatosensory evoked potential (SSEP) at ≥ 24 h from ROSC in combination with other indices to predict poor outcome in adult patients who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).

- We suggest against using the absence of EEG background reactivity alone to predict poor outcome in adult patients who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).
- We suggest using suppression or burst-suppression on EEG to predict poor outcome in adult patients who are comatose and who are off sedation after cardiac arrest (weak recommendation, very low-certainty evidence).

[h4] Electroencephalography (EEG)

Electroencephalography (EEG) is one of the most widely used and studied methods to assess brain function and prognosis after cardiac arrest.[359] EEG is also important for diagnosing and treating seizures. The main aspects of assessing EEG for neuroprognostication are background activity, superimposed discharges, and reactivity. The EEG background continuity is most important for the prognosis and is commonly categorised as continuous, discontinuous, burst suppression (50-99% suppression periods) or suppression (>99% activity <10 μV amplitude).[360] A standardised terminology for critical care EEG has been proposed by the American Clinical Neurophysiology Society (ACNS).[187]

Immediately after a cardiac arrest, the EEG background is suppressed in many patients, but it returns to a continuous normal voltage EEG within the first 24 h in most patients who ultimately achieve a good outcome.[361,362] The time for this restitution is correlated with the outcome.[360,363] The EEG background is often discontinuous and of low frequency on its first appearance.[361,364] Sedative drugs affect background continuity and have the potential to induce discontinuous or burst-suppression background in a dose-dependent manner.[365,366]

[h4] Background patterns

[h5] Suppression

A suppressed (<10μV) or low-voltage (<20μV) background, based on the the American Clinical Neurophysiology Society terminology,[187] is relatively common during the first day after a cardiac arrest in patients who later recover (Figure 5).[337,361,362] However, 24 h after ROSC, a suppressed EEG background <10μV is a reliable sign of a poor prognosis, with a false positive rate of 0.4% (95% confidence interval 0.04-1.46%),[367-372] although two false-positive predictions by this pattern 48-72 h after cardiac arrest were reported in a total of 1351 patients included in the systematic review informing these guidelines [327]. There was moderate interrater agreement for suppressed background among senior neurophysiologists.[369,373]

[h5] Burst suppression

According to the American Clinical Neurophysiology Society terminology, burst suppression is defined as 50-99% of the recording consisting of suppression alternating with bursts. The terminology does not have any amplitude criteria for the bursts, but these may be defined further as 'highly epileptiform bursts', based on appearance.[187] 'The presence of 'identical bursts' (either the first 0.5 seconds of each burst or each stereotyped cluster of ≥2 bursts appear visually similar in >90% of bursts) portends a poor prognosis in post-anoxic coma.[374] A substantial portion of patients with burst suppression during the first 24 h and occasional patients with burst suppression-pattern after 24 h still have a good outcome, which is possibly related to sedation use.[339,361,367-369,375-377] American Clinical Neurophysiology Society-defined suppression and burst-suppression are highly specific for predicting poor outcome after cardiac arrest, especially when these patterns are recorded after 24 h from ROSC.[368,378-380] However, in a large substudy of the multicentre TTM2 trial including 845 patients, the specificity of these 'highly malignant' patterns assessed locally at each participating centre was only 93%, suggesting a possible suboptimal implementation.[381] Limited evidence shows that suppression with periodic discharges and burst-suppression with identical bursts are more specific and less time-dependent than suppression and heterogeneous burst-suppression [382-386] There is substantial interrater agreement among experienced neurophysiologists for burst-suppression.[369]

[h5] Reactivity

EEG reactivity is a measurable change in amplitude or frequency upon external stimulation (auditory and pain). Interrater agreement for the assessment of EEG reactivity varied from slight to almost perfect.[369,387] A proposal for international consensus on reactivity testing exists.[388] The prognostic performance of this feature varied substantially between studies.[327,389] Absence of EEG-reactivity during the first 24 h after cardiac arrest is an indicator of a poor outcome with high sensitivity but low specificity (41.7-87.5%).[377,390-392] After 24 h, the sensitivity of absent reactivity remains high, but the specificity varied from 50% to 100%.[367,369,375,377,391-395] In a recent substudy on 821 comatose patients from the multicentre TTM2 trial, the absence of reactivity on EEG at 24 h to 14 days from ROSC predicted poor neurological outcome at 6 months with 79 [76-82]% sensitivity but only 60 [55-66]% specificity.[381]

[h4] Superimposed patterns

[h5] Periodic discharges

A 'periodic' pattern is a waveform that occurs repeatedly, with a quantifiable interval between discharges. If no such interval exists, the pattern is termed 'rhythmic'.[187] Periodic discharges may be superimposed on various backgrounds and are related to a worse prognosis. Generalised periodic discharges are a sign of a poor prognosis with limited specificity.[367,368,371,375] In general, the background on which periodic discharges appear is more related to the neurological outcome.[360] Periodic discharges on a continuous and reactive EEG background should not be considered as an indicator of a poor outcome.[192]

[h5] Sporadic epileptiform discharges

'Sporadic epileptiform discharges' describes sharp waves or spikes resembling those seen in patients with epilepsy but without the regularity of a periodic pattern. The frequency by which they appear may vary extensively from 'rare' (<1/h) to 'abundant' (≥1/10s), bordering on periodic discharges. While their appearance is related to a worse outcome, their specificity to predict poor outcome ranges from 66.7 to 100%,[327] and reports on the potentially important frequency or number of discharges were lacking in studies.[337,369,371,372] Presence of sporadic epileptiform discharges is *not* a reliable indicator of a poor neurological prognosis.

[h5] Electrographic seizures and electrographic status epilepticus

The American Clinical Neurophysiology Society defines 'unequivocal seizures' as epileptiform discharges >2.5Hz for ≥10 seconds or any pattern with definite evolution lasting ≥10 seconds.[187] This definition was inconsistently used in studies. Seizures had a low sensitivity but high specificity for a poor outcome regardless of timing.[367,369,371,375,396]

The term 'electrographic status epilepticus' defines an electrographic seizure for ≥10 continuous minutes or for a total duration of ≥20% of any 60-minute period of recording. This definition has been included for the first time in the 2021 update of the American Clinical Neurophysiology Society terminology, and none of the currently available prognostic studies has incorporated it yet. Some studies based their definition of electrographic status epilepticus on the American Clinical Neurophysiology Society classification of unequivocal seizures extending ≥30 min but also included epileptiform discharges ≥1 Hz,[208,363] and in one study ≥0.5 Hz as electrographic status epilepticus.[397] Other studies had an unclear definition of electrographic status epilepticus.[339,375,376,391] The proportion of patients classified with electrographic status epilepticus varied considerably between studies, possibly reflecting differences in definitions. One study showed that electrographic status

epilepticus evolves from high-frequency discharges early after onset to progressively slower frequencies during the following days and weeks.[198] While electrographic status epilepticus is associated with hypoxic-ischaemic brain injury after cardiac arrest, it is not as specific and consistent as suppression and burst-suppression.[207,208,210] Probably, this is partly because of its inconsistent definition in the available literature. As with periodic discharges, it is important to consider if the EEG-background is continuous and reactivity is present, which are both favourable features.[208,210] Because of the lack of a standardised classification, we recommend avoiding the term 'status epilepticus' for assessments of prognosis but instead classify the EEG background and superimposed discharges and unequivocal seizures according to the standardised American Clinical Neurophysiology Society terminology.[187]

[h4] Quantitative EEG-indices

Automated assessment of quantitative EEG features such as the burst-suppression amplitude ratio and reactivity has been tested in individual studies.[398,399] Combinations of quantitative EEG features include the Bi-spectral index (BIS) and the Cerebral Recovery Index.[400] The threshold value and specificity for BIS to predict poor outcome varied widely between studies.[401-403] Automated EEG assessments may decrease subjectivity. Prospective multi-centre studies are needed to assess the prognostic performance after cardiac arrest.

[h4] Evoked potentials

[h5] Somatosensory evoked potentials (SSEPs)

When performing SSEPs, the median nerve is electrically stimulated and the ascending signals are recorded from the peripheral plexus brachialis, cervical level, subcortical level and the sensory cortex (N20-potential) (Figure 6a). SSEPs may be depressed by barbiturate coma but are preserved with other sedative drugs such as propofol and midazolam.[404] A bilateral absence of the short-latency N20-potentials over the sensory cortex (Figure 6b) is a reliable sign of a poor prognosis after cardiac arrest with high specificity both within 48h (99.7; 85% confidence interval 98.2 – 100.0%) and at 48–96 h (99.8; 95% confidence interval 99.0–100.0) after cardiacarrest.[212,213,339,349,372,376,390,392,393,399,405-416] with a sensitivity ranging between 37.7% (95% confidence interval 34.4–41.1%) and 45.2% (95% confidence interval 40.8–49.7%). Occasional false positive predictions were reported.[417] The interrater reliability for interpretation of SSEPs was moderate to good.[418,419] The recording quality is critical, and noise from muscle activity is an important limiting factor that neuromuscular blocking drugs may eliminate.[404,418]

Recent studies have shown that very low cortical SSEP amplitudes predict poor outcome with similar specificity as absent N20-potential.[420-424] In most studies, the N20 amplitude threshold for 100% specificity was <0.5 µV. However, because of the documented variability in thresholds and SSEP montage across studies and the potential interference from sedation, low N20 amplitude is not yet recommended for predicting poor outcome after cardiac arrest.[425]

[h3]Biomarkers

These guidelines are supported by evidence derived from a systematic review on prognostication and the 2025 ILCOR CoSTRs.[327] The relevant 2025 ILCOR treatment recommendations (which have been adopted by the ERC/ESICM) are:

- We recommend that neuroprognostication always be undertaken using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).
- We suggest using neuron-specific enolase (NSE) within 72 h after ROSC, in combination with other tests, for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very-low-certainty evidence).
- We suggest against using S-100B protein for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, low-certainty evidence).
- We suggest against using serum levels of glial fibrillary acidic protein (GFAP), serum tau protein, or neurofilament light chain (NfL) for predicting poor neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).

Protein biomarkers released following injury to neurons and glial cells may be measured in blood and are likely to correlate with the extent of brain injury and neurological outcome. Neuron-specific biomarkers include NSE, NfL, and tau protein, while S100B and glial fibrillary acidic protein originate from astrocytes. Neuron-specific enolase has been recommended for assessment of brain injury and to help prognosticate outcome after cardiac arrest since 2015.[2] Several reports on novel biomarker candidates have been published since 2020.[335,426-432]

Importantly, a multimodal approach should be used for assessment of comatose survivors after cardiac arrest. Advantages of biomarkers include quantitative results, the relative ease of sampling and interpretation and their independence from the effects of sedatives. Limitations include availability, limited knowledge of their kinetics, and lack of standardisation across analytical methods. Most of the available evidence is limited to a time span of up to 72 h after cardiac arrest,

which is relevant for most patients. However, very limited evidence supports using biomarkers after 72 hours in patients who fail to awaken.

Biomarker blood values are continuous rather than dichotomous (categorical) variables. Results are dichotomised to calculate the sensitivity and specificity of these biomarkers by establishing a threshold that divides positive from negative results. Consequently, test sensitivity and specificity depend on the threshold chosen: a high threshold increases the test's specificity and decreases the sensitivity, and vice versa. Biomarkers are released with different latency and speed following acute brain injury. Although the kinetics of NSE after cardiac arrest is incompletely known, studies have shown that NSE blood levels increase up to 72 h in patients with unfavourable outcome and tend to decrease in patients with favourable outcome.[433,434]

Large studies investigating and validating promising novel biomarkers are needed to confirm their predictive value, assess their reproducibility outside specialised laboratories, and identify consistent thresholds for a specificity that should be close to 100%. The rationale for accepting a specificity of less than 100% would be that when using blood biomarkers, there will always be outliers that must be taken into consideration, e.g. due to poor calibration or issues with laboratory standards, haemolysis (for NSE) or due to poor technique in handling of samples. Demanding 100% specificity from a blood biomarker will lower the sensitivity to levels where their clinical use can be questioned, while allowing an FPR of 1% or 2% will increase their clinical relevance. With a multimodal approach, every prognostic method used to assess an individual patient must point in the same direction to be trusted. This may be particularly true for biomarkers because of their continuous nature; normal or mildly elevated levels (at the correct sampling time) should always alert the clinician of potential error in other methods, indicating poor prognosis.

[h4]Neuron-specific enolase (NSE)

Neuron-specific enolase has been studied extensively after cardiac arrest. A large substudy of the TTM-trial identified a threshold of 48 ug L^{-1} at 48 h and a threshold of 38 ug L^{-1} at 72 h with a false positive rate of 2% (95% confidence intervals 1–5%) for poor neurological outcome at 6 months.[334]

The 2021 guidelines suggest using a threshold of 60 µg L^{-1} at 48h and 72 h to predict poor outcome after cardiac arrest. In 2022, a validation study of these guidelines in 660 patients found no falsely pessimistic prediction (specificity 100 [83-100]) for an NSE >60 µg L^{-1} in comatose patients with a GCS motor score no better than 3 at ≥72 h after ROSC.[331] In the 2025 ILCOR evidence update[8] NSE values between >60 µg L^{-1} and 87 µg L^{-1} at 48h from ROSC predicted poor neurological outcome with a specificity ranging from 95% to 100%,[430,433-437] while NSE values between 46.2 µg L^{-1} and 60 µg L^{-1} at

72 h from ROSC predicted poor neurological outcome with a specificity ranging from 94% to 100%.[433,434,436,438] In another study, NSE with a threshold of 50.2 ug L^{-1} on day 4 predicted poor neurological outcome at one month with 100% specificity and 42.1% sensitivity.[439]

NSE decreases after 24 h in patients with good outcome and typically increases in patients with a poor outcome to peak at 48-96 h. NSE performs poorly at 24 h and best at 48 or 72 h.[334,415,439-444] However, an NSE measurement at 24 is useful as a baseline value to detect the NSE trend during the two following days. Increasing NSE from 24-48 or 48-72 h is a reliable indicator of a poor prognosis with similar performance as the absolute value.[445] Different chemiluminescence immonoassays were used in the included studies, which may have affected the NSE detection limits and the reference intervals [446]. Thresholds for high NSE values must be established in collaboration with the local laboratory considering the analytical method. Red blood cells contain NSE, so haemolysis (free haemoglobin) must be measured, and samples discarded if the haemolysis index threshold is exceeded because this may generate a falsely high NSE value.[446] The half-life of free haemoglobin is approximately 2-4 h compared with the 30-h half-life of NSE. Thus, the NSE value may be inappropriately increased (by NSE from red blood cells) when free haemoglobin is no longer detectable, which is a concern when using NSE for prognostication after cardiac arrest.[446]

[h4]S100B

Two observational studies investigated S100B immediately after ROSC and identified threshold values ranging from 3.56 to 16.6 with 100% specificity of poor outcome but low sensitivities of 2.8% to 26.9%.[442,443] In the largest study, S100B discriminated best at 24 h with a threshold value of 2.59 ug/L for 100% specificity, but with a low sensitivity of 10%, the corresponding sensitivity for 98% specificity (2% FPR) was 32% (threshold value 0.36 ug/L).[447] The authors concluded that S100B did not add real value to present prognostication models with or without NSE. S100B is rarely used in clinical practice and is not included in our recommendations.

[h4]Glial fibrillary acidic protein (GFAP)

Five studies published after the 2020 review evaluated the ability of the blood values of Glial Fibrillary Acidic Protein (GFAP) measured between 12 and 72 h after ROSC to predict poor neurological outcome in comatose patients after CA.[426,429,431,448,449] In these studies, high GFAP values predicted poor neurological outcome with 98-100% specificity at all time points, but the thresholds for this prediction varied widely. GFAP blood values rise earlier than NSE after cardiac arrest [450] and

can achieve an area under the receiver operating characteristic (ROC) curve of 0.85 at 12-24 h after ROSC,[426,449] higher than that of NSE.[448]

[h4]Serum Tau

Tau is a microtubule stabilising protein expressed predominately in the unmyelinated axons of the central nervous system.[450] Three recent studies showed that tau blood levels of >502.5 pg mL^{-1} at 12 after ROSC in one study[426] and 40 pg mL^{-1} in one study[431] or >131 pg mL^{-1} in another study[449] predicted poor neurological outcome with 100% specificity and 20-25% sensitivity. All three studies measured tau using the ultrasensitive single molecular array (SIMOA) assay.

[h4]Serum neurofilament light chain (NfL)

There is an increasing interest in assessing NfL to predict neurological outcome. After the publication of the 2020 systematic review informing the 2021 guidelines,[327] several studies evaluated the ability of the blood values of NfL measured between 24 h and 72 h after ROSC to predict poor neurological outcome.[335,428-430,436,451] One study[428] investigated NfL at 12 after ROSC. In this study, NfL values of 90 pg mL^{-1} in OHCA and 207 pg mL^{-1} in IHCA predicted poor functional outcome at 2-6 months with 100% specificity and sensitivity of 53 [48-59]% and 29 [20-39]%, respectively. Other studies investigated NfL at 24 h,[335,429,430,449,451] showing that values between 242 and 609 pg mL^{-1} predicted poor neurological outcome between hospital discharge and 12 months with 100% specificity and sensitivity ranging from 54 [47-61]% and 66 [54-76]%. At 48h from ROSC, NfL values between 330 and 4660 pg mL^{-1} predicted poor neurological outcome between hospital discharge and 12 months with 100% specificity and sensitivity ranging from 35 [26-45]% to 83 [69-91]%.[335,429,430,436,449,451] Fewer studies investigated NfL at 72 h after ROSC.[335,429,449] In these studies, NfL values between 244 and 970,1 pg mL^{-1} predicted poor outcome with 99-100% specificity and a sensitivity ranging from 74 [62-83]% to 85 [76-90]%. The prognostic performance of NfL was superior to that of NSE across all time points. Most studies included fewer than 100 patients. In larger studies, the Area Under Curve–Receiveing Operating Characteristic (AUROC) of NfL ranged between 0.88 and 0.97 at 48h after ROSC.[428,430,452] Unlike NSE, NfL is not affected by haemolysis. The kinetics of NfL after cardiac arrest are largely unknown. As for NSE, a source of confounding for NfL is the presence of different assays, which may create different results across measuring methods. Blood values of NfL after cardiac arrest are comparatively lower than those of NSE, and most studies used the ultrasensitive single molecular array (SIMOA) assay. At least four assays for NfL are commercially available, and a process to standardise methods is ongoing.[453]

[h3] Recommendations on NfL, GFAP, and tau for neuroprognostication after cardiac arrest

Recent evidence has shown that novel biomarkers of brain injury, such as NfL, GFAP, or tau, have comparable or superior accuracy than NSE for predicting neurological outcome in patients who are comatose after resuscitation from cardiac arrest. This is especially true for NfL, whose AUROC was 0.90 or greater in some studies.[430,452] However, these biomarkers are still not widely available. In addition, there is little information on their kinetics in the acute phase after cardiac arrest. Finally, no consistent thresholds for predicting poor neurological outcome have been identified. For this reason, at present, the ERC/ESICM do not recommend using NfL, GFAP and tau for neuroprognostication after cardiac arrest. Further research is ongoing, and it is likely that this recommendation will be revised in the near future.

[h3]Imaging

These guidelines are supported by evidence derived from a systematic review on prognostication and 2025 ILCOR CoSTRs . The relevant treatment recommendations in the 2025 ILCOR CoSTR (which have been adopted by the ERC/ESICM) are:

- We recommend that neuroprognostication always be undertaken using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).
- We suggest using brain imaging studies for prognostication only in centres where specific experience is available (weak recommendation, very-low-quality evidence).
- We suggest using the presence of a marked reduction of the grey matter/white matter (GM/WM) ratio on brain CT within 72 h after ROSC or the presence of extensive diffusion restriction on brain MRI at 2 to 7 days after ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with TTM (weak recommendation, very low-quality evidence).

[h4] Computed tomography (CT) of the brain

Following cardiac arrest, hypoxic-ischaemic brain injury causes cytotoxic oedema, which appears as an attenuation of the GM/WM interface, and vasogenic oedema leading to brain swelling, visible as an effacement of cortical sulci.[454] Measurement of the ratio between the GM and the WM densities (GWR), expressed in Hounsfield units, is a method to quantify the degree of oedema. The density of

the GM is higher than that of the WM, so GWR is normally higher than 1. The lower the GWR, the greater the severity of brain oedema.

GWR reduction occurs early in patients with severe hypoxic-ischaemic brain injury. Most studies on reduced GWR showed that this sign was 100% specific for poor neurological outcome as early as 1h after ROSC.[327] However, the sensitivity of brain CT to predict poor outcome increases over time. In one study on 2204 unconscious patients who underwent brain CT in the first 24 hours after ROSC, the sensitivity of GWR for predicting in-hospital mortality increased over the first four hours post-arrest, reaching a maximum of 25% after five hours, while false positive rates remained <5% at all time points.[455] In a substudy of the TTM trial on 356 patients undergoing brain CT within seven days after ROSC, brain oedema was more common (46% vs 10%) at >24 h to 7 days than within 24 h after ROSC. Sensitivity increased from 14% to 57% and specificity from 97% to 100% across these two time points. Among 36 patients with repeated brain CT, 15/36 had oedema at the second CT (median 77h after ROSC), while only one ot the 15 patients with a positive result on the second CT had oedema at the first brain CT 2h after ROSC.[456] These results were replicated by a similar study in 95 patients.[457] In another study comparing brain CT performed within six hours (n= 76) or 72-96 hours (n=54) after ROSC, the area under the receiver operating characteristics (AUCs) of GWR increased from 0.70 to 0.92. Nonquantitative signs of brain oedema, such as the presence of sulcal effacement, loss of boundary between grey and white matter at the basal ganglia level, and presence of the pseudo subarachnoid sign, were also more common in brain CTs performed 72-96 h after ROSC.[458]

The methods for GWR measurement varied across studies. In most of them, GWR was calculated between GM and WM areas within the basal ganglia.[327,457-461] In others, measurements within the cerebrum (centrum semiovale and high convexity area) were performed.[462-464] Finally, other studies calculated an average of the GWR in the two previous areas.[460,465,466] In almost all studies, a GWR threshold for 100% specificity was identified. However, its value varied across studies,[327] probably reflecting differences between scanners and software,[467] and in calculation methods.

In recent studies, methods for automated GWR assessment to measure brain oedema on CT in cardiac arrest patients have been investigated. These methods showed comparable [468] or superior accuracy compared to manual GWR assessment.[469,470] Automated GWR measurement holds promise for standardising the assessment of the severity of HIBI after cardiac arrest with brain CT, making it less operator-dependent. However, the optimal method has not been established, and the evidence is limited to a few studies.

[h4] Magnetic resonance imaging (MRI) of the brain

Along with CT, magnetic resonance imaging (MRI) of the brain is the most investigated imaging-based predictive index in patients who are comatose after cardiac arrest.[327] Brain MRI is more challenging to perform in ventilated ICU patients, and MRI was generally performed later than brain CT, usually at 48h or later from ROSC. On brain MRI, cytotoxic oedema from hypoxic-ischaemic brain injury appears as a hyperintensity on diffusion-weighted imaging (DWI) sequences.[471] In several studies, the presence of DWI lesions is associated with poor neurological outcome after cardiac arrest.[462,472-475] However, the assessment was done qualitatively, and specificity was inconsistent (range 55.7-100%). Apparent diffusion coefficient (ADC) enables a semiquantitative assessment of DWI changes, therefore limiting subjectivity. However, the ADC metrics in prognostication studies varied.[327] The two more common measures are the lowest mean ADC,[461,466,476,477] and the proportion of brain volume (percentage of voxels) below a given ADC threshold.[461,466,476-481] All these studies identified an ADC threshold for 100% specificity, often with sensitivities above 50%. All studies on ADC MRI had a small sample size, which limited their precision. In many studies, imaging was performed at the treating physician's discretion, which may have introduced a selection bias. Unlike clinical examination and EEG, imaging studies are not prone to interference from sedative drugs. In addition, they can be assessed blindly. Their major limitation is the lack of standardisation of measurement techniques. Despite the available studies showing high accuracy for both brain CT and MRI, the number of studies was limited, with a wide variability in the adopted measurement techniques, which significantly limits the reproducibility of their results. For this reason, it is reasonable to reserve the use of imaging studies for prognostication only in centres where specific experience is available. Since there is currently no standard for CT-GWR or MR-ADC measurements, these techniques can be recommended to confirm the presence of generalised and extensive ischemic injury apparent from conventional visual analysis by an experienced neuroradiologist. Finally, imaging studies cannot be performed at the bedside, and MRI may not be feasible in the most unstable patients, which limits its applicability, especially in the early post-resuscitation period. In patients undergoing ECPR, the strong magnetic field of conventional MRI may interfere with the functioning of the ECMO pump.

[h3]Multimodal prognostication

The 2021 ERC-ESICM Guidelines on Post-Resuscitation Care included an algorithm for the prediction of poor neurological outcome in patients who are comatose after cardiac arrest.[3] This algorithm recommended that, in patients who are comatose with a motor response no better than abnormal

flexion at ≥72 h from ROSC after major confounders have been excluded, poor neurological outcome was predicted when at least two concordant signs indicating poor outcome are present. These signs were:

- Bilaterally absent pupillary and corneal reflex 72 hours or later after ROSC; use of an automated pupillometer, when available, is recommended;
- A bilaterally absent N20 SSEP wave;
- Highly malignant EEG patterns, defined as a suppressed background ± periodic discharges or burst-suppression according to American Clinical Neurophysiology Society, after 24 h from ROSC;
- NSE blood values above 60 µg/L at 48 and/or 72 h after ROSC; increasing NSE blood levels between 24-48h or 24/48 and 72 h further support a likely poor outcome;
- Status myoclonus, defined as continuous and generalised myoclonus for more than 30 minutes in the first 72 hours after ROSC;
- Signs of diffuse and extensive anoxic injury on brain CT or MRI.

This algorithm was subsequently validated in three multicentre studies on a total of 1791 patients.[331,482,483] All these studies confirmed that the 2021 ERC-ESICM prognostication algorithm predicts poor outcome with a 0% false positive rate (95% confidence intervals 0-3.7%). One of these studies was conducted in the KOHRNPRO 1.0 registry in Korea, where withdrawal of life-sustaining therapy was reported in only 12 patients (0.9% of the total cohort) with a consequent low risk of self-fulfilling prophecy bias.[331] However, this algorithm also had limitations:

- In validation studies, almost half of patients remained with indeterminate outcome after applying the 2021 algorithm.[484]
- The 2021 algorithm was focused only on predicting poor neurological outcome and did not include evidence from the ERC/ESICM endorsed systematic review on the prediction of good neurological outcome published in 2022. Although the 2021 guidelines recommend caution if discordant signs indicate a potentially good outcome, no guidance was provided on incorporating these signs in a specific prognostic strategy. In studies validating the 2021 guidelines, 21% of patients with indeterminate outcome had neurological recovery after applying the algorithm.
- No guidance was provided on the timing of SSEP or imaging. For SSEP, evidence from prognostication studies showed that a bilaterally absent wave accurately predicted poor outcome at 24 h or earlier after ROSC.[422,485,486] For imaging, the evidence mentioned above showed that the sensitivity of brain CT increased after 24 from ROSC.

The 2025 writing group changed the suggested prognostication algorithm to overcome the limitations above (Figure 4). The changes were based mainly on evidence published after 2021 and on a recent study designed to improve the sensitivity of the previous algorithm, reduce indeterminate outcome, and allow the prediction of good neurological outcome.

[h3] Prediction of good neurological outcome

Predicting good neurological outcome after cardiac arrest has several advantages. Firstly, it can reduce uncertainty in prognostication. Recent evidence shows that the prognosis remains indeterminate in about half of the cases when using an algorithm based uniquely on prediction of poor neurological outcome.[1,484] Secondly, detecting a chance of good neurological recovery can reassure patients' relatives and inform their discussions with clinicians. Thirdly, it may help inform decisions about escalation of organ support. Finally, it may counterbalance a falsely pessimistic signal from predictors of poor neurological outcome. In fact, no single test predicts poor outcome with absolute certainty.[327] The 2021 guidelines for post-resuscitation care acknowledged these limits and suggested using caution and repeating the assessment when discordance is present, i.e., if signs indicating a poor outcome coexist with signs indicating a potential for recovery.

Based on an ERC-ESICM-endorsed systematic review of 36 studies in 7149 adult patients with post-anoxic coma,[487] the 2025 ILCOR CoSTR identified six signs predicting neurological recovery in comatose cardiac arrest survivors.[8] These include a withdrawal or localising response to pain (motor score of the Glasgow Coma Scale [GCS-M] 4-5) in the first 4 days after ROSC, normal (<17 mcg/L) NSE blood values within 72 h after ROSC, absence of diffusion restriction on MRI between 72 hours and 7 days after ROSC, and a continuous or nearly continuous normal-voltage EEG background without periodic discharges or seizures within 72 hours from ROSC. Similar to unfavourable EEG patterns, the ILCOR 2025 CoSTR recommends using the American Clinical Neurophysiology Society (ACNS) EEG terminology[187].

The ERC-ESICM review also identified a high (>4 µV) amplitude of the N20 SSEP wave as a good neurological outcome predictor after cardiac arrest.[353,423,488] However, ILCOR does not recommend using this sign yet because of variability in the methods to calculate it and concern regarding potential interference from sedative drugs. Normal (<55 pg/mL) blood levels of NfL at 24-72 h from ROSC predicted good outcome with high specificity and sensitivity. However, the evidence was limited to two studies where NfL was measured in the same laboratory using a high-sensitivity technique, which is not widely available.[335,336]

Two cohort studies have investigated the ability of ILCOR-recommended good outcome predictors to counterbalance discordant poor prognostic signs [+ Lagebrant 2025].[483] In one of these studies,[483] the coexistence of one good outcome predictor with one ERC-ESICM-recommended [489] poor outcome predictor was associated with neurological recovery in 11% of cases, compared to 3% when only a poor outcome predictor was present. In another study [Lagebrant 2025 - submitted], among 2245 patients who underwent prognostication, one unfavourable predictor and one or more favourable predictors coexisted in 104, of whom 33 (32%) had a good neurological outcome at six months.

[h3] Suggested prognostication strategy

Prognostication is a continuous process that starts immediately, even if the prognostic balance is made at 72 h or later after ROSC (Figures 4 and 7). Some indices, such as the EEG signs of potential recovery, are best detected within 24-36h from ROSC, while others, such as the NSE blood levels, must be recorded daily to determine their trend. Even if the accuracy of NSE values for predicting poor outcome is highest at 48-72 h, NSE values at 24 h provide a baseline.

Prognostic assessment should start with an accurate clinical examination.[490] Its main scope is to confirm that the patient is comatose because of hypoxic-ischaemic brain injury. Clinical examination should be performed daily to detect signs of neurological recovery, such as purposeful movements or to identify a clinical picture suggesting impending brain death. The latter may include fixed, dilated pupils, diabetes insipidus, and cardiovascular changes suggesting herniation, such as bradycardia associated with hypertension or unexplained haemodynamic instability. Brain death occurs in 5-10% of patients who die after cardiac arrest resuscitated with conventional CPR and in about 25% of patients who die after resuscitation with extracorporeal CPR.[317,489] In most cases, brain death occurs during the first 3-4 days after ROSC. A suggested algorithm for brain death screening after cardiac arrest is shown in Figure 9.

Awakening from post-anoxic coma typically occurs within 3-4 days from ROSC.[213,277] However, patients who are initially unconscious following cardiac arrest are usually treated with sedatives and neuromuscular blocking drugs to facilitate temperature management, mechanical ventilation and other life support measures. Therefore, to enable a reliable clinical examination, these drugs should be stopped for sufficient time to avoid interference from their effects. The World Brain Death Project consensus group recommends that clinical examination be delayed until at least five elimination half-lives of the drug administered with the longest half-life.[491] Although this recommendation has been made in the context of diagnosing brain death, it can be equally suitable

for prognostic assessment. Short-acting drugs are preferred whenever possible but even a short-acting drug such as propofol has a half-life of 2.3 – 4.7 h, which implies the need to stop sedatives for at least 24 h in most cases. This will be much longer if there is renal and/or hepatic impairment or if longer acting drugs have been given. When residual sedation or paralysis is suspected, consider using antidotes to reverse the effects of these drugs. Use caution when administering flumazenil to reverse the effect of benzodiazepines because this may precipitate seizures. Apart from sedation and neuromuscular blockade, other major confounders include hypothermia, severe hypotension, sepsis, and metabolic or respiratory derangements.

A motor response no better than abnormal flexion (M≤3) of the Glasgow Coma Scale was the entry point of the 2021 prognostication algorithm, based on its high sensitivity for poor outcome prediction. However, this low threshold leaves out most patients destined to neurological recovery. Recent evidence (Lagebrant 2025) showed that using M<6 as an entry point increases the ability of the algorithm to identify patients with good outcome without reducing specificity for poor outcome. Hence, the prognostication strategy described below applies to unconscious patients, defined as not being awake and obeying commands (M<6) at ≥72 h after ROSC. Results of earlier prognostic tests are also considered at this time.

In an unconscious patient at ≥72 h from ROSC, in absence of confounders, poor outcome is very likely when two or more of the following predictors are present: no pupillary and corneal reflexes at ≥72 h, bilaterally absent N20 SSEP wave at ≥24 h, highly malignant EEG at >24 h, NSE >60 µg/L at 48 h and/or 72 h, status myoclonus ≤72 h, or a diffuse and extensive anoxic injury on brain CT/MRI. Most of these signs can be recorded before 72 h from ROSC. However, their results will be evaluated only when the prognosis is formulated (Figure 7). In one study,[492] a strategy of using ≥2 predictors had 0[0-8]% FPR compared with 7[1-18]% of the 2015 ERC-ESICM stepwise strategy (due to false positives for pupillary light reflexes).

Evidence from the 2013 and 2020 reviews showed that a bilaterally absent N20 SSEP wave is the most widely documented predictor of poor outcome and the most consistently associated with 100% specificity. However, false-positive predictions have occasionally been reported. In some of these cases, the cause of a false positive result was an incorrect reading of the SSEP record because of artefacts.[493] Neuromuscular blockade improves readability of SSEPs, and it should be considered whenever possible.[494] Time after ROSC does not affect the specificity of SSEPs, which can be recorded from day 1.

Based on expert opinion, we suggest that both pupillay and corneal reflexes should be absent at the time of prognostic assessment to predict poor outcome reliably. Unlike SSEPs, ocular reflexes are

prone to interference from sedation. Evidence in post-anoxic coma shows that automated pupillometry is more sensitive than standard pupillary light reflex in detecting pupil response to light when pupil size is small, reducing the risk of false positive results.[349] Unlike standard pupillary light reflex, automated pupillometry delivers a stimulating light source with standard characteristics (intensity, duration, and distance from the eye) and quantitatively measures pupillary response, ensuring reproducibility. For this reason, we suggest detecting the absence of pupillary light reflex with a pupillometer, if available.

Status myoclonus is a prolonged period of myoclonic jerks. Although there is no universal definition for status myoclonus, based on our previous definition,[1] we suggest that, in comatose survivors of cardiac arrest, status myoclonus should be defined as a continuous and generalised myoclonus persisting for 30 minutes or more. Aside from duration and continuity, other clinical features of myoclonus suggest poor outcome. These include a generalised (vs. focal), axial (vs. distal), or stereotyped (vs. variable) distribution. Conversely, some EEG features, such as a continuous or reactive background or the presence of spike-wave discharges synchronised with the myoclonic jerks indicate a potential for good outcome.[192] We suggest recording an EEG in patients with post-arrest status myoclonus to identify an epileptiform activity and detect signs associated with potential recovery.

Among unfavourable EEG patterns, those more consistently associated with poor neurological outcome are suppression and burst suppression ('highly malignant' patterns). According to the American Clinical Neurophysiology Society, a suppressed EEG background is defined as >99% of activity having a voltage less than 10 µV, while burst-suppression is defined as 50-99% of the record consisting of suppression, alternated with bursts.[187] During the first 12-24 h after ROSC, these patterns are more prevalent but have a higher risk of false-positive prediction. Confounding from sedatives may contribute to this. We suggest using these EEG patterns for prognostication only after 24 h from ROSC. The absence of EEG background reactivity has an inconsistent specificity for poor neurological outcome, and we no longer recommend using it for this purpose.

High blood NSE values are a sign of neuronal cell damage and have long been recommended as a predictor of poor neurological outcome after cardiac arrest.[495] While prediction with 0% FPR can be achieved anytime from 24 h to 7 days after ROSC, the sensitivity of an individual NSE measurement for prediction of poor neurological outcome with 0% FPR is highest at 48-72 h after ROSC.[327] However, the NSE threshold value for 0% FPR is inconsistent because of a few patients with good neurological outcome despite very high NSE values. The presence of these outliers can be partly explained by the release of NSE from extracerebral sources, such as red blood cells or

neuroendocrine tumours. Repeated blood sampling and careful exclusion of extracerebral sources is recommended when using NSE for neuroprognostication. Another cause of variability for the NSE thresholds is represented by the different measurement techniques used.[446] In the 2020 ERC/ESICM review, the highest recorded NSE thresholds for 0% FPR at 48 and 72 h from ROSC were 120 µg/L and 79 µg/L, respectively. However, these data refer to outliers, and in most studies the 0% FPR threshold was 60 µg/L and 50 µg/L, respectively. Based on these data, we presume that the risk of a false-positive prediction associated with an NSE value of 60 µg/L is minimal, especially because at least another predictor should confirm the NSE signal. Increasing NSE values between 24 h and 48 h or between 24/48 h and 72 h also suggests a poor outcome even if the incremental prognostic value of adding NSE trends to a single NSE value is uncertain.[327,441,445] We suggest performing serial NSE samples at 24, 48, and 72 h after ROSC to detect NSE trends and minimise confounding from occasional haemolysis.

Signs of diffuse and extensive hypoxic-ischaemic brain injury on brain CT can be present very early after ROSC,[327] several studies have shown that sensitivity or brain CT to detect hypoxic-ischemic brain injury increases during the first week after ROSC.[456-458,496,497] Patients who are admitted to hospital after OHCA often have their brain CT performed in the emergency department. We suggest repeating brain CT if the patient is unconscious at the time of prognostication (72 h–96 h after ROSC) and the first brain CT does not show signs of hypoxic-ischemic brain injury.

Cytotoxic oedema reduces water diffusivity, which appears on magnetic resonance imaging (MRI) as a hyperintensity on diffusion-weighted imaging (DWI) with corresponding low apparent diffusion coefficient (ADC) values Because measurement methods are not standardised and multicentre validation studies using comparable measurement techniques are lacking, we suggest that predictive indices based on neuroimaging are used only in places where specific experience is available. We also suggest that centres using neuroimaging for prognostication after cardiac arrest create their own normal and threshold values based on the technique.

When none of the criteria for poor outcome described above are present, patients should be assessed for signs of *potential recovery*. These include a GCS motor score of 4 or 5 at 72-96 h after ROSC, normal blood values of neuron-specific enolase (NSE) at 24 h-72 h after ROSC, a continuous background without discharges on EEG within 72 h from ROSC, and absent diffusion restriction in the cortex or deep grey matter on MRI on days 2–7 after ROSC. In a recent study on 2445 patients with GCS-M ≤5 and no concordant signs of poor functional outcome, more than 60% of patients with at least one of these signs had a favourable outcome at six months. In those with two concordant

favourable signs and no signs of poor outcome, the neurological recovery rate was >80% [Lagebrant 2025].

When neither concordant unfavourable signs nor favourable signs are present, the neurological outcome remains *indeterminate*. Although the prognosis will be poor in most of these patients, neurological recovery is still possible. [483][Lagebrant 2025] We, therefore, suggest observing and re-evaluating patients with indeterminate outcome over time to detect signs of awakening (Figure 4). In three studies, the prevalence of late awakening, defined as a recovery of consciousness at ≥48 h from the suspension of sedation, was 20/89 (22%),[498] 56/194 (29%),[277] and 78/228 (34%).[216] Last awakening occurred on day 11, day 12, and day 23 from the suspension of sedation, respectively. The rates of good neurological outcome among late awakeners were 80%, 90% and 73%, respectively. In two other studies, the last patient awoke on day 22 and day 29.[499,500] Organ dysfunction, such as post-resuscitation shock or renal failure [216,277] and use of midazolam instead of propofol for sedation[216,284] were associated with a higher likelihood of late awakening, which suggests that at least some of these cases may have been due to a reduced clearance of sedation. In a before-and-after study comparing two sedative regimens (propofol-remifentanil versus midazolam-fentanyl) in 460 comatose resuscitated patients undergoing temperature control targeted at hypothermia, use of propofol-remifentanil was associated with significantly lower odds of delayed awakening after adjustment (OR 0.08 [0.03–0.2]),[277] confirming indirect evidence from a previous smaller study[235].

Late awakening does not preclude full neurological recovery. However, the likelihood of awakening in resuscitated patients who remain comatose decreases progressively with time and the rates of good neurological outcome are generally lower in late vs. early awakeners.[216,277,499,501]

[h3] Neuroprognostication in extracorporeal cardiopulmonary resuscitation

Hypoxic-ischaemic brain injury (HIBI) is common in patients resuscitated with ECPR. Because ECPR is used in patients with refractory cardiac arrest, those who are admitted to the ICU with ECPR have prolonged resuscitation times, which may increase the risk of severe HIBI.[502] In a systematic review of 23,388 resuscitated patients in 32 studies, the prevalence of brain death was three times higher in patients resuscitated with ECPR vs. those resuscitated with conventional resuscitation (27.9 vs. 8.3 %).[317] There is no validated neuroprognostication strategy for patients with HIBI after ECPR, and the general neuroprognostic principles apply to these patients. However, some special considerations are necessary in this category of patients.

Clinical examination in patients undergoing ECPR is often hampered by profound and prolonged sedation. Sedation and muscle relaxants only minimally affect the pupillary light reflex, which can provide valuable prognostic information. In a study of 100 patients undergoing veno-arterial ECMO (of whom 49 with refractory cardiac arrest and 51 with refractory cardiogenic shock), an neurological pupil index (NPi) below 3 (abnormal) anytime from 24 h to 72 h was 100% specific for predicting 90-day mortality with 53% sensitivity.[503]

Regarding biomarkers, one important concern is haemolysis due to extracorporeal circulation, which may lead to a release of NSE from the red blood cells and cause false positive results. NSE values are linearly correlated with the degree of haemolysis and the free haemoglobin levels.[504] Although a continuous NSE release from haemolysis due to ECPR should result in persistently high NSE, a study on 129 ECMO patients, most of whom underwent ECPR,[505] showed that NSE decreases in patients who had neurological recovery and increased in those who had poor neurological outcome, therefore showing a similar kinetic to that in patients resuscitated from conventional CPR. Similar trends were observed during the first 48h in another study on 190 ECPR patients.[506]

Prognostic accuracy studies on ECPR patients suggest that the NSE threshold for predicting poor outcome may be higher than in patients resuscitated with conventional CPR. In a study on 256 OHCA patients from the Prague trial,[507] the median NSE blood values at 24 h, 48h, and 72 h were significantly higher in ECPR patients than in conventional CPR patients, despite the rates of good neurological outcome being not significantly different between the two groups (conventional CPR 29.3% vs ECPR 21.7%; p = 0.191). The AUROCs for outcome prediction were not significantly different, suggesting that NSE had comparable overall accuracy in both groups. However, the NSE values corresponding to 95% specificity for predicting poor neurological outcome were higher in the ECPR group at all three time points (84 µg/L at 24 h and 48h and 129 µg/L at 72 h, compared with 60 µg/L, 65 µg/L and 57 µg/L, respectively, in the conventional CPR group). In a study of 159 patients treated with venoarterial ECMO, of whom 101 (64%) had cardiac arrest, six of the 36 patients with good neurological outcome at 29 months had an NSE >100 µg/L 48h after the start of ECMO.[508] The optimal NSE thresholds for predicting poor outcome with a minimal risk of falsely pessimistic prediction in patients resuscitated with ECPR are currently unknown.

Unlike NSE, NfL is unaffected by haemolysis, and it can be particularly advantageous for neuroprognostication in ECPR patients. However, the evidence in ECPR patients is still preliminary. One study of 98 patients undergoing venoarterial ECMO, of whom 74 were in cardiac arrest, showed that suppression or burst-suppression on EEG in these patients were associated with poor neurological outcome.[509] Recording EEG is helpful in ECPR patients because of the high rate of

neurological injury, prolonged sedation and paralysis confounding neurological examination, and the risk of epileptiform activity from HIBI.[510]

Performing MRI in ECPR patients is difficult because the strong magnetic fields (1.5–3 Tesla) of conventional MRI are incompatible with extracorporeal life support circuits. Portable MRI with lower magnetic fields has been used to identify brain injury (but not hypoxic-ischaemic brain injury) in ECPR patients.[511] However, their spatial resolution is lower than that of conventional MRI. At the time of this writing, there are no published studies on MRI for prognostication in comatose ECPR patients.

Brain CT can be safely performed in patients undergoing ECPR. In a study on 30 ECPR patients GWR had an AUROC for predicting neurological outcome ranging from 0.848 to 0.952, depending on the calculation method used.[512] In a substudy of the Prague ECPR trial including 45 patients GWR calculated at the caudate and putamen levels on brain CT performed within 36h from arrest predicted neurological outcome at six months with AUROCs of 0.86 and 0.77 respectively.[513] GWR was not significantly different between patients resuscitated with ECPR vs conventional CPR. Another study, however, showed a low accuracy of brain CT performed early (<3h from ROSC) for assessing the severity of HIBI in ECPR patients. A substudy of the Prague OHCA trial showed that GWR measured at the basal ganglia level performed poorly as a measure of brain oedema on brain CT performed at a median of 4.3 hours after arrest. Almost all (93%) patients had contrast agents administered for coronary angiography before brain CT.[513] None of the above mentioned studies assessed cerebral postanoxic oedema with common visual assessment criteria used by neuroradiologists, such as the presence of sulcal effacement, loss of boundary at the basal ganglia level, or pseudo-subarachnoid haemorrhage sign described in other studies.[456,458]

Only a few studies specifically investigated the accuracy of standard neuroprognostic tests in predicting neurological outcomes in patients undergoing ECPR. On the other hand, there is no specific pathophysiologic reason for these tests to perform differently in comatose ECPR patients as compared to those resuscitated with conventional CPR. Pending further research, we suggest using a multimodal approach for prognostication in comatose ECPR patients. We recommend paying particular attention to the risk of confounding from haemolysis when using NSE (see above). The optimal NSE threshold to predict poor outcome is currently unknown. Imaging studies require transport to the imaging suite, which implies technical difficulties and potential risk in ECPR patients. Standard MRI carries the additional risk of interference with extracorporeal circuit from the strong magnetic field. Specific prospective studies are needed to assess the optimal prognostication

strategy in patients resuscitated with ECPR. Assessment of cerebral oedema on brain CT using GWR in ECPR patients is insufficiently supported by available evidence.

[h2] Withdrawal of life-sustaining therapy (WLST)

While a minority of the resuscitated patients treated in an ICU die during the first few days due to cardiovascular collapse or massive brain swelling causing brain death, most deaths will be secondary to a decision to withdraw life-sustaining therapy (WLST).[316,318,341,514] Generally, a presumption that the final neurological outcome of the patient will be poor is central to this decision.[318] Pre-existing co-morbidities may also contribute to a WLST decision.[514] The clinical team discussing the prognosis of an individual patient need to consider that inaccurately pessimistic prognostication could lead to WLST in patients who might otherwise achieve a good functional outcome but also that overly conservative prognostication could leave patients in a severely disabled state undesired by themselves and their relatives.[515] Patients may not receive specific treatments because they are not available, or because there is an active decision to withhold them. The main reasons for withholding treatments are that they will not benefit the patient or, if known, the patient's wishes not to have a specific treatment.[515,516] There are few data on withholding life-sustaining therapies in post-cardiac arrest patients specifically.

The practice of WLST varies widely across Europe and impacts the proportion of CA-patients surviving with severe brain injury (CPC 3-4). Lacking high-quality data, this fraction appears to vary widely from approximately 10-50%.[230,337,344] The most apparent effects are seen for patients who remain in an unresponsive wakefulness/vegetative state (CPC 4). As an example, 1/243 (0.4%) survivors in a northern European study[230] compared with 61/195 (31%) in an Italian multi-centre study[337] were in CPC 4 at 6 months. Evidence for variation in WLST practice across Europe was also found in the ETHICUS Study: physicians from southern Europe were less prone to withdraw treatment compared with those from northern Europe, and there was also an effect of religion.[517] The Ethicus-2 Study has shown that the frequency of WLST and withholding decisions among general ICU patients has increased over the last 15–20 years.[518]

Studies using propensity score matching indicate that premature (<72 h from cardiac arrest) WLST for neurological reasons (WLST-N) are common and may be the cause of death for a substantial proportion of patients who might have recovered to a good outcome if their intensive care treatment had been prolonged.[519,520] A recent study found that the practice of WLST-N <72 h varied between 20-60% among nine US hospitals and was inversely related to the rate of neurological consultation.[521] A similar variation in the practice of early WLST was found in a nationwide UK

study.[19] A high frequency of early WLST-N may indicate prognostic pessimism and lower healthcare quality.

The brain stem is more resistant to hypoxic-ischaemic injury than the cerebrum, and the recovery of functions such as spontaneous breathing and sleep-wake cycle is part of the trajectory towards an unresponsive wakefulness/vegetative syndrome. The period when the patient is still dependent on intensive care is sometimes referred to as the 'window of opportunity for death'.[522] This perception may cause a sense of urgency for the relatives and treating team, indirectly impacting decisions on premature WLST.[523,524] One qualitative study identified limitations in family-team communication as an important factor for premature WLST after cardiac arrest.[524] Caregivers' inappropriate avoidance of uncertainty may also be important, leading to overly pessimistic perceptions of the prognosis.[525] Although some tests show high specificity for predicting a poor outcome before 72 h, we recommend that, in general, conclusions about the neurological prognosis are postponed until at least 72 h after the cardiac arrest and the influence of sedative and metabolic factors have been ruled out. This will enable most patients with good outcome to awaken before the prognostic assessment, decreasing the risk of false predictions.[284] We encourage local protocols on how to collect information about the extent of brain injury during the first days. Use all available resources to inform a multimodal assessment.[60,327] Relatives will require regular, clear, and structured information and an understanding of their role in decision-making. Early indicators of poor prognosis may be conveyed in a balanced fashion to inform relatives that the situation is grave and enable time for adjustment before critical decisions are made. The bedside nurses are confronted by grieving caregivers, which may be very stressful.[524] Allocate sufficient time for communication around the prognosis within the team and with the relatives.[526]

While the assessment of post-cardiac arrest neurological prognosis and discussions about WLST are most often linked, try to separate these processes in discussions and documentation. Decisions about WLST need to consider several aspects other than the perceived brain injury; for example, age, co-morbidities and the prognosis for general organ function.[514] Consequently, for ethical reasons, WLST may be considered for patients in whom the neurological prognosis is uncertain or even favourable. Conversely, intensive care may be prolonged despite dismal neurological prognosis because absolute certainty is unobtainable for an individual patient.[527] The patient's preferences are central. Since the patient cannot be asked and advance directives are rare among cardiac arrest victims, the relatives are usually the primary source of information about the patient's likely wishes. Once a decision on WLST has been made, the ERC/ESICM recommend a transition to a structured end of life care, to address patient symptoms, the caregiver situation and potential for organ

donation. Guidelines on end of life and palliative care in the ICU were recently updated by the ESICM.[528]

[h2] Long-term outcome after cardiac arrest

[h3] Long-term outcome

In settings where WLST is rare, poor outcomes because of severe hypoxic-ischaemic brain injury are common.[529,530] In contrast, in countries practising WLST, most survivors (82–91%) experience a 'good' functional outcome and return home; just 1-10% require long-term care.[529,530] At one-year and beyond, evidence suggests that general health status approximates normal population values.[531] However, such generic health assessments may lack sufficient granularity to capture the breadth of problems.[322,532] Cardiac arrest survivors often continue to experience symptoms such as memory difficulties, anxiety, fatigue and physical limitations which can impact their health-related quality of life and societal participation.[529-531,533-536] Supplementing generic assessment with condition or problem-specific assessment is therefore recommended.[322] Older age, female sex, anxiety, depression, and impaired neurocognitive function are significantly associated with poorer health-related quality of life following OHCA.[534] A registry-based study reported significantly worse health-related quality of life in IHCA (n=1369) survivors when compared to OHCA (n=772) survivors.[537]

[h4] Cognition

A recent review of neurocognitive function following OHCA highlighted the substantial heterogeneity in outcome reporting and use of different cut-points,[533] with possible cognitive impairment ranging between 0-88%. Most common impairments affect episodic memory, executive functioning, and processing speed.[533,538] Most cognitive recovery occurs within the first three to six-months after the cardiac arrest.[529,530,539]

[h4] Fatigue

Up to 70% of cardiac arrest survivors report fatigue.[529,530,540] Limited evidence suggests no significant difference in fatigue levels between 1-5 yrs after OHCA.[540] Both physical and mental fatigue is widely described and associated with cognitive deficits, anxiety, depression.[538,540] and low levels of physical activity.[541]

[h4] Emotional wellbeing

A review of IHCA and OHCA survivors described little change in the prevalence of short (<6-months) and long-term (>6-months) anxiety (22-24%) and depression (19%).[535] A further review, of OHCA survivors only, reported similar levels of anxiety (26%), depression (19%) and post-traumatic stress disorder (20%), with symptom prevalence appearing to increase over time for anxiety and depression.[536] For OHCA, age and female sex are non-significant moderators for anxiety and depression.[536] However, younger survivors (<60 years) are at a higher risk of developing depressive symptoms within six-months. [535]

[h4] Physical function

Survivors frequently experience mobility limitations over both the short and longer-term,[537,542-545] which are more common compared to both general[530] and matched cardiac populations.[542] Problems are more common in older individuals, females, and those with cognitive impairment, anxiety or depression.[542] Similarly, at six-months post-OHCA, one-third of survivors in the TTM2 trial self-reported low levels of physical activity,[543] an important cardiovascular risk factor,[546] which were more common in those who were obese or, for example, had mobility problems or cognitive impairment.[543]

[h4] Pain

Pain is reported by 21-58% of survivors at 3-6-months,[545,547,548] and in 53% of IHCA survivors at 12-months.[549]

[h4] Societal Participation and return to work

Limitations in usual activities are reported at 3-6 months,[544,547] and 12-months.[549] Up to 50% self-report difficulties performing work or other activities due to physical (50%) or emotional (35%) problems at six-months.[545] Self-reported restrictions in societal participation are greater when compared to matched cardiac patients.[550] Cognitive impairment, depression, fatigue and restricted mobility negatively affect societal participation.[550] Younger patients also report more restrictions in returning to societal activities.[551]

Approximately 50% return to previous work levels within six-months, rising to 63% with reduced hours; median return time is around 80 days.[551] Although a smaller sample size, similar percentages of return have been reported by others; for example, 42% and 55% at six and 12-months respectively.[552] Factors reducing work return include cognitive impairment, fatigue, and female sex.[550,553-555]

[h4] Family members and close friends

Family members and close friends, often referred to as co-survivors, particularly those who witness or participate in the resuscitation, commonly experience anxiety, posttraumatic stress, and sleep disturbance.[556,557] Higher acute traumatic stress in the partners of cardiac arrest survivors was associated with symptoms of post-traumatic stress at both 3-months and 1-year.[558] These symptoms were greater in partners than in survivors. Bereaved family members also experience high levels of emotional burden.[556]

[h2] Rehabilitation and follow-up after cardiac arrest

[h3] Rehabilitation during hospitalisation

Although are no ICU rehabilitation studies for cardiac arrest specifically, there are rehabilitation guidelines for post-intensive care syndrome and these recommend early mobilisation, delirium management and ICU diaries. [559,560] Early mobilisation (e.g., functional/resistance exercises) within 72 hours of ICU admission may reduce ventilation duration, length of stay, delirium and muscle strength.[559] Information on the type, dose and length of mobilization is limited and evidence for long term outcomes is lacking.

An RCT (N=750) compared usual levels of ICU mobilisation (mean 8.8 (SD 9.0) minutes/day) with increased early mobilization (mean 20.8 (SD 14.6) minutes/day).[561] Whilst there were no significant effects in any of the prespecified outcomes, the intervention group showed a trend towards more adverse events. No cardiac arrest survivors were included. A subsequent systematic review and meta-analysis report mobilisation in the ICU to be safe, and with no overall increase of adverse events.[562]

Delirium is common among cardiac arrest survivors (up to 92%).[563] Multimodal prevention strategies and assessment, as described for general intensive care patients may be relevant.[559,564] The Confusion Assessment Method for the ICU or the Intensive Care Delirium Screening Checklist are recommended assessment approaches.[559] Physical and non-physical assessments before hospital discharge are recommended.[3,559] Early screening of cognitive and emotional status to predict later problems in OHCA survivors is widely supported.[565-569]

[h3] Specialised in-patient neurological rehabilitation

In-patient rehabilitation for cardiac arrest survivors is provided within general brain injury rehabilitation programmes, informed by multiple clinical practice guidelines for different types of

acquired brain injuries, including hypoxic or traumatic brain injury and stroke.[570-572] Even small improvements may reduce the burden of care on family and society.

A review of five observational studies of in-patient rehabilitation for adult cardiac arrest survivors with acquired brain injury (N=187) reported low quality evidence of positive effects for functional and neurological outcome (standardised mean difference 0.71, 95% CI 0.45-0.96).[573] Additional observational studies of HIBI report similar findings.[574-576] Whilst worse recovery in HIBI patients when compared to other acquired brain injury groups has been reported,[575] where baseline function was similar, outcomes were not statistically different.[577] For those who are comatose or in an unresponsive wakefulness state, outcome was unfavourable, and they rarely recover.[578-580]

[h3] Cardiac rehabilitation

Many, but not all, cardiac arrest survivors are eligible for generic cardiac rehabilitation programs.[581] These typically include aerobic exercise, sometimes with addition of resistance training, for 20-90 minutes/ 1-7 sessions a week,[582] delivered at an institution, home-based or electronically.

A recent metanalysis including 85 RCTs (>23 000 patients) confirmed that exercise-based cardiac rehabilitation for patients with coronary heart disease reduces cardiovascular mortality, recurrent cardiovascular events and hospitalization; some evidence suggests cost-effectiveness and improvements in health-related quality of life.[582] Whilst there is no evidence of specific benefit following cardiac arrest, two small observational studies (N=33) included in a recent review suggest that exercise-based rehabilitation is safe for survivors and without adverse events.[573] Moreover, exercise duration (but not capacity) increased (mean difference 3.7 min (95% CI 0.5–7.0), p=0.02). Cognitive and emotional problems are inadequately addressed in traditional cardiac rehabilitation programmes,[583] and access remains limited for cardiac arrest survivors.[581]

[h3] Follow up

Based on limited evidence,[584-587] a structured follow-up including screening of fatigue, cognitive and emotional status, and information provision is suggested to identify the problems and care needs of both cardiac arrest survivors and co-survivors (Figure 8).[1,3,556] Asking about physical impairment should also be considered.[542] Information should cover both medical subjects such as cardiac disease, risk factors, medication and ICD and other topics such as potential physical, cognitive and emotional changes and fatigue, resuming daily activities, driving and work, relationship and sexuality.[3] Some useful links include: Heartsight (https://ourheartsight.com/), Sudden Cardiac Arrest UK (https://suddencardiacarrestuk.org/), and Life After Cardiac Arrest (https://www.hlr.nu/wp-

content/uploads/2022/04/livetefterhjartstopp_ENG.pdf). Whilst patient forums report on the benefit and value of peer support networks,[588] published studies on the effectiveness of such networks or virtual/online forums are not available.[589,590]

[h3] Screening and management of cognitive, emotional and physical status, and fatigue

[h4] Cognitive issues

Screening should include asking the survivor about cognitive complaints. Family members or close friends can provide useful insight. Formal screening is recommended when possible. Evidence supports use of the Montreal Cognitive Assessment (MoCA) (Table 2);[591,592] sensitivity improves when used in combination with the Symbol Digit Modalities Test (Table 2).[591] For those that screen positive, consider referral to a healthcare professional with experience in brain injury-related impairments – e.g., an occupational therapist or neuropsychologist.

Cognitive rehabilitation aims to reduce the impact of cognitive impairments on daily life.[593] Psychoeducation is an essential part of this approach. There are no studies of cognitive rehabilitation for cardiac arrest,[573] but clinical practice guidelines in other acute brain injury patients are useful.[593,594] For example, compensatory memory strategies[593,595] and metacognitive strategy training.[593,596,597] Examples of integrated cardiac and cognitive rehabilitation for cardiac arrest survivors are described but not evaluated.[583,598]

[h4] Emotional issues

The Hospital Anxiety and Depression Scale (HADS) is widely used in cardiac arrest,[535,536] but there are few psychometric evaluations of its performance in this population. [599,600] However, there is strong evidence to support the use of the Hospital Anxiety and Depression Scale in the general population and in patients with cardiac disease[601] (Table 2). Although the Impact of Events Scale-revised[558,565] and the Post-Traumatic Stress Disorders Checklist (Table 2) have been used in cardiac arrest,[567,568] evidence of psychometric properties in this population is limited. For those who screen positive, consider referral to a specialist in the management of emotional problems - e.g., general practitioner, psychologist, psychiatrist, social worker. It is also important to monitor the wellbeing of family members and close friends.[3,529,530] Emotional difficulties could be treated in line with symptom specific pharmacological and non-pharmacological recommendations.

There is limited evidence that psychosocial interventions specifically designed for cardiac arrest survivors can be of value.[573] A single RCT (121 of the 301 patients were cardiac arrest survivors) of a

social-cognitive intervention suggests that when delivered to cardiac patients and partners, a more positive impact on emotional wellbeing is reported than when delivered to patients alone.[602,603] A small study confirmed the feasibility of an individual acceptance and mindfulness-based exposure therapy delivered digitally for cardiac arrest survivors with post-traumatic stress disorder (n=11); the potential for outcome improvement was described.[604]

[h4] Screening and management of fatigue

Whilst assessment guidance in this population is lacking, the most widely used measures include the Modified Fatigue Impact Scale (MFIS),[605-608] the Multi-dimensional Fatigue Inventory-20 items (MFI-20),[538,606] and the Fatigue Severity Scale (FSS)[607-609] (Table 2). Evidence from other populations (e.g., multiple sclerosis) suggests where both mental and physical fatigue are important the Modified Fatigue Impact Scale is preferable to the Fatigue Severity Scale.[610] For those that screen positive, consider referral to specialist in fatigue and fatigue management - e.g. psychologist, occupational therapist, physiotherapist, rehabilitation medicine physician.

Limited evidence suggests that a telephone-delivered energy conservation and problem-solving therapy may benefit cardiac arrest survivors.[607,608] Clinical practice guidelines in other patient groups, may be useful;[611,612] including for example, behavioural interventions such as pacing and prioritising activities. And whilst fatigue is a survivor-reported barrier to returning to work following OHCA,[555] compensatory strategies, such as modified work tasks and flexible work hours, can be helpful.[552,555]

[h4] Screening and management of physical challenges

Assessment guidance for physical function or physical activity in this population is lacking. Whilst patient self-reports, such as those described in a recent trial,[613,614] may over-estimate the amount of physical activity engaged in,[615] they could be useful indicators of where cardiac arrest survivors could benefit from physical activity interventions (Table 2). For those reporting low levels of physical activity or limitations in physical function, consider referral to a physiotherapist or an occupational therapist.

[h3] Rehabilitation and interventions to increase societal participation and overall health-related quality of life

Comprehensive care pathways should be multi-factorial, multi-disciplinary, and tailored to an individual's needs based on the biopsychosocial model. The ultimate goals of care should support

survivors towards optimal psychological recovery, relative independence, re-integration into society and an improved health-related quality of life.

However, underpinned by the low-quality of evidence, a recent review of rehabilitation interventions was unable to determine intervention effectiveness on the secondary consequences of cardiac arrest survival including health-related quality of life and neurological function.[573] Among cardiac arrest survivors working prior to the event almost half report an unmet rehabilitation need at six-months.[552] Further high-quality studies are urgently needed.[546,573] A small pilot study (n=40) tested a residential and home-based rehabilitation programme including education, physical activity training, and psychosocial support.[573] Whilst recruitment rates were less than expected and the specialised residential component may not be feasible in many settings, patient and clinician's satisfaction was high. Initial reports suggest a positive impact on depression, disability, and life activities.

[h4] Family members and close friends

Prior to hospital discharge and at follow-up, enhanced communication with family and close friends is important to highlight 'what to expect', signpost to helpful resources including survivor/patient organisations and, where appropriate, to seek further help from, for example, a general practitioner.[556]

[h2]Organ donation

These recommendations encourage providing patients and their families with the opportunity to donate organs in the event of brain death or the decision to WLST (Figure 9). In the face of the increasing shortage of transplant organs, it is important to remember that a significant proportion of patients who will not survive cardiac arrest represent a potential source of solid organ donors. All health systems should develop, implement and evaluate protocols designed to optimise organ donation opportunities for patients who have had a cardiac arrest.

Recent CPR is not a barrier to organ donation. A recent ILCOR systematic review identified 35 observational studies of organ donation after donor cardiac arrest.[8] For all organ grafts studied (heart, lung, kidney, pancreas, liver, intestine) there was no significant difference in graft function or recipient survival with organs from donors who died after an initially successful resuscitation, compared with donors who had not received CPR.

Organ donation policies and practices vary internationally, and clinicians must respect local legal and ethical requirements. There are different pathways for patients with cardiac arrest to become organ

donors.[616] These guidelines specifically address organ donation after brain death (DBD) or controlled donation after circulatory death (cDCD: Maastricht category III donors) in patients with ROSC or who have been treated with ECPR.[617] Challenges in implementing uncontrolled donation protocols after cardiac arrest (Maastricht category I/II donors) are discussed in the ERC Guidelines 2025 Adult Advanced Life Support, and ethical aspect in the ERC Guidelines 2025 on Ethics in Resuscitaiton.[172,618]

A systematic review identified 26 studies that showed that the prevalence of brain death in ventilated comatose patients with hypoxic-ischemic brain injury who died after cardiopulmonary resuscitation was 12.6% (95% CI 10.2–15.2%), with a higher prevalence after ECPR [27.9% (19.7–36.6%) vs. 8.3% (6.5–10.4%)], and that approximately 40% of them donated organs.[317] The median time to diagnosis of brain death was 3.2 days. Patients who remain comatose after resuscitation from cardiac arrest, especially when resuscitated by ECPR, should be actively evaluated for signs of brain death. Scoring systems that may enable early detection of patients with a high probability of brain death after cardiac arrest may help increase organ donation after out of hospital cardiac arrest.[619,620] High-volume centres are more likely to refer and procure transplantable organs from patients with non-survivable OHCA.[621]

Even in the absence of brain death, some patients may be evaluated as possible cDCDs when WLST is considered. Donation after controlled circulatory determination of death is an increasingly important organ donation source. For kidneys, the proportion of cDCDs has increased from 17% to 31% in Australia between 2009 and 2019,[622] and from 21% to 46% between 2009 and 2023 in the UK.[623] However, cDCDs after cardiac arrest are probably underreported. Two recent controlled studies investigated the outcomes of organs from cDCDs after cardiac arrest resuscitation and showed that the survival of kidneys[624] or hearts[625] donated by cDCDs after cardiac arrest was not inferior to that of non-CPR donors.

Implementation of ECPR to treat refractory OHCA is associated with increased organ donation and an excellent outcome of transplanted organs.[626] Thus, ECPR has a potential to increase not only the number of survivors of prolonged cardiac arrest but also the number of organ donors.[489,627,628] The Utstein OHCA template includes organ donation as a supplementary outcome and we suggest that cardiac arrest registries report if organ donation after initial resuscitation from cardiac arrest occurred.[629]

[h2]Investigating sudden unexplained cardiac arrest

Unexplained cardiac arrest refers to cases where no diagnosis is evident after initial ECG, echocardiography, and coronary assessment in sudden cardiac arrest survivors.[630] Recent registry

data suggest that 12.3% of sudden cardiac arrest survivors had no diagnosis after the initial assessment, with higher rates observed in younger or exercise-related cases.[631 632] Further testing may identify a specific diagnosis in 41 to 61% of patients.[632,633] Possible diagnoses include primary electrical disorders like Brugada and long QT syndromes, latent genetic cardiomyopathies (e.g. arrhythmogenic RV, hypertrophic and dilated cardiomyopathies), inflammatory heart disease (e.g. myocarditis, sarcoidosis), ischaemia without atherosclerotic coronary artery disease (e.g. coronary spasm) and conduction system abnormalities.

A thorough diagnosis after unexplained cardiac arrest is important for patient clarity, tailored treatment, and identifying at-risk family members. The latest ESC guidelines standardise sudden cardiac arrest survivor evaluations before diagnosing idiopathic ventricular fibrillation and emphasise a multidisciplinary approach.[180] Recommended diagnostic testing of patients with unexplained cardiac arrest includes blood sample collection for toxicology and genetic testing, data retrieval from cardiac implantable electronic devices and wearable monitors, repeated 12 lead ECG and continuous cardiac monitoring, cardiac MRI, sodium channel blocker tests, and exercise testing.[180]

Genetic testing plays an important role in identifying heritable causes of unexplained cardiac arrest.[634] A confirmed diagnosis of a heritable condition should prompt targeted genetic testing, focusing on genes with strong evidence of causative links with diagnostic yields varying by condition (e.g., ~20% in Brugada Syndrome to ~80% in Long QT Syndrome).[180,634] However, a negative result does not rule out a genetic cause, and family screening may still be necessary. The role of genetic testing in unexplained cardiac arrest survivors without a clear diagnosis remains uncertain, with diagnostic yields up to 17% in unexplained cardiac arrest and ~10% after detailed clinical assessment.[180] Long-term follow-up of unexplained cardiac arrest patients is recommended because of the high risk of recurrence of arrhythmia (16–26%) often within the first few years. Risk is higher in those lacking a thorough initial evaluation.[635] In the absence of diagnosis at the initial phase, prolonged follow-up and repetition of investigations can help isolate a diagnosis, most often related to an electrical heart disorder.[636]

[h2]Cardiac Arrest Centres

There is wide variation among hospitals in the availability and type of post-resuscitation care, as well as clinical outcomes, which has given rise to the concept of the cardiac arrest centre as a means of providing post-cardiac arrest patients with uniform, high-quality treatment according to current standards of care.[637-639] Definitions of a cardiac arrest centre vary, but an expert consensus paper

published by the Association for Acute Cardiovascular Care of the European Society of Cardiology, European Association of Percutaneous Coronary Interventions, European Heart Rhythm Association, European Resuscitation Council, European Society for Emergency Medicine and European Society of Intensive Care Medicine, states that the minimum requirements for a cardiac arrest centre are 24/7 availability of an on-site coronary angiography laboratory, an emergency department, an intensive care unit (ICU), imaging facilities (such as echocardiography, computed tomography, and magnetic resonance imaging), as well as a network organization.[640]

ILCOR suggests that adult patients with non-traumatic OHCA cardiac arrest should be cared for in cardiac arrest centres and this recommendation had been adopted by the ERC/ESICM.[39] The weak recommendation is based on low-certainty evidence from a systematic review that used the European position paper to define cardiac arrest centres.[641] The systematic review included one RCT [642] and 15 observational studies.[643-657] Of these, 12 reported better survival to hospital discharge and one showed no difference. However, the studies were very heterogeneous, and their interpretation is problematic because all were at moderate or serious risk of bias. The one RCT was undertaken in London, UK and randomised OHCA patients with ROSC and without ST elevation on their ECGs to be transferred to cardiac arrest centre or to the nearest acute hospital.[642] There was no difference in 30-day mortality (primary outcome), but there was also little difference in the treatment provided in the acute hospitals and cardiac arrest centres.

It is likely that the optimal configuration of cardiac arrest centres will vary among different countries and regions but in many healthcare systems the trend is to regionalise the care of cardiac arrest patients in a similar way to the regionalisation of major trauma. Despite only low-certainty evidence supporting cardiac arrest centres, major European scientific organisations are general supportive of their implementation. Further details on the system behing cardiac arrst centers ar ein the ERC Guidelines 2025 System Saving Lives.[658]

[h1]Conflict of interest statement

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[h1]Legends

Figure 1. Post-resuscitation care for unconscious patients.

Abbreviations PCI percutaneous coronary intervention; ICU intensive care unit; EEG electroencephalogram; ICD implantable cardioverter defibrillator

Figure 2. Haemodynamic and ventilation targets for the comatose post-cardiac arrest patient.

Abbreviations MAP mean arterial pressure; TV tidal volume

Figure 3. Multiple modalities used for the prediction of neurological outcome in the comatose post-cardiac arrest patient.

Abbreviations EEG electroencephalogram; SSEPs somatosensory evoked potentials; NSE neurone specific enolase; CT computed tomography; MRI magnetic resonance imaging.

Figure 4. Algorithm for neurological prognostication in patients who are comatose after cardiac arrest

This algorithm is designed specifically for predicting neurological prognosis and does not account for extracerebral factors that may influence patient outcomes.

Abbreviations - CT: computed tomography; EEG: electroencephalography; GCS-M: Glasgow Coma Scale Motor score; MRI: magnetic resonance imaging; NSE: neuron-specific enolase; SSEP: short-latency somatosensory evoked potentials.

NOTES

[1] Major confounders may include analgo-sedation, neuromuscular blockade, hypothermia, severe hypotension, hypoglycemia, sepsis, and metabolic and respiratory derangements.

[2] Use a pupillometer, when available, to determine if the pupillary light reflex is absent.

[3] Perform serial NSE samples at 24, 48, and 72 h after ROSC to detect NSE trends and minimise confounding from occasional haemolysis. Increasing NSE values between 24-48h or 24/48 h and 72 h further support a likely poor outcome.

[4] Defined as continuous and generalised myoclonus persisting for 30 minutes or more.

Figure 5. EEG patterns with high specificity for poor neurological outcome at 24 h or later after ROSC.

A. Suppressed EEG background. Based on the American Clinical Neurophysiology Society (ACNS) 2021 terminology,[187] this is defined as a very low-voltage background with more than 99% of the activity having an amplitude below 10 µV.
B. Suppressed EEG background with periodic discharges.
C. Burst-suppression with identical bursts. Burst-suppression is defined as 50-99% of the recording consisting of suppression alternating with bursts. When either the first 0.5 seconds of each burst or each stereotyped cluster of ≥2 bursts appear visually similar in >90% of bursts, these bursts are defined as identical.
D. Burst-suppression with heterogeneous bursts (variable burst appearance).

Figure 6. Short-latency somatosensory evoked potentials (SSEP) in a patient with preserved SSEP cortical activity (left tracing) and in a patient with severe HIBI (right tracing).

SSEP of the upper limb are obtained after bipolar transcutaneous electrical stimulation of the median nerve at the wrist. In each SSEP recording, the four tracings represent the electrical neural activity induced by the stimulus at various anatomical levels during its central propagation along the somatosensory pathway. Positive waves are downward deflections of the tracing from the baseline, and negative waves are upward deflections. Each positive or negative wave is indicated by a P or N letter, respectively, followed by a number indicating its latency from the stimulus in milliseconds. The more distal the generator of a wave from the stimulus site, the longer its latency is.

The four tracings represent, from top to bottom: brachial plexus on the same side of the stimulus (EP or Erb); cervical cord (N13); cervicomedullary junction (P14) and upper midbrain and thalamus (N18); primary somatosensory cortex on the opposite side of the stimulus (N20 and P25).
On the left-hand side of the figure, the N20 is present. The tracing on the right-hand side, from a patient with severe HIBI, shows no cortical N20/P25 waves.

Figure 7. Simplified timeline showing suggested timings for recording multimodal predictors and formulating neurological prognosis in patients who are comatose after resuscitation from cardiac arrest.

Abbreviations – CT: computed tomography; MRI: magnetic resonance imaging; NSE: neuron-specific enolase.

Figure 8. Recommendations for in-hospital functional assessments, follow-up and rehabilitation after cardiac arrest.

Figure 9. Organ donation algorithm after cardiac arrest.
ROSC: return of spontaneous circulation; WLST: withdrawal of life-sustaining treatment.

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