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POST-RESUSCITATION THERAPY

AUSTRALIAN RESUSCITATION COUNCIL

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EMA

Post-resuscitation Therapy in Adult Advanced Life Support. ARC and NZRC Guideline 2010

Australian Resuscitation Council, New Zealand Resuscitation Council

Background

After the return of a spontaneous circulation (ROSC), resuscitation DOES NOT STOP. It is essential to continue maintenance of airway, breathing and circulation. ROSC is just the first step toward the goal of complete recovery from cardiac arrest. Interventions in the post-resuscitation period are likely to significantly influence the final outcome. A comprehensive treatment protocol including multiple interventions provided in a structured way may improve survival after cardiac arrest.[1]

Hypoxic brain injury, myocardial injury or subsequent organ failure are the predominant causes of morbidity and mortality after cardiac arrests.[2]

The aims of therapy after initial resuscitation are to:

- Continue respiratory support.
- Maintain cerebral perfusion.
- Treat and prevent cardiac arrhythmias.
- Determine and treat the cause of the arrest.

In addition treatable causes of cardiac arrest need to be addressed. These include:

- Hypoxaemia
- Hypovolaemia
- Hypo/Hyperkalaemia and other metabolic disorders including acidosis and disturbances of magnesium and calcium
- Hypo/Hyperthermia
- Tension pneumothorax
- Tamponade: pericardial
- Toxins/poisons/drugs including carbon monoxide, and cyclic antidepressants
- Thrombosis: pulmonary embolus /acute myocardial infarction

A full history and examination will guide the possible investigations. Electrolyte disorders such as hypo- and hyper-natraemia may cause continuing cerebral damage. Serum electrolytes, arterial blood gases and ECG should be performed to guide further treatment.[1]

Treatment recommendations

Blood pressure

It is imperative to ensure an adequate systemic arterial blood pressure as soon as practicable after return of spontaneous circulation. Despite limited clinical data, the known pathophysiology of post-cardiac arrest syndrome provides a rationale for titrating hemodynamics to optimize organ perfusion.[1]

Aim for a blood pressure equal to the patient's usual blood pressure or at least a systolic pressure greater than 100 mg Hg. If the blood pressure falls, a vasopressor may be given by small intravenous increments (eg. adrenaline 50 to 100 mcg) or infusion until fluid status and the need for intravascular volume expansion can be assessed. [Class A; Expert consensus opinion]

There is insufficient evidence to support or refute the routine use of intravenous fluids following sustained return on spontaneous circulation after cardiac arrest. Rapid infusion of cold 0.9% saline or lactacted Ringers appears to be well tolerated when used to induce therapeutic hypothermia. Based on the pathophysiology of post-cardiac arrest syndrome,[2] it is reasonable to use intravenous fluids as part of a package of post-cardiac arrest care.[1]

There is insufficient evidence to support or refute the routine use of vasopressors and/ or inotropes for improving survival in adult patients with cardiovascular dysfunction after resuscitation from cardiac arrest.[1] If vasoactive drugs are used, then as soon as possible any vasoconstricting drugs should be given by a dedicated central venous line. [Class A; Expert consensus opinion]

There is insufficient evidence to support or refute the use of mechanical circulatory support (eg. an intra-aortic balloon pump) in post-cardiac arrest patients who have cardiovascular dysfunction.[1]

Intubation and ventilation are continued in the immediate post arrest period guided by appropriate monitoring.

Oxygenation

Recent studies have recognized the potential harm caused by hyperoxaemia after ROSC.[1,3] Once ROSC has been established and the oxygen saturation of arterial blood (SaO2) can be monitored reliably (by pulse oximetry and/ or arterial blood gas analysis), it is reasonable to titrate the inspired oxygen to achieve a SaO2 of 94 – 98%. [Class A; LOE III-2]

Control of arterial carbon dioxide

Five studies in adults and numerous animal studies documented harmful effects of hypocapnia (cerebral ischemia) after cardiac arrest. Two studies provide neutral evidence There are no data to support the targeting of a specific $PaCO_2$ after resuscitation from cardiac arrest. Data extrapolated from patients with brain injury however, imply that ventilation to normocarbia (eg. $PaCO_2$ 35 to 40 mmHg) is appropriate.[4] Routine hyperventilation may be detrimental (eg. result in cerebral vasoconstriction) and should be avoided. [Class A; Extrapolated evidence] Arterial blood gas measurements should be used to titrate ventilation in the immediate post-resuscitation period, rather than End Tidal CO_2 levels.[1]

Blood glucose control

Several human studies have documented a strong association between high blood glucose after resuscitation from cardiac arrest and poor neurologic outcome. There is good evidence that persistent hyperglycemia after stroke is associated with a worse neurologic outcome.

One human randomized interventional study that prospectively evaluated strict glucose control (72–108 mg/dl, 4–6 mmol/l]) compared to moderate glucose control (108–144 mg/dl, 6–8 mmol/l) in patients resuscitated from prehospital cardiac arrest with ventricular fibrillation found no survival benefit with strict glucose control. Five retrospective studies in post-cardiac arrest patients suggested an association of higher glucose levels with increased mortality and worse neurological outcomes, but these findings may be related to other factors.

Based on these studies, the suggested target ranges for glucose values have been variable. A good randomized trial of intensive glucose control versus conventional glucose control in the largest number of ICU patients to date reported increased mortality in patients treated with intensive glucose control. Two meta-analyses of studies of tight glucose control versus conventional glucose control in critically ill patients showed no significant difference in mortality but found tight glucose control was associated with a significantly increased risk of hypoglycemia.[1]

The optimal blood glucose target in critically ill patients has not been determined. Comatose patients were at particular risk from unrecognized hypoglycemia, and the risk of this complication occurring increases as the target blood glucose concentration is lowered.[1]

Recommendation

Providers should monitor blood glucose frequently after cardiac arrest and should treat hyperglycemia (>10 mmol/l) with insulin but avoid hypoglycemia.[1] [Class B; LOE II]

Prophylactic anti-arrhythmics

No studies specifically and directly addressed the prophylactic use of antiarrhythmic therapy started immediately after resuscitation from cardiac arrest. Six studies documented inconsistent improvement in long-term survival when prophylactic antiarrhythmics were given to survivors of cardiac arrest from all causes.

It may be reasonable to continue an infusion of an antiarrhythmic drug that successfully restored a stable rhythm during resuscitation (e.g. lignocaine 2–4 mg/min or amiodarone 0.6 mg/kg/hr for 12–24 hours). [Class B; LOE Expert opinion] If no antiarrhythmic drug was used during resuscitation from a shockable rhythm, an antiarrhythmic drug may be considered to prevent recurrent VF. [Class B; LOE Expert opinion]

Temperature control

Induced hypothermia has been shown to be beneficial in some patients still comatose after return of spontaneous circulation. When actively rewarming a severely hypothermic patient, practitioners should take this information into account. Hyperthermia should be avoided. [Class A; LOE II]

Coagulation control

Despite good theoretical reasons why fibrinolysis following cardiac arrest in patients with suspected pulmonary embolism might be beneficial, there is no direct evidence to that effect. Several studies showed no significant increase in survival to hospital discharge. There was an increase in bleeding complications following fibrinolysis in most of those studies. One study suggested that the risk of major haemorrhage was further increased in patients who have undergone CPR.

Recommendation

In patients with diagnosed or suspected pulmonary embolism after ROSC following cardiac arrest, there is inadequate evidence to recommend for or against the use of fibrinolytic therapy.[1]

Sedation and paralysis

Apart from the data related to induced hypothermia, there were no data to support or refute the use of a defined period of ventilation, sedation, and neuromuscular blockade after cardiac arrest. One observational study in adults documents increased incidence of pneumonia when sedation is prolonged beyond 48 hours after prehospital or in-hospital cardiac arrest.[4]

There is insufficient data to recommend for or against the use of neuroprotective drugs (such as thiopental, glucocorticoids, nimodipine, lidoflazine, or diazepam) in comatose cardiac arrest post return of spontaneous circulation not treated with hypothermia or as an adjunct to therapeutic hypothermia in the post arrest treatment of adult cardiac arrest.[1]

Seizure control

No controlled clinical trials directly addressed prophylactic treatment for seizures after cardiac arrest. Five studies documented a 3–44% incidence of seizures after sustained return of spontaneous circulation.[1] Seizures increase the oxygen requirements of the brain and can cause life-threatening arrhythmias and respiratory arrest.

Two studies reported no difference in neurologic outcome after use of single dose diazepam or magnesium or both; or thiopental given after sustained return of spontaneous circulation. There are no studies addressing prompt and aggressive treatment after the first seizure occurring after circulation was restored. Seizures in the post arrest period may be refractory to multiple medications. There are insufficient data to support or refute the use of specific anti seizure medication in the prevention or treatment of seizures in after return of spontaneous circulation.[1]

Maintenance therapy should be started after the first event once potential precipitating causes (e.g. intracranial haemorrhage, electrolyte imbalance, etc) are excluded. [Class A; LOE Expert opinion]

Treatment of underlying cause of the cardiac arrest

If not already undertaken, management should be directed toward the treatment of underlying causes that have been identified (eg. correction of electrolyte abnormalities, treatment of tension pneumothorax etc.).

Myocardial infarction

There is evidence of underlying ischemic heart disease in the majority of patients who have an out-of-hospital cardiac arrest.
Acute coronary artery occlusion is known to be the precipitating factor in many of these patients. While coronary artery occlusion after cardiac arrest is associated with ECG ST elevation or LBBB, it can also occur in the absence of these findings.[5]

Recommendations

In patients with STEMI or new LBBB on ECG following ROSC after OHCA, immediate angiography and percutaneous coronary intervention (PCI) should be considered. [Class A; LOE III-3]
It is reasonable to perform immediate angiography and PCI in selected patients, despite the absence of ST segment elevation on the ECG or prior clinical findings, such as chest pain. [Class A; LOE III-3]
Clinical findings of coma in patients prior to PCI are commonly present in OHCA patients, and should not be a contraindication to consider immediate angiography and PCI.
It is reasonable to include cardiac catheterization in standardized post-cardiac arrest protocols as part of an overall strategy to improve neurologically intact survival in this patient group. [Class A; LOE III-3]
Therapeutic hypothermia is recommended in combination with primary PCI, and should be started as early as possible, preferably prior to initiation of PCI. [Class A; LOE III-3]

Pulmonary embolus

Despite good theoretical reasons why fibrinolysis following cardiac arrest in patients with suspected pulmonary embolism might be beneficial, there is no direct evidence to that effect. Several studies showed no significant increase in survival to hospital discharge. There was an increase in bleeding complications following fibrinolysis in most of those studies. One study suggested that the risk of major haemorrhage was further increased in patients who have undergone CPR.[1]
In patients with diagnosed or suspected pulmonary embolism after return of spontaneous circulation following cardiac arrest, there is inadequate evidence to recommend for or against the use of fibrinolytic therapy in addition to heparin. The mortality with surgical embolectomy for suspected or diagnosed pulmonary embolism is high if it follows cardiac arrest and it should be avoided in patients who have received CPR. There are few data on percutaneous mechanical thromboembolectomy, but it may be beneficial and may be considered in patients sustaining cardiac arrest from a pulmonary embolism who are not candidates for fibrinolytic therapy.[1]

Resuscitation related injuries

Rib fractures and other injuries are common[7] but acceptable consequences of CPR given the alternative of death from cardiac arrest. After resuscitation all patients should be reassessed and re-evaluated for resuscitation-related injuries. The extent of injuries is often underestimated by standard investigations (eg. chest radiograph).[8] Other complications of resuscitation (eg. incorrect placement of tubes) should be identified and treated. Intravascular lines inserted under emergency conditions may need to be replaced. [Class B; Expert opinion]

Resuscitation centres

While extrapolation from randomized and observational studies of systems of care for other
acute time-sensitive conditions (trauma, ST elevation MI, stroke) suggests that specialist cardiac arrest centres and systems of care may be effective, there is insufficient direct evidence to recommend for or against their use.[6]

Prognosis

It is impossible to predict accurately the degree of neurological recovery during or immediately after a cardiac arrest. After cessation of sedation (and/or induced hypothermia) the probability of awakening decreases with each day of coma.

Prognostication during a cardiac arrest

Five studies documented some ability to predict outcome in adults when neurologic examination is undertaken during cardiac arrest, but there is insufficient negative predictive value for this assessment to be used clinically. Relying on the neurologic exam during cardiac arrest to predict outcome is not recommended and should not be used.[4]

Prognostication after cardiac arrest in patients not treated with hypothermia

Clinical examination

In adult patients comatose after cardiac arrest who have not been treated with therapeutic hypothermia, the following parameters predicted poor outcome (Cerebral Performance Category <2 or death) with false positive rate of 0%:

- absent vestibulo-ocular reflexes at ≥24 hours [95%CI 0–14%]
- absence of pupillary light and corneal reflex at 72 hours [95% CI 0–9%]
- Glasgow Coma Scale <5 at 48 hours (95% CI 0–13%) and on day 3 (95% CI 0–6%) and
- a clinical examination score <15 on day 4 [95% CI 0–18%)

However, in one study an absent motor response (Glasgow Coma Scale motor=1) at 72 hours after cardiac arrest predicted poor outcome with a false positive rate of 5% [95%CI 2–9%]%].
The presence of myoclonus status in adults was strongly associated with poor outcome but rare cases of good neurological recovery have been described and accurate diagnosis was problematic.

Recommendations

There are no clinical neurological signs that reliably predict poor outcome <24 hours after cardiac arrest.
In adult patients who are comatose after cardiac arrest, and who have not been treated with hypothermia and who do not have confounding factors (such as hypotension, sedatives or neuromuscular blockers), the absence of both pupillary light and corneal reflex at ≥72 hours reliably predicts poor outcome.

Absence of vestibulo-ocular reflexes at ≥24 hours and a GCS motor score of 2 or less at ≥72 hours are less reliable. Other clinical signs, including myoclonus, are not recommended for predicting poor outcome.

Prognostication based on laboratory analyses

Evidence does not support the use of serum or cerebrospinal fluid biomarkers (eg. NSE, S-100b, base deficit, glucose, or soluble P-selectin) alone as predictors of poor outcomes in comatose patients after cardiac arrest with or without treatment with therapeutic hypothermia. Limitations included small numbers of patients and/or inconsistency in cut-off values for predicting poor outcome.[1]

Prognostication based on Somato-Sensory Evoked potentials

The bilateral absence of the N20 component of Somatosensory Evoked Potentials measured between 4 hours and 2 weeks after cardiac arrest were associated with poor outcome in fourteen studies. In a meta-analysis of patients not treated with therapeutic hypothermia, absence of cortical N20 response to median nerve stimulation at 24–72 hours after cardiac arrest predicted poor outcome (death or Cerebral Performance Category 3–5) with a false positive rate of 0.7% (95% CI: 0.1–3.7).[1]

Recommendation

No electrophysiologic study reliably predicts outcome of comatose patient after cardiac arrest in the first 24 hours treated without therapeutic hypothermia. After 24 hours, bilateral absence of the N20 cortical response to median nerve stimulation predicts poor outcome in comatose cardiac arrest survivors not treated with therapeutic hypothermia.[1]

Prognostication based on EEG

Electroencephalography predicts poor outcome in comatose survivors of cardiac arrest within 1 week after CA in twelve studies. In a meta-analysis, EEG showing generalized suppression to less than 20 μV, burst-suppression pattern associated with generalized epileptic activity, or diffuse periodic complexes on a flat background 12–72 hours after sustained return of spontaneous circulation predicted a poor outcome (false positive rate of 3%, 95% CI 0.9–11%) in patients not receiving therapeutic hypothermia.[1]

Recommendation

In the absence of confounding circumstances such as sedatives, hypotension, hypothermia or hypoxemia, it is reasonable to use unprocessed electroencephalography interpretation (specifically identifying generalized suppression to less than 20 μV, burst suppression pattern with generalized epileptic activity, or diffuse periodic complexes on a flat background) observed between 24 and 72 hours after sustained return of spontaneous circulation to assist the prediction of a poor outcome in comatose survivors of cardiac arrest not treated with hypothermia.[1] [Class B; LOE IV]

Neuroimaging

Apart from their use in confirmation of brain death, there is insufficient evidence to recommend the routine use of neuroimaging to predict outcome of adult cardiac arrest survivors.[1]

Prognostication after cardiac arrest in patients treated with hypothermia

There is inadequate evidence to recommend a specific approach to prognosticating poor outcome in post-cardiac arrest patients treated with therapeutic hypothermia.[1] There are no clinical neurological signs, electrophysiologic studies, biomarkers, or imaging modalities that can reliably predict neurological outcome in the first 24 hours after cardiac arrest.[1]

Beyond 24 hours, no single parameter for predicting poor neurologic outcome in post-cardiac arrest patients treated with hypothermia is without reported false positives. Based on limited available evidence, potentially reliable prognosticators of poor outcome in patients treated with therapeutic hypothermia after cardiac arrest include:

- bilateral absence of N20 peak on somato-sensory evoked potential ≥24 hours
- unreactive electroencephalogram background at 36–72 hours
- the absence of both corneal and pupillary reflexes >72 hours after cardiac arrest.[1]

Limited available evidence also suggests that Glasgow Motor Score of 2 or less at 3 days after sustained return of spontaneous circulation and the presence of status epilepticus are potentially **unreliable** prognosticators of poor outcome in post-cardiac arrest patients treated with therapeutic hypothermia.[1]

Serum biomarkers such as neuron specific enolase are potentially valuable as adjunctive studies in prognostication of poor outcome in patients treated with hypothermia, but their reliability is limited by the relatively few patients who have been studied and lack of assay standardization. Given the limited available evidence, decisions to limit care should not be made based on the results of a single prognostication tool. [Class A; LOE IV]

Outcome of Resuscitation

Resuscitation after cardiac arrest produces a good quality of life in most long-term survivors. There is little evidence to suggest that resuscitation leads to a large pool of survivors with an unacceptable quality of life. Cardiac arrest survivors may experience post-arrest problems including anxiety, depression, post-traumatic stress, and difficulties with cognitive function. Clinicians should be aware of these potential problems, screen for them and, if found, treat them.[6] [Class A; LOE Expert opinion]

Organ donation

Adult patients who progress to brain death after resuscitation from out-of-hospital cardiac arrest should be considered for organ donation.[1] [Class A; LOE Expert opinion]

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