Targeted Temperature Management Post Cardiac Arrest
A Learning Resource for Intensive Care Nursing Staff

Pages 1 to 4: ICU Guidelines

Page 4 to end: Pathophysiology; Post-cardiac arrest syndrome; Oesophageal probe placement; Algorithm for immediate treatment; Immediate interventions; Targeted Temperature Management using the Arctic Sun; Prognostication and testing methods; Organ donation; Supporting the family.

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GUIDANCE FOR TARGETED TEMPERATURE MANAGEMENT AFTER CARDIAC ARREST

INTENSIVE CARE UNIT RAIGMORE HOSPITAL

Introduction:

Targeted Temperature Management (TTM) previously known as therapeutic hypothermia is an active treatment aimed at achieving and maintaining a specific core body temperature for a specific duration of time to improve clinical outcome following resuscitation from cardiac arrest.

A recently published study by Nielsen et al. (2013) demonstrated no advantage for TTM of 33°C in comparison with a TTM of 36°C. Strict TTM is essential to avoid hyperthermia.

Indications:

Adult patients presenting with the following:

- Presenting rhythm ventricular fibrillation/tachycardia*
- Return of spontaneous circulation (ROSC)
- Persistent coma in the emergency department as defined by GCS < 9
- Witnessed arrest
- Less than 15 minutes of down time prior to arrival of emergency medical services
- Less than 60 minutes of advanced cardiac life support prior to ROSC

*Patients who present in a rhythm other than VT/VF should be considered for treatment providing that they would otherwise be admitted to the intensive care unit (ICU).

Other indications at the discretion of the ICU Consultant:

- Including non-VF or in-hospital cardiac arrests.
- Particularly primary cause of cardiac arrest in previously fit patients.

Exclusions:

- Time from ROSC to initiation of TTM > 8 hours
- Greater than 30 minutes of MAP less than 60 mmHg
- Persistent shock in spite of vasopressors (systolic < 90 mmHg)
- History of terminal illness
- Other possible cause of coma
- Poor prognosis due to co-morbidity, poor functional status or prolonged time without CPR. Lack of any neurological response, including brain stem activity is likely to indicate a poor prognosis.

Pregnant females may be included at the discretion of the consultant in charge.
Goals of care:

- Determining and treating the cause of cardiac arrest.
- Minimising brain injury using neuroprotective measures.
- Managing cardiovascular dysfunction.
- Managing problems that may arise from global ischaemia and reperfusion injury.
- Rapidly achieve and maintain a core body temperature of 36°C when circulation is restored after arrest. TTM should be initiated as soon as possible and within 4 hours of ROSC.
- Maintain this temperature at a steady state for 12 – 24 hours after the initiation of temperature control.
- Involvement of Cardiologist for appropriate procedures e.g. urgent coronary revascularisation.

Immediate interventions:

- Intubation and mechanical ventilation. Change humidifier temperature control setting to mask mode.
- Insertion of central venous catheter and arterial cannula.
- Insertion of naso-gastric tube: consider enteric feeding following completion of TTM i.e after 12-24hrs.
- Insertion of oesophageal temperature probe to monitor core temperature. Avoid rectal temperature as this may be slow to reflect a change in core temperature.
- Obtain admission bloods: U/Es, LFTs, Ca2+, Mg+, PO4, Glucose, CRP, Troponin, Cholesterol, TFTs, FBC and coagulation screen.
- Obtain ABG and glucose.
- Record GCS including pupillary size and response.
- Record sedation score (RASS).
- 12-lead ECG.
- Early echocardiogram.
- Administer sedative infusion(s) as prescribed.
- Prepare arctic sun device. Perform thorough skin assessment prior to applying the pads. Choose the appropriate pad size for the patient.
- If patient presents cold, allow controlled slow rewarming to 36°C at a rate of 0.5°C per hour using the arctic sun device.

Record the following when commencing TTM:

- Record the patient’s core temperature prior to starting treatment. Hourly temperature assessment should be confirmed with a secondary monitoring device i.e. tympanic thermometer. Document both core and tympanic temperature recordings.
- Record the exact time when the treatment is commenced.
- Record the exact time when the patient’s core temperature reaches 36°C.
- Record the proposed length of time for maintaining the temperature at 36°C i.e. 12 hours or 24 hours.
- Record water and patient temperature hourly as displayed on the arctic sun.
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## ASSESSMENT AND MONITORING PRIORITIES DURING TARGETED TEMPERATURE MANAGEMENT

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| **Neurological control**                        | • Allow the patient to remain completely rested and avoid unnecessary interventions during TTM e.g. avoid change of position, routine tracheal suctioning, routine bed bathing.  
  • Maintain head of bed elevation > 30°.  
  • Check pupil size and response every hour: absent pupillary or corneal reflexes or motor response to pain at 72 hours are predictors of poor outcome.  
  • Report any signs of seizures to medical staff: anti-convulsants may be prescribed if seizing is diagnosed.  
  • EEG needs to be considered in order to assess brain cortical activity and diagnose seizures.                                                                                                                                                                                                 |
| **Control of shivering (less likely at 36°C)**   | • Monitor for signs of shivering and treat to prevent increase in metabolic rate.  
  • Review RASS: titrate sedation to maintain RASS -5.  
  • Treatment may include magnesium bolus or NMBA bolus.  
  • If NMBA continuous infusion is prescribed use peripheral nerve stimulator to monitor hourly train-of-four (TOF): aim for TOF 1/4 to 2/4.                                                                                                                                                                                                 |
| **Acute Coronary Syndrome management and follow-up care.** | • Investigate and treat acute coronary syndromes: thrombolysis and antiplatelet drugs may be given as usual provided there are no contraindications.  
  • Commence medications as per acute coronary syndrome guidelines. Consider NG aspirin and clopidogrel.  
  • Daily 12-lead ECG.  
  • 2nd troponin to be obtained 12 hours after admission.  
  • Echocardiogram if not already done on admission.                                                                                                                                                                                                                                                                 |
| **Potential for organ donation and withdrawal of life-sustaining therapies.** | • Organ donation should be considered in those who have achieved ROSC and who fulfil criteria for death using neurological criteria.  
  • In those comatose patients in whom a decision is made to withdraw life-sustaining therapy, organ donation should be considered after circulatory death occurs.  
  • Discussions about potential organ donation should be initiated with the specialist nurse for organ donation (SNOD) at the time the criteria in recommendation is met.  
  • A multi-disciplinary team (MDT) should be responsible for planning the approach and discussing organ donation with those close to the patient.  
  • The MDT should include the medical and nursing staff involved in the care of the patient led throughout the process by and identifiable consultant; the SNOD; local faith representative(s) where relevant. |
Introduction:

- Successful return of spontaneous circulation (ROSC) is the first step towards the goal of complete recovery from cardiac arrest. The complex patho-physiological processes that occur following whole body ischaemia during cardiac arrest and the subsequent reperfusion response during CPR and following successful resuscitation have been termed the **post-cardiac arrest syndrome**.

- Depending on the **cause of the arrest**, and the severity of the post-cardiac arrest syndrome, many patients will require multiple organ support and the treatment they receive during this post-resuscitation period influences significantly the overall outcome and particularly the quality of neurological recovery.

- The post-resuscitation phase starts at the location where ROSC is achieved but, once stabilised, the patient is transferred to the most appropriate high-care area (e.g. emergency room, cardiac catheterisation laboratory or intensive care unit (ICU)) for continued diagnosis, monitoring and treatment. The post-resuscitation care algorithm outlines some of the key interventions required to optimise outcome for these patients.

- Of those comatose patients admitted to ICUs after cardiac arrest, as many as 40–50% survive to be discharged from hospital depending on the cause of arrest, system and quality of care. Of the patients who survive to hospital discharge, the vast majority have a good neurological outcome although many have subtle cognitive impairment.

The post-cardiac arrest syndrome comprises:

2. Post-cardiac arrest myocardial dysfunction: this can be severe and recovery is usual after 48 to 72 hours.
3. Systemic ischaemia/reperfusion response: tissue reperfusion can cause programmed cell death potentially affecting all organ systems.
4. Persistent precipitating pathology: coronary artery disease is the most common precipitating cause following out of hospital cardiac arrest.

Effects:

- The severity of this syndrome will vary with the duration and cause of cardiac arrest. It may not occur at all if the cardiac arrest is brief.

- Post-cardiac arrest brain injury manifests as coma, seizures, myoclonus, varying degrees of neurocognitive dysfunction and brain death.

- Among patients surviving to ICU admission but subsequently dying in-hospital, brain injury is the cause of death in approximately two thirds after out-of hospital cardiac arrest and approximately 25% after in-hospital cardiac arrest.

- Cardiovascular failure accounts for most deaths in the first three days, while brain injury accounts for most of the later deaths.
Withdrawal of life-sustaining therapy is the most frequent cause of death (approximately 50%) in patients with a prognosticated bad outcome, emphasising the importance of the prognostication plan.

Post-cardiac arrest brain injury may be exacerbated by microcirculatory failure, impaired autoregulation, hypotension, hypercarbia, hypoxaemia, hyperoxaemia, pyrexia, hypoglycaemia, hyperglycaemia and seizures.

Significant myocardial dysfunction is common after cardiac arrest but typically starts to recover by 2–3 days, although full recovery may take significantly longer.

The whole body ischaemia/reperfusion of cardiac arrest activates immune and coagulation pathways contributing to multiple organ failure and increasing the risk of infection. Thus, the post-cardiac arrest syndrome has many features in common with sepsis, including intravascular volume depletion, vasodilation, endothelial injury and abnormalities of the microcirculation.

**Aim of targeted temperature management:**

- To reduce brain injury and improve neurological outcome.
- To slow the cellular reactions that can cause brain and other organ damage after the heart restarts.

**Pathophysiology:**

- The brain has a small amount of oxygen stores.
- Cerebral perfusion and oxygen delivery stop during cardiac arrest and oxygen stores are rapidly depleted.
- After oxygen is depleted, the brain turns to anaerobic metabolism to sustain function.
- Glucose and adenosine triphosphate (ATP) levels rapidly deplete if return of blood flow is not achieved.
- This causes ion pumps that use ATP to fail resulting in electrolyte imbalances that include potassium, sodium and calcium, resulting in cellular oedema and cell death.

**Effects of reperfusion:**

- Reperfusion initiates chemical processes that lead to inflammation and continued injury in the brain.
- This is known as reperfusion injury.
- Reperfusion injury is thought to include the release of free radicals, nitric oxide, cathecholamines, cytokines and calcium shifts, which all lead to mitochondrial damage and cell death.
- This process may last as long as 24 to 48 hours.
- In low perfusion states, the blood-brain barrier is disrupted, leading to worsening cerebral oedema.
**Benefits:**

The complete benefits of targeted temperature management are not well understood but the following are suggested:

- Reduced intracranial pressure.
- The cerebral metabolic rate is decreased by 6% to 7% for every 1°C decrease in the body temperature. Decreasing the cerebral metabolic rate decreases cerebral oxygen consumption.
- TTM helps to stabilise the influx of calcium and glutamate by slowing the neuro-excitatory processes, thereby reducing the disruptions in the blood-brain barrier and preventing premature cell death.
- TTM is also thought to decrease many of the chemical reactions that occur during reperfusion, such as free radical production.

**Why are mitochondria important?**

- Mitochondria are often referred to as the powerhouses of the cells.
- Mitochondria are tiny organelles inside cells that take in nutrients, break them down and **create energy** for the cell.
- Creating cell energy is referred to as cellular respiration.
- Most of the chemical reactions involved in cellular respiration happen in the mitochondria.
- The energy made by the mitochondria is in the form of a chemical called adenosine triphosphate (ATP). Sugar molecules are broken down to release ATP which is used to transport energy within the cell for metabolism.
- Mitochondria are able to take up calcium, store it and release it when it is required.
- Dysfunction of mitochondria can affect the production of cell-specific products that are essential for proper cell functioning and energy production. This can eventually lead to cell death and failure of the organ system. Hence the importance of preventing mitochondrial dysfunction.
The Apoptotic Pathway:

- ATP and other high-energy metabolites breakdown leading to increased intracellular levels of lactate, H+ ions, and phosphates resulting in intracellular acidosis.
- Calcium influx induces mitochondrial dysfunction.
- Glutamate is an important neurotransmitter and plays the principal role in neural activation. Prolonged glutamate exposure causes neuron hyperexcitability.
- Excessive glutamate release can overstimulate the brain and lead to excitotoxicity causing cell death resulting in seizures or strokes.

What are free radicals??

- Every moment, as we breathe in oxygen and our cells produce energy through our normal everyday living processes, molecules inside our cells react with the oxygen we breathe in. This is called oxidative stress.
- It is exactly as oxygen reacting with certain metals (e.g. on a car) producing rust. The scientific name for rust is oxidation.
- That same “rust” (oxidation) happens in every single one of our cells as we breathe in oxygen. The oxidation also occurs through our normal everyday internal processes such as metabolism and immune defence.
- As these molecules within our cells react with the oxygen (oxidation) they become free radicals.
- So now this free radical molecule that is a molecule that has at least one unpaired electron and is therefore very unstable and highly reactive.
• The free radical (unstable molecule) now goes around the cell literally stealing electrons from other healthy molecules.

• This is where antioxidants come in to play. An antioxidant is a natural biochemical substance that protects living cells from free radicals and the damage they cause. Antioxidant means “against oxidation”.

• Free radicals are not just formed through breathing and other normal bodily processes, but there are many outside influences that dramatically further produce free radicals in the cells e.g. stress, toxins, chemicals.

• Free radicals in the cells are like little fires. Once a free radical is formed that “small fire” begins to grow just like a real fire.

• If this fire is not extinguished by antioxidants, then serious damage occurs in the cells, tissues and organs.

• Free radicals will damage cell membranes, enzymes, blood lipoprotein, unsaturated fatty acids in the cell membranes and even damage chromosomes and DNA. All of this damage will eventually lead to premature aging and disease.
Indications for therapeutic hypothermia:

Adult patients presenting with the following:

- Presenting rhythm ventricular fibrillation/tachycardia *
- Return of spontaneous circulation (ROSC).
- Persistent coma in Emergency Department as defined as GCS < 9.
- Witnessed arrest.
- Less than 15 minutes of down time prior to arrival of Emergency Medical Services.
- Less than 60 minutes of advanced cardiac life support (ACLS) prior to ROSC.

* Patients who present in a rhythm other than VF/VT should be considered for treatment providing that they would otherwise be admitted to the Intensive Care Unit.

Other indications at the discretion of ICU Consultant:

- Including non-VF or in-hospital arrests.
- Particularly primary cardiac cause of arrest in previously fit patients.

Exclusions:

- Time from ROSC to initiation of TTM > 8 hours
- Greater than 30 minutes of MAP less than 60 mmHg
- Persistent shock in spite of vasopressors (systolic < 90 mmHg)
- History of terminal illness
- Other possible cause of coma
- Poor prognosis due to co-morbidity, poor functional status or prolonged time without CPR. Lack of any neurological response, including brain stem activity is likely to indicate a poor prognosis.

Pregnant females may be included at the discretion of the consultant in charge.

Goal:

- To reach target temperature of 36°C within 4 hours of ROSC.
- For every hour delay to onset of cooling, mortality increases by 20%
- This temperature should be maintained for 12 to 24 hours.
Priorities:

- The patient is sedated, intubated and mechanically ventilated. Keep head of bed elevation 30-45° and keep the neck straight to avoid venous congestion. Use zinc oxide tape, rather than Velcro tapes to avoid venous constriction.

- Monitoring: ECG monitoring, CVP and arterial blood pressure monitoring, oxygen saturations*, end-tidal CO2 monitoring. Train-of-four monitoring is needed if neuromuscular blocking agents (pharmacological paralysis) are used.

- Insert: NG tube, urinary catheter, oesophageal temperature probe. Avoid rectal probe as rectal temperature is generally 0.5-1.0 °C higher than core temperature because of bacterial fermentation. Response time is slow because of insulation by faeces.

- Cooling should be initiated as quickly as possible: i.e. within 4 hours of ROSC.

- Discuss with medical staff and cool for 12-24 hours and target temperature 36°C.

- Coronary reperfusion: coronary angiography or administer thrombolysis as appropriate.

Instructions for inserting the oesophageal temperature probe:

Placement:

- Proper placement of the oesophageal probe is essential for accurate measurement of core temperature.
- If it is too high in the oesophagus, the reading will be affected by tracheal air.
- Placement in the lower third of the oesophagus, in proximity to the heart and the aorta, will reflect core temperature. In this position, the probe is not affected by cooler tracheal temperatures.

Contra-indications:

- Known oesophageal stricture.
- Oesophageal perforation.
- Oesophageal varices.

First determine the length:

- Measure from the corner of the patient’s mouth to the earlobe ~ and from the earlobe to the upper part of the sternum.
- Mark the measurement on the probe.
- Lubricate the tip of the probe with water-soluble lubricant gel.
- Insert the temperature probe into the oral cavity and advance.
- Continue to advance the probe until the area previously marked on the probe reaches the patient’s lips. If resistance is met, withdraw the probe and gently advance again. Avoid forcing the probe.
- Secure the probe to the patient’s skin.
- Connect the cable from the monitoring device to the probe.
- Observe the temperature displayed.
- Placement may be verified with radiograph.
Hyperoxia:

- Unnecessary hyperoxia should be avoided. Excessive oxygen harms post-ischaemic neurons by causing oxidative stress in the early stages of reperfusion.

- Monitor and titrate oxygen levels by using arterial blood gases and by continuous saturation monitoring. Adjustment of FiO₂ to produce an arterial oxygen saturation of 94% to 96% can prevent acute hyperoxia.

- Adjust oxygen saturation alarm to 97%.
Immediate Treatment, Diagnosing And Optimising Recovery

**Immediate treatment**
- Airway and Breathing
  - Maintain SpO2 94 – 98%
  - Advanced airway
  - Waveform capnography
  - Ventilate lungs to normocapnia
- Circulation
  - 12-lead ECG
  - Obtain reliable intravenous access
  - Aim for SBP > 100 mmHg
  - Fluid (crystalloid) – restore normovolaemia
  - Intra-arterial blood pressure monitoring
  - Consider vasopressor/ inrope to maintain SBP
- Control temperature
  - Constant temperature ≤ 36°C
  - Sedation; control shivering

**Diagnosis**

- Likely cardiac cause? (branching decision)
  - No
    - Consider CT brain and/or CTPA
      - Treat non-cardiac cause of cardiac arrest
  - Yes
    - ST elevation on 12 lead ECG?
      - No
        - Consider Coronary angiography ± PCI
      - Yes
        - Coronary angiography ± PCI
          - Cause for cardiac arrest identified? (branching decision)
            - No
              - ICU management
                - Temperature control: constant temperature ≤ 36°C for ≥ 24 h; prevent fever for at least 72 h
                - Maintain normoxia and normocapnia; protective ventilation
                - Optimise haemodynamics (MAF, lactate, ScvO2, CO/CI, urine output)
                - Echocardiography
                - Maintain normoglycaemia
                - Diagnose/treat seizures (EEG, sedation, anticonvulsants)
                - Delay prognostication for at least 72 h
            - Yes
              - Follow-up and rehabilitation

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**Optimising recovery**
- Secondary prevention
  - e.g., ICD, screen for inherited disorders, risk factor management

**Follow-up and rehabilitation**
This section explores the recommended care for patients deemed suitable for active treatment by a senior decision maker, within the first 72 hours following cardiac arrest and ROSC.

Airway and Ventilation:

- Patients with reduced level of consciousness, agitation indicative of cerebral irritation or those with respiratory compromise should be sedated, their airway secured via tracheal intubation and lung protective ventilation commenced.

- Ventilation should be tailored to the patient using tidal volumes 6–8ml per ideal bodyweight. Although protective lung ventilation strategies have not been studied specifically in post-cardiac arrest patients, given that these patients develop a marked inflammatory response, it seems rational to apply protective lung ventilation: tidal volume 6–8 mL kg ideal body weight and positive end expiratory pressure 4–8 cm H$_2$O.

- Hypoxaemia and hypercarbia both increase the likelihood of a further cardiac arrest and may contribute to secondary brain injury. Several animal studies indicate that hypoxaemia early after ROSC causes oxidative stress and harms post-ischaemic neurones.

- A recent study of air versus supplemental oxygen in ST-elevation myocardial infarction (STEMI) showed that supplemental oxygen therapy increased myocardial injury, recurrent myocardial infarction and major cardiac arrhythmia and was associated with larger infarct size at six months.

- Given the evidence of harm after myocardial infarction and the possibility of increased neurological injury after cardiac arrest, patients should be ventilated with inspired oxygen concentrations required to achieve normal paO$_2$ between 8 to 12 kPa and with target oxygen concentrations of 94 to 98%.

- Avoid hypoxaemia, which is also harmful – ensure reliable measurement of arterial oxygen saturation before reducing the inspired oxygen concentration.

- Give adequate doses of sedative, which will reduce oxygen consumption. Assess sedation level every hour using the RASS.

- Hypocarbia causes cerebral vasoconstriction and a decreased cerebral blood flow. After cardiac arrest, hypocapnia induced by hyperventilation causes cerebral ischaemia.

- It is reasonable to adjust ventilation to achieve normocarbia and to monitor this using the end-tidal CO$_2$ and arterial blood gas values.

- Insert a gastric tube to decompress the stomach; gastric distension caused by mouth-to-mouth or bag-mask ventilation will splint the diaphragm and impair ventilation.

- A chest x-ray will be required to:
  - Check the lung fields for signs of aspiration or pulmonary oedema.
  - Confirm the position of the endotracheal tube, nasogastric tube and any invasive lines that have been inserted.
  - Detect complications of CPR such as rib fractures or pneumothorax.
- Shivering is less likely when targeted temperature is 36°C. Infusions of neuromuscular blocking drugs interfere with clinical examination and may mask seizures. However if shivering occurs, a bolus dose of neuromuscular blocking drug may be required. Alternatively, magnesium sulphate, a naturally occurring N-methyl-D-aspartate (NMDA) receptor antagonist, that reduces the shivering threshold slightly, can also be administered.

- Continuous electroencephalography (EEG) is recommended to detect seizures in these patients, especially when neuromuscular blockade is used.

**Investigation for the pathological cause of arrest:**

- All patients should be rapidly evaluated and assessed for any reversible cause of cardiac arrest. This assessment should include a clinical examination concerning the 4H’s and 4T’s as defined by the Advanced Life Support Group, followed by a set of mandatory investigations to include the following:

  - Blood tests to include full blood count, clotting profile, urea and serum electrolytes, magnesium, troponin, TFTs, cholesterol.
  - 12-Lead ECG
  - Chest x-ray
  - Blood gas analysis.

- Additional investigations to be considered on a per-patient basis following the exclusion of ischaemic heart disease should include:
  - CT brain.
  - CT Pulmonary Angiography.
  - Echocardiography.

- Indications and timing of computed tomography (CT) scanning:
  - Cardiac causes of OHCA have been extensively studied in the last few decades; conversely, little is known about non-cardiac causes. Early identification of a respiratory or neurological cause can be achieved by performing a brain and chest CT scan at hospital admission, before or after coronary angiography.
  - In the absence of signs or symptoms suggesting a neurological or respiratory cause (e.g. headache, seizures or neurological deficits for neurological causes, shortness of breath or documented hypoxaemia in patients suffering from a known and worsening respiratory disease) or if there is clinical or ECG evidence of myocardial ischaemia, undertake coronary angiography first, followed by CT scan in the absence of causative lesions.
Percutaneous coronary intervention following ROSC with ST-elevation:

- Urgent angiography and percutaneous coronary artery intervention (PCI) should be strongly considered in all patients who have ROSC following out-of-hospital cardiac arrest (OOHCA) where the initial ECG is indicative of an ST elevation myocardial infarction or where there is evidence of left bundle branch block.

- Conscious level following OOHCA should not be used to determine suitability for PCI. These patients can be ventilated and sedated. NICE guidance is clear “Do not use level of consciousness after cardiac arrest caused by suspected acute STEMI to determine whether a person is eligible for coronary angiography.

- Observational studies also indicate that optimal outcomes after OHCA are achieved with a combination of TTM and PCI, which can be included in a standardised post-cardiac arrest protocol as part of an overall strategy to improve neurologically intact survival.

Percutaneous coronary intervention following ROSC without ST-elevation:

- Urgent angiography and PCI should also be considered in patients who have ROSC following OOHCA, whose initial ECG does not show ST elevation myocardial infarction, but in whom a cardiac cause is strongly suspected. This can be guided by history of presentation, strong past medical history of cardiac disease, exclusion of non-cardiac causes and supportive evidence of ischaemia on ECG or echocardiography if available.

- Factors such as patient age, duration of CPR, haemodynamic instability, presenting cardiac rhythm, neurological status upon hospital arrival, and perceived likelihood of cardiac aetiology can influence the decision to undertake the intervention in the acute phase or to delay it until later in the hospital stay.

Haemodynamic management:

- Haemodynamic instability and impaired myocardial function is very common post cardiac arrest. This can result in hypotension, low cardiac output, arrhythmias and impaired organ perfusion. Invasive arterial monitoring is necessary to evaluate blood pressure and manage it accordingly.

- Administration of fluids, vasopressors and inotropes may be required. Therefore central venous access is advisable. Cardiac output monitoring may help to guide treatment in haemodynamically unstable patients but there is no evidence that its use affects outcome.

- Use of echocardiography can be extremely helpful in assessing right and left ventricular performance post arrest and can be used to guide drug therapy and evaluate myocardial function pre and post intervention.

- Hypotension following cardiac arrest can be multifactorial, including hypovolaemia, cardiac stunning and pump failure, or vasodilatation resulting from the inflammatory response. Vasopressor and inotropic support is often required.

- In cases of refractory cardiogenic shock, urgent echocardiography should be requested.

- Arrhythmias should be treated aggressively optimisation of fluid and electrolyte status and administration of a suitable pharmacological agent.

- There is no definitive data to suggest targeting a specific blood pressure improves outcome. Most clinicians would aim for a blood pressure that results in a minimum urine output of 0.5ml/kg/hr with evidence of ability to clear lactate accordingly.
• Immediately after a cardiac arrest there is typically a period of hyperkalaemia. Subsequent endogenous catecholamine release and correction of metabolic and respiratory acidosis promotes intracellular transportation of potassium, causing hypokalaemia. Hypokalaemia may predispose to ventricular arrhythmias. Give potassium to maintain the serum potassium concentration between 4.0 and 4.5 mmol L⁻¹.

Implantable cardioverter defibrillators:
• Consider insertion of an implantable cardioverter defibrillator (ICD) in ischaemic patients with significant left ventricular dysfunction, who have been resuscitated from a ventricular arrhythmia that occurred later than 24–48 h after a primary coronary event.
• ICDs may also reduce mortality in cardiac arrest survivors at risk of sudden death from structural heart diseases or inherited cardiomyopathies.

Disability (optimising neurological recovery):

Cerebral perfusion:
• Animal studies show that immediately after ROSC there is a short period of multifocal cerebral no-reflow followed by transient global cerebral hyperaemia lasting 15–30 min. This is followed by up to 24 h of cerebral hypoperfusion while the cerebral metabolic rate of oxygen gradually recovers.
• After asphyxial cardiac arrest, brain oedema may occur transiently after ROSC but it is rarely associated with clinically relevant increases in intracranial pressure.
• In many patients, autoregulation of cerebral blood flow is impaired (absent or right-shifted) for some time after cardiac arrest, which means that cerebral perfusion varies with cerebral perfusion pressure instead of being linked to neuronal activity.
• In one study autoregulation was disturbed in 35% of post-cardiac arrest patients and the majority of these had been hypertensive before their cardiac arrest; this tends to support the recommendation made in the 2010 ERC Guidelines: after ROSC, maintain mean arterial pressure near the patient’s normal level.

Sedation:
• Although it has been common practice to sedate and ventilate patients for at least 24 h after ROSC, there are no high-level data to support a defined period of ventilation, sedation and neuromuscular blockade after cardiac arrest.
• Patients need to be sedated adequately during treatment with TTM, and the duration of sedation and ventilation is therefore influenced by this treatment.
• The length of sedation is dictated by treatment and management of potential complications post cardiac arrest. It is therefore advisable that short acting sedatives and opioids such as propofol with alfentanil be used to allow early assessment of neurological function.
Control of seizures:

- Seizures are common after cardiac arrest and occur in approximately one-third of patients who remain comatose after ROSC. In the context of targeted temperature management and the use of active cooling devices, diagnosing true seizure activity can be challenging.

- Routine seizure prophylaxis in post-cardiac arrest patients is not recommended because of the risk of adverse effects and the poor response to anti-epileptic drugs among patients with clinical and electrographic seizures.

- Seizures can exacerbate brain injury as they increase cerebral metabolic rate and as such they should be treated aggressively.

- Myoclonus is most common and occurs in up to 25%, the remainder having focal or generalised tonic-clonic seizures or a combination of seizure types. **True myoclonus can be particularly difficult to treat**; phenytoin is often ineffective. Propofol is effective to suppress post-anoxic myoclonus. Clonazepam, sodium valproate and levetiracetam are antimyoclonic drugs that may be effective in post-anoxic myoclonus.

- Use intermittent electroencephalography (EEG) to detect epileptic activity in patients with clinical seizure manifestations. Consider continuous EEG to monitor patients with a diagnosed status epilepticus and effects of treatment. In comatose cardiac arrest patients, EEG commonly detects epileptiform activity: post-anoxic status epilepticus was detected in 23–31% of patients using continuous EEG-monitoring.

- Patients with electrographic status epilepticus may or may not have clinically detectable seizure manifestations that may be masked by sedation. Whether systematic detection and treatment of electrographic epileptic activity improves patient outcome is not known.

Glucose control:

- There is a strong association between high blood glucose after resuscitation from cardiac arrest and poor neurological outcome.

- Tight glucose control (4.5–6.0 mmol L) has been shown to increase morbidity and mortality in ICU patients, mainly as a result of hypoglycaemic episodes.

- Based on the available data, following ROSC maintain the blood glucose at ≤ 10 mmol L and avoid hypoglycaemia. Do not implement strict glucose control in adult patients with ROSC after cardiac arrest because it increases the risk of hypoglycaemia.
Targeted temperature management:

- Hyperthermia following cardiac arrest is common and several studies have demonstrated an association between post arrest pyrexia and poor outcome. Post ROSC pyrexia should be managed with anti-pyretics or active cooling measures.

- The term targeted temperature management or temperature control is now preferred over the previous term therapeutic hypothermia. The Advanced Life Support Task Force of the International Liaison Committee on Resuscitation (ILCOR) made several treatment recommendations on targeted temperature management:
  - Maintain a constant, target temperature at 36°C.
  - TTM is recommended for adults after OOHCA with an initial shockable rhythm who remain unresponsive after ROSC.
  - TTM is suggested for adults after OOHCA with an initial nonshockable rhythm who remain unresponsive after ROSC.
  - TTM is suggested for adults after IHCA with any initial rhythm who remain unresponsive after ROSC.

- Following the TTM trial, many intensive care clinicians in the UK have elected to use 36°C as the target temperature for post cardiac arrest temperature control. This has several advantages compared with a target temperature of 33°C:
  - There is a reduced need for vasopressor support.
  - Lactate values are lower (the clinical significance of this is unclear).
  - The rewarming phase is shorter.
  - There is reduced risk or rebound hyperthermia after rewarming.

- Temperature management should be started as soon as possible after sustained ROSC has been achieved.
How to control temperature:

- Temperature management should be started as soon as possible after sustained ROSC has been achieved.

- Methods of inducing and/or maintaining TTM include:
  - Simple ice packs and/or wet towels are inexpensive; however, these methods may be more time consuming for nursing staff, may result in greater temperature fluctuations, and do not enable controlled rewarming. Ice cold fluids alone cannot be used to maintain hypothermia, but even the addition of simple ice packs may control the temperature adequately.
  - Cooling blankets or pads.
  - Water or air circulating blankets.
  - Intravascular heat exchanger, placed usually in the femoral or subclavian veins.
  - Extracorporeal circulation (e.g. cardiopulmonary bypass, ECMO).
  - Surface cooling pads i.e. Arctic Sun

- The temperature is typically monitored from a thermistor placed in the oesophagus. As yet, there are no data indicating that any specific cooling technique increases survival when compared with any other cooling technique; however, internal devices enable more precise temperature control compared with external techniques.

Plasma electrolyte concentrations, effective intravascular volume and metabolic rate can change rapidly during rewarming, as they do during cooling. Rebound hyperthermia is associated with worse neurological outcome. Thus, rewarming should be achieved slowly: the optimal rate is not known, but the consensus is currently about 0.25–0.5°C of rewarming per hour. Choosing a strategy of 36°C will reduce this risk.

Record the following once TTM is commenced:

- Record the patient’s core temperature prior to commencing treatment. Hourly temperature assessment should be confirmed with a secondary monitoring device i.e. tympanic thermometer. Document both core and tympanic recordings.

- Record the exact time when the treatment is commenced.

- Record the exact time when the patient’s core temperature reaches 36°C.

- Record the proposed length of time for maintaining the temperature at 36°C i.e. 12 hours or 24 hours.

- Record the water and patient temperature hourly as displayed on the arctic sun.
Cardiac arrest

Controlled temperature

Rewarming

Exclude confounders, particularly residual sedation

Unconscious patient, M=1-2 at ≥72 h after ROSC

One or both of the following:
- No pupillary and corneal reflexes
- Bilaterally absent N20 SSEP wave

No

Yes

Wait at least 24 h

Two or more of the following:
- Status myoclonus ≤48 h after ROSC
- High NSE levels
- Unreactive burst-suppression or status epilepticus on EEG
- Diffuse anoxic injury on brain CT/MRI

No

Yes

Indeterminate outcome
Observe and re-evaluate

Poor outcome likely

Use multimodal prognostication whenever possible

(1) At ≥24 h after ROSC in patients not treated with targeted temperature
(2) See text for details.
Prognostication recommendations following active treatment and the tools that guide clinical decision making:

Ultimately, the decisions regarding prognostication and the suitability of ongoing care rest with the attending consultant.

**Prognosis of early physiological recovery:**

Following cardiac arrest and the post cardiac arrest syndrome a number of vital organs can be affected with the potential for ensuing renal, hepatic and cardiac failure. Evaluating the patient’s overall clinical condition and their prognosis following cardiac arrest can be complex and warrants a multi-disciplinary approach with frequent assessment.

Continuation of therapeutic measures, such as TTM may need to be reappraised within the first 24-48 hour period if there are signs of irreversible organ damage or significant changes in the patient’s clinical condition.

**Prognosis of neurological recovery:**

Hypoxic-ischaemic brain injury is common after resuscitation following cardiac arrest and about 60% of patients who die following admission to ICU after OOHCA do so as a result of neurological injury. The majority of these deaths are due to withdrawal of treatment based on the likelihood of a poor neurological outcome. It is therefore of great importance to take a multimodal and considered approach to the prognostication of neurological outcome post cardiac arrest.

The joint ERC/ESICM Advisory Statement on Neurological Prognostication in comatose survivors of cardiac arrest suggests that multiple tests of brain injury can be employed and that prognostication should be delayed sufficiently to enable full clearance of sedatives and optimise neurological assessment. In the majority of circumstances where the patient is actively managed, this period would at least be 72 hours following cardiac arrest.

There are a number of available testing methods which can aid prognostication of neurological recovery. Specialist input from the neurology team can also be considered for complex cases.

**Testing methods:**

Clinical Signs:

- Bilateral absence of pupillary light and corneal reflexes at 72 hours post ROSC confers a poor prognosis.
- Absence or extensor motor response to pain at 72 hours post ROSC is around 75% sensitive in predicting a poor outcome.
- Myoclonic status epilepticus (continuous and generalised myoclonus for more than 30 minutes duration) within the first 48 hours is consistently associated with a poor outcome.
Electrophysiology:

- Bilateral absence of short latency somatosensory evoked potentials (SSEP’s) at > 72 hours from ROSC is reliably predictive of poor outcome in those patients treated with TTM.
- Bilateral absence of short latency somatosensory evoked potentials (SSEP’s) at > 24 hours from ROSC is likely to be predictive of poor outcome in those patients NOT treated with TTM.
- EEG based predictors such as absence of reactivity to external stimuli, presence of burst suppression or refractory status epilepticus at > 72 hours post ROSC can be predictive of poor outcome when used in combination or when combined with other predictors.
- EEG is not recommended as a prognostic tool during active TTM or during the first 36 hours post ROSC. However, continuous monitoring can be helpful to elucidate level of consciousness and active non-convulsive seizure activity, which may occur in 25% of patients.

Imaging:

- CT may be used to diagnose global anoxic-ischaemic cerebral injury, conferred by the presence of sulcal effacement and an attenuation of the grey/white matter interface. These findings within 24 hours from ROSC suggest a poor neurological outcome, but should only be used for prognostication in combination with other predictors. False positive rates of up to 8% have been reported when CT is considered in isolation.
- MR brain imaging is more sensitive than CT for detecting global axonal cerebral injury, although use may be limited by patient instability.

Biochemical markers:

- Neuron specific enolase (NSE) and S-100B are protein biomarkers that are released in response to neuronal and glial cell damage, respectively.
- The rise and extent of rise in blood values of NSE and S-100B following cardiac arrest is likely to represent the extent of ischaemic neurological damage and has been shown in several studies to correlate with the severity of anoxic brain injury.
- At the present there is no clear evidence to suggest a threshold of values that would consistently predict poor outcome. This may well change in the future. Current international guidelines suggest that ‘high serum values’ of NSE at 48-72 hours, when used in combination with other predictors can be useful in prognostication of poor neurological outcome.

Diffusion-weighted magnetic resonance imaging:

Diffusion-weighted magnetic resonance imaging scan of a 68-year-old man who suffered a ventricular fibrillation cardiac arrest with prolonged resuscitation.
Diffuse cortical hyperintensities are observed, consistent with severe global anoxic injury.
Multimodal approach to assess prognosis in comatose survivors after cardiac arrest treated with hypothermia.

The multimodal approach to assess prognosis in comatose survivors after cardiac arrest treated with hypothermia should ideally include neurological examination combined with the use of electroencephalography (EEG) and somatosensory evoked potentials (SSEPs), the measurement of biomarkers (neuron-specific enolase (NSE) and S-100β protein) and magnetic resonance imaging (MRI).

**Somatosensory evoked potentials:**

(A) In comatose survivors after cardiac arrest, somatosensory evoked potentials are elicited by transcutaneous electrical stimulation applied to the median nerve and then recorded at Erb’s point (N9), the cervical medulla (N13) and the contralateral cortex (N20).

(B) Example of present N20 cortical response (C3’) in two comatose patients after cardiac arrest.

(C) Example of absent N20 cortical response (C3’) in two comatose patients after cardiac arrest.
Organ donation:

Post cardiac arrest patients who do not survive represent an opportunity to increase the organ donor pool, either after brain death or as non-heart-beating donors.
**Information For Supporting The Family:**

**What is Targeted Temperature Management?**

Targeted Temperature Management (TTM) is considered an important therapy for a comatose survivor of cardiac arrest. Cardiac arrest is a life-threatening event and medical help must be called for immediately.

Cardiac arrest occurs when the patient’s heart stops beating. However, the heart may be restarted during cardiopulmonary resuscitation (CPR) but the patient may remain minimally responsive immediately after the event. Neurological problems can develop as a consequence because of the lack of blood and oxygen to the brain. Poor blood flow may be due to cardiac arrest or the blockage of an artery by a clot. If the cause is a blocked artery supplying blood to the heart, the patient may need to undergo a special procedure to unblock the artery. The procedure to unblock the artery is carried out in the Coronary Angiography Suite.

Early intervention using TTM as soon as possible after return of circulation may improve brain function and survival. It is an active treatment that tries to achieve and maintain a specific body temperature i.e. 36°C in the patient for a specific duration of time. The procedure for this is carried out in the Intensive Care Unit.

**What happens to the patient in the Intensive Care Unit?**

Close monitoring of the patient is needed. When the patient first arrives in the ICU, nursing and medical staff will need access to the patient to provide immediate care. This can take some time so please allow at least 90 minutes. During this time the patient will be kept unconscious with sedation; a breathing tube will be needed so that the patient can be attached to a mechanical ventilator (breathing machine); and temperature, blood pressure and heart rate will be continuously monitored. Many blood tests and procedures will be performed during the first 24 hours.

**How does Targeted Temperature Management work?**

The exact way in which controlling the temperature works in protecting the brain is unknown, however, maintaining the body temperature at 36°C for a specific duration of time is thought to work by reducing the risk of tissue injury or brain injury following lack of blood flow. TTM helps to protect the brain and other vital organs by limiting the release of toxins that build up in the blood, which can impair consciousness.

**How is the treatment carried out?**

The patient is attached to a breathing machine and is kept unconscious with sedation. Keeping the body temperature at 36°C is achieved by applying adhesive pads to the patient’s body. Water at a set temperature circulates through the pads in response to the patient’s temperature and at a set target temperature on the automated temperature control device. The device is referred to as the Arctic Sun® 5000 Temperature Management System.
How long with the treatment continue for?

The treatment should begin as soon as possible and the body temperature will be maintained at 36°C continue for a minimum of 12 hours. The patient is kept unconscious with sedation for the duration of the procedure. At the end of the procedure, and at a time agreed by the medical staff, the patient’s sedation will be switched off.

Will the patient be brain damaged?

It is difficult to predict this with certainty as some time will be needed to allow for potential recovery to occur. More tests and investigations will be needed.

Will the patient survive?

Cardiac arrest is an extremely critical condition and there is no guarantee that recovery or survival will be possible. Despite controlling the body temperature at 36°C, not all patients after cardiac arrest will survive. From the first moment that the patient collapses, the impact of neurological damage may be so severe that despite treatment, the patient may unfortunately die. It is impossible to predict as every patient is different. Indeed recovery or survival occurs on an individual basis. Some patients wake up very quickly after the sedative infusions have been stopped whilst others can take longer to begin waking up. Some patients may have significant impairment in functions as a result of brain injury.

Although neurological outcome is considered to be good for the majority of cardiac arrest survivors, fatigue, cognitive problems (memory and attention) and emotional problems are common. These can have significant impact and can affect a patient’s daily functioning, return to work and quality of life. Therefore, follow-up care after hospital discharge is necessary.
**References:**

Chan et al. (2016) Association between therapeutic hypothermia and survival after in-hospital cardiac arrest. JAMA 316(13), pp. 1375-1382


