AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council WHAKAHAUORA AOTEAROA

ANZCOR Guideline 11.7 – Post-resuscitation Therapy in Adult Advanced Life Support

Summary

This guideline provides advice on post-resuscitation care because a comprehensive treatment protocol including multiple interventions provided in a structured way may improve survival after cardiac arrest

Who does this guideline apply to?

This guideline applies to adults who require advanced life support

Who is the audience for this guideline?

This guideline is for health professionals and those who provide healthcare in environments where equipment and drugs are available.

Recommendations

The Australian and New Zealand Committee on Resuscitation (ANZCOR) make the following recommendations:

1. ANZCOR suggests hemodynamic goals (e.g., mean arterial pressure [MAP], systolic blood pressure [SBP]) be considered during postresuscitation care and as part of any bundle of post-resuscitation interventions.
2. ANZCOR recommends avoiding hypoxia in adults with ROSC after cardiac arrest in any setting.
3. ANZCOR suggests avoiding hyperoxia in adults with ROSC after cardiac arrest in any setting.
4. Once ROSC has been established and the oxygen saturation of arterial blood (SaO2) can be monitored reliably (by pulse oximetry [SpO2] and/or arterial blood gas analysis [SaO2]), it is reasonable to titrate the inspired oxygen to achieve a target saturation between 94 – 98%.
5. ANZCOR suggests maintaining $PaCO_2$ within a normal physiological range as part of a post-ROSC bundle of care.
6. ANZCOR suggests no modification of standard glucose management protocols for adults with ROSC after cardiac arrest.
7. Providers should monitor blood glucose frequently after cardiac arrest and should treat hyperglycemia (>10 mmol/l) with insulin but avoid hypoglycemia.
8. 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).

9. If no antiarrhythmic drug was used during resuscitation from a shockable rhythm, an antiarrhythmic drug may be considered to prevent recurrent VF.
10. ANZCOR recommends targeted temperature management (TTM) for adults victims of cardiac arrest who remain unresponsive after ROSC (see Guideline 11.9 for details).
11. ANZCOR suggests against routine seizure prophylaxis in post–cardiac arrest patients.
12. ANZCOR recommends the treatment of seizures in post–cardiac arrest patients.
13. Maintenance therapy for seizures should be started after the first event and potential precipitating causes (e.g. intracranial haemorrhage, electrolyte imbalance, etc) should be excluded.
14. In patients with STEMI or new LBBB on ECG following ROSC after OHCA, immediate angiography and percutaneous coronary intervention (PCI) should be considered.
15. ANZCOR recommends emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients with ROSC after OHCA of suspected cardiac origin with ST elevation on ECG.
16. 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.
17. ANZCOR suggests emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients who are comatose with ROSC after OHCA of suspected cardiac origin with-out ST elevation on ECG.
18. 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.
19. Targeted temperature management is recommended in combination with primary PCI, and should be started as early as possible, preferably prior to initiation of PCI.
20. After resuscitation all patients should be reassessed and re-evaluated for resuscitation-related injuries. The extent of injuries is often underestimated by standard investigations (e.g. chest radiograph). Other complications of resuscitation (e.g. incorrect placement of tubes) should be identified and treated. Intravascular lines inserted under emergency conditions may need to be replaced.
21. ANZCOR suggests that OHCA patients should be considered for transport to a specialist cardiac arrest center as part of wider regional system of care for management of patients with OHCA.

Prognostication and cardiac arrest

22. Relying on the neurologic exam during or immediately after cardiac arrest to predict outcome is not recommended and should not be used.

Prognostication with TTM

23. ANZCOR suggest against the use of clinical criteria alone before 72 hours after ROSC to estimate prognosis.

24. ANZCOR suggests that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings.

25. ANZCOR recommends using bilaterally absent pupillary light reflexes (PLRs) or the combined absence of both pupillary and corneal reflexes at least 72 hours after ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM.

26. ANZCOR suggests against using an absent (M1) or extensor motor response to pain (M2) alone to predict poor outcome, given its high FPR. However, due to its high sensitivity, this sign may be used to identify the population with poor neurologic status needing prognostication or to predict poor outcome in combination with other more robust predictors.

27. ANZCOR suggests against the use of myoclonus during the first 72 hours from ROSC as a predictor for prognosticating a poor neurologic outcome.

28. ANZCOR suggests that the presence of status myoclonus during the first 72 hours from ROSC be considered at 72 hours after ROSC (in combination with other factors) as a predictor for prognosticating a poor neurologic outcome.

29. ANZCOR suggests prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized. We recommend that the earliest time to prognosticate a poor neurologic outcome is 72 hours after ROSC, and should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination.

30. ANZCOR recommends using bilateral absence of N20 somatosensory evoked potentials (SSEP) wave measured at least 72 hours after ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM.

31. AZCOR suggests using persistent absence of EEG reactivity to external stimuli at 72 hours or longer after ROSC, presence of persistent burst suppression after rewarming, or intractable and persistent status epilepticus (SE) to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM.

32. ANZCOR recommends against using Bispectral Index (BIS) to predict poor outcome during TTM in patients who are comatose after resuscitation from cardiac arrest and are treated with TTM.

33. ANZCOR suggests using utmost care and preferably sampling at multiple serial time points (24–72 hours) when assessing neuron-specific enolase (NSE), to avoid false-positive results due to hemolysis.

34. ANZCOR suggests using serial high-serum values of NSE at 48 to 72 hours from ROSC in combination with other predictors for predicting poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with TTM.

35. ANZCOR suggests using brain imaging studies for prognostication only in centers where specific experience is available.

36. ANZCOR suggests using the presence of a marked reduction of the gray matter/white matter (GM/WM) ratio on brain CT within 2 hours after ROSC or the presence of extensive diffusion restriction on brain MRI at 2 to 6 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.

Prognostication without TTM

37. ANZCOR suggest against the use of clinical criteria alone before 72 hours after ROSC to estimate prognosis.

38. ANZCOR suggests that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings.

39. ANZCOR recommends using the absence of PLR (or the combined absence of both pupillary and corneal reflexes) at 72 hours or greater from ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM.

40. ANZCOR suggests against using an absent or extensor motor response to pain (M≤2) alone to predict poor outcome, given its high FPR.

41. ANZCOR suggests using the presence of myoclonus or status myoclonus within 72 hours from ROSC in combination with other predictors to predict poor outcome in comatose survivors of cardiac arrest.

42. ANZCOR suggests prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized.

43. ANZCOR recommends using bilateral absence of the N20 SSEP wave within 72 hours from ROSC to predict poor outcome in patients who are comatose after cardiac arrest and who are not treated with TTM.

44. ANZCOR suggests using the presence of burst suppression on EEG at 72 hours from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are not treated with TTM.

45. ANZCOR suggests against using EEG grades for prognostication due to the inconsistencies in their definitions.

46. ANZCOR suggests against using low-voltage EEG for prognostication, given the potential interferences of technical factors on EEG amplitude.

47. ANZCOR suggests using high serum values of NSE at 24 to 72 hours from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are not treated with TTM.

48. ANZCOR suggests using the presence of a marked reduction of the GM/WM ratio on brain CT within 48 hours after ROSC or the presence of extensive reduction in diffusion on brain MRI at 2 to 6 days after ROSC only in combination with other more-established predictors for prognosticating a poor neurologic outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM).

49. ANZCOR suggests using brain-imaging studies for prognostication only in centers where specific experience is available.

Outcome for Survivors

50. 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.

Organ Donation

51. ANZCOR recommends that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated for organ donation.

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]

1.1 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]

Recommendations

ANZCOR suggests hemodynamic goals (e.g., mean arterial pressure [MAP], systolic blood pressure [SBP]) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions (CoSTR 2015, weak recommendation, low-quality evidence).[3]

There is insufficient evidence to recommend specific hemodynamic goals; such goals should be considered on an individual patient basis and are likely to be influenced by post-cardiac arrest status and pre-existing comorbidities (CoSTR 2015, weak recommendation, low-quality evidence).[3]

Values and preferences

In making these recommendations, we place a higher value on the recognition that while hemodynamic goals are likely important to optimize outcome, specific targets remain unknown and likely vary depending on individual physiology and comorbid status.[3]

Aim for a blood pressure equal to the patient's usual blood pressure or at least a systolic pressure greater than 100mg Hg. If the blood pressure falls, a vasopressor may be given by small intravenous increments (e.g. 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 postcardiac 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 (e.g. 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.

1.2 Oxygenation

Recommendations

ANZCOR recommends avoiding hypoxia in adults with ROSC after cardiac arrest in any setting (CoSTR 2015, strong recommendation, very low quality evidence).[3]

ANZCOR suggests avoiding hyperoxia in adults with ROSC after cardiac arrest in any setting (CoSTR 2015, weak recommendation, very low quality evidence).[3]

Once ROSC has been established and the oxygen saturation of arterial blood (SaO2) can be monitored reliably (by pulse oximetry [SpO2] and/or arterial blood gas analysis [SaO2]), it is reasonable to titrate the inspired oxygen to achieve a target saturation between 94 – 98%. [Class A; LOE III-2, Expert consensus opinion]. See also Guideline 11.6.1.

1.3 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 (e.g. $PaCO_2$ 35 to 40 mmHg) is appropriate.[4]

Routine hyperventilation may be detrimental (e.g. 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]

Recommendations

ANZCOR suggests maintaining $PaCO_2$ within a normal physiological range as part of a post-ROSC bundle of care (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

Values and preferences

There is no good evidence to suggest or recommend either hypercarbia or hypocarbia. In the absence of evidence to that end, combined with a potential suggestion of harm, we suggest maintaining normocarbia. Many physiological considerations may influence selection of $PaCO_2$ goals for individual patients.

1.4 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

ANZCOR suggests no modification of standard glucose management protocols for adults with ROSC after cardiac arrest (CoSTR 2015, weak recommendation, moderate-quality evidence).[3]

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]

1.5 Prophylactic anti-arrhythmic agents

No studies specifically and directly addressed the prophylactic use of antiarrhythmic therapy started immediately after resuscitation from cardiac arrest. Observational studies document inconsistent improvement in long-term survival when prophylactic antiarrhythmics were given to survivors of cardiac arrest from all causes.[3]

Recommendation

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; Expert consensus 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; Expert consensus opinion]

1.6 Temperature control

Targeted temperature management 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.[3]

Recommendation

ANZCOR recommends targeted temperature management for adults victims of cardiac arrest who remain unresponsive after ROSC (CoSTR 2015, strong recommendation, low-quality evidence) (see Guideline 11.9 for details).[3]

1.7 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 targeted temperature management in the post arrest treatment of adult cardiac arrest.[1]

1.8 Seizure control

Studies document 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.

Studies report no difference in neurologic outcome after use of single dose diazepam or magnesium or both; or thiopental given after sustained return of spontaneous circulation.[5-7]

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]

Recommendation

ANZCOR suggests against routine seizure prophylaxis in post–cardiac arrest patients (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

ANZCOR recommends the treatment of seizures in post–cardiac arrest patients (CoSTR 2015, strong recommendation, very-low-quality evidence).[3].

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

1.9 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 (e.g. management of myocardial infarction, 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.[8]

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.

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]

ANZCOR recommends emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients with ROSC after OHCA of suspected cardiac origin with ST elevation on ECG (CoSTR 2015, strong recommendation, low-quality evidence).[3] Also see Guideline 11.3

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]

ANZCOR suggests emergency cardiac catheterization laboratory evaluation in comparison with cardiac catheterization later in the hospital stay or no catheterization in select adult patients who are comatose with ROSC after OHCA of suspected cardiac origin with-out ST elevation on ECG (CoSTR 2015, weak recommendation, very-low-quality evidence).

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]

Targeted temperature management 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]

1.10 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]

1.11 Resuscitation related injuries

Rib fractures and other injuries are common[9] but acceptable consequences of CPR given the alternative of death from cardiac arrest.

Recommendation

After resuscitation all patients should be reassessed and re-evaluated for resuscitation-related injuries. The extent of injuries is often underestimated by standard investigations (e.g. chest radiograph).[10] Other complications of resuscitation (e.g. incorrect placement of tubes) should be identified and treated. Intravascular lines inserted under emergency conditions may need to be replaced. [Class B; Expert consensus opinion]

1.12 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.[11]

Recommendation

ANZCOR suggests that OHCA patients should be considered for transport to a specialist cardiac arrest center as part of wider regional system of care for management of patients with OHCA (CoSTR 2015, weak recommendation, low-quality evidence).[11]

Values and preferences

In making this recommendation, we recognize the development of cardiac arrest centers may be considered as a health improvement initiative, as has been performed for other critical conditions, including myocardial infarction, stroke, and major trauma, without the evidence of randomized trials.[3]

2 Prognosis

Many comatose post-cardiac arrest patients die or will survive with a poor neurologic outcome. Therefore, reliable methods to assess prognosis are needed to prevent continued unnecessary treatment and accurately inform families. Post-cardiac arrest prognostication was extensively reviewed in the 2010 and 2015 CoSTR processes.[1,3] The consensus of the task forces was that multimodal assessments should be used, should never rely on a single prognostication element, and supplementary tests should be considered in the context of the clinical examination. The most reliable combination and timing for assessments have not been fully determined.[3]

Recommendations address prognostication of comatose post-cardiac arrest patients treated with hypothermic TTM and patients not treated with hypothermic TTM. This approach was chosen because hypothermic TTM may alter the natural history of coma and may delay recovery of CNS function. Patients may be exposed to large doses of sedative and neuromuscular blockade during TTM. The metabolism of these agents maybe delayed during hypothermic TTM. Prognostic elements that are reliable in comatose post-cardiac arrest patients not treated with hypothermic TTM may be less reliable at the same time point inpatients treated with TTM.

Clinical signs, neurophysiological measurements, blood or cerebrospinal fluid markers, and imaging studies with high specificity for poor neurologic outcome, defined as death, vegetative state, or severe cerebral disability (CPC 3–5) have been assessed. These assessments are justified because they are likely to be used to justify limiting life-sustaining treatments. To quantify the specificity of the findings, CoSTR 2015 examined the false positive rate (FPR) of each sign for predicting unfavorable neurologic outcome, with a goal of 0% FPR. The 95% CI of the FPR was calculated, and the tendancy was to recommend a finding as useful if the FPR was less than 5%, and suggest that a finding might be useful if the FPR was less than 10%. In most cases, clinical signs and findings were considered individually, because few studies considered combinations of clinical findings.[3]

2.1 Prognostication during a cardiac arrest

Studies document 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. 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.

Recommendation

Relying on the neurologic exam during cardiac arrest to predict outcome is not recommended and should not be used.[4] [Class A, Expert consensus opinion]

3 Prognostication for comatose cardiac arrest victims treated with TTM

Recommendations

ANZCOR suggest against the use of clinical criteria alone before 72 hours after ROSC to estimate prognosis (CoSTR 2015, weak recommendation, low-quality evidence).[3]

ANZCOR suggests that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings (CoSTR 2015, weak recommendation, low-quality evidence). [3]

3.1 Clinical Examination

ANZCOR recommends using bilaterally absent pupillary light reflexes (PLRs) or the combined absence of both pupillary and corneal reflexes at least 72 hours after ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM (CoSTR 2015, strong recommendation, low-quality evidence). [3]

ANZCOR suggests against using an absent (M1) or extensor motor response to pain (M2) alone to predict poor outcome, given its high FPR. However, due to its high sensitivity, this sign may be used to identify the population with poor neurologic status needing prognostication or to predict poor outcome in combination with other more robust predictors (CoSTR 2015, weak recommendation, very low-quality evidence). [3]

ANZCOR suggests against the use of myoclonus during the first 72 hours from ROSC as a predictor for prognosticating a poor neurologic outcome (CoSTR 2015, weak recommendation, low-quality evidence). [3]

ANZCOR suggests that the presence of status myoclonus during the first 72 hours from ROSC be considered at 72 hours after ROSC (in combination with other factors) as a predictor for prognosticating a poor neurologic outcome (CoSTR 2015, weak recommendation, low-quality evidence). [3]

ANZCOR suggests prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized.

ANZCOR recommends that the earliest time to prognosticate a poor neurologic outcome is 72 hours after ROSC, and should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination (CoSTR 2015, weak recommendation, low-quality evidence). [3]

3.2 Electrophysiology

ANZCOR recommends using bilateral absence of N20 smatosensory evoked potentials (SSEP) wave measured at least 72 hours after ROSC to predict poor outcome in patients who

are comatose after resuscitation from cardiac arrest and who are treated with TTM (CoSTR 2015, strong recommendation, low-quality evidence).[3]

SSEP recording requires appropriate skills and experience, and utmost care should be taken to avoid electrical interference from muscle artifacts or from the ICU environment, as well as confounding drugs. This test is only ordered in the appropriate clinical context.

AZCOR suggests using persistent absence of EEG reactivity to external stimuli at 72 hours or longer after ROSC (weak recommendation, low-quality evidence), presence of persistent burst suppression after rewarming, or intractable and persistent status epilepticus (SE) (CoSTR 2015, weak recommendation, very-low-quality evidence) to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are treated with TTM.[3]

ANZCOR recommends against using Bispectral Index (BIS) to predict poor outcome during TTM in patients who are comatose after resuscitation from cardiac arrest and are treated with TTM (CoSTR 2015, strong recommendation, very-low-quality evidence).[3]

3.3 Blood Markers

ANZCOR suggests using utmost care and preferably sampling at multiple serial time points (24–72 hours) when assessing neuron-specific enolase (NSE), to avoid false-positive results due to hemolysis (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

ANZCOR suggests using serial high-serum values of NSE at 48 to 72 hours from ROSC in combination with other predictors for predicting poor neurologic outcome in patients who are comatose after cardiac arrest and who are treated with TTM (CoSTR 2015, weak recommendation, verylow-quality evidence). However, no threshold-enabling prediction with 0 FPR can be recommended, and NSE levels are insufficiently specific to be used alone for estimating prognosis.[3]

3.4 Imaging

ANZCOR suggests using brain imaging studies for prognostication only in centers where specific experience is available (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

ANZCOR suggests using the presence of a marked reduction of the gray matter/white matter (GM/WM) ratio on brain CT within 2 hours after ROSC or the presence of extensive diffusion restriction on brain MRI at 2 to 6 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 (CoSTR 2015, weak recommendation, very-low-quality evidence).

Early imaging markers of poor prognosis should not prevent support for a sufficient period of time to observe other clinical features, although some extreme CT scan findings are consistent with herniation and brain death.[3]

4 Prognostication for comatose cardiac arrest victims not treated with TTM

ANZCOR suggest against the use of clinical criteria alone before 72 hours after ROSC to estimate prognosis (CoSTR 2015, weak recommendation, low-quality evidence).

ANZCOR suggests that multiple modalities of testing (clinical exam, neurophysiological measures, imaging, or blood markers) be used to estimate prognosis instead of relying on single tests or findings (CoSTR 2015, weak recommendation, low-quality evidence).

4.1 Clinical Examination

ANZCOR recommends using the absence of PLR (or the combined absence of both pupillary and corneal reflexes) at 72 hours or greater from ROSC to predict poor outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM (CoSTR 2015, strong recommendation, very-low-quality evidence).[3]

ANZCOR suggests against using an absent or extensor motor response to pain (M≤2) alone to predict poor outcome, given its high FPR (CoSTR 2015, weak recommendation, very-low-quality evidence). However, due to its high sensitivity, this sign may be used to identify the population with poor neurologic status needing prognostication or to predict poor outcome in combination with other more-robust predictors.[3]

ANZCOR suggests using the presence of myoclonus or status myoclonus within 72 hours from ROSC in combination with other predictors to predict poor outcome in comatose survivors of cardiac arrest (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

ANZCOR suggests prolonging the observation of clinical signs when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false-positive results is minimized (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

4.2 Electrophysiology

ANZCOR recommends using bilateral absence of the N20 SSEP wave within 72 hours from ROSC to predict poor outcome in patients who are comatose after cardiac arrest and who are not treated with TTM (CoSTR 2015, strong recommendation, very-low-quality evidence). SSEP recording requires appropriate skills and experience, and utmost care should be taken to avoid electrical interference from muscle artifacts or from the ICU environment.[3]

ANZCOR suggests using the presence of burst suppression on EEG at 72 hours from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are not treated with TTM (CoSTR 2015, strong recommendation, very-low-quality evidence).[3]

ANZCOR suggests against using EEG grades for prognostication due to the inconsistencies in their definitions (CoSTR 2015, weak recommendation, very-low-quality evidence).[3]

ANZCOR suggests against using low-voltage EEG for prognostication, given the potential interferences of technical factors on EEG amplitude (CoSTR 2015, weak recommendation, very-low quality evidence).[3]

4.3 Blood Markers

ANZCOR suggests using high serum values of NSE at 24 to 72 hours from ROSC in combination with other predictors for prognosticating a poor neurologic outcome in patients who are comatose after cardiac arrest and who are not treated with TTM (CoSTR 2015, weak recommendation, very-low-quality evidence). However, no threshold-enabling predictionwith 0 FPR can be recommended. We suggest using utmost care and preferably sampling at multiple time points when assessing NSE, to avoid false-positive results due to hemolysis. [3]

4.4 Imaging

ANZCOR suggests using the presence of a marked reduction of the GM/WM ratio on brain CT within 48 hours after ROSC or the presence of extensive reduction in diffusion on brain MRI at 2 to 6 days after ROSC only in combination with other more-established predictors for prognosticating a poor neurologic outcome in patients who are comatose after resuscitation from cardiac arrest and who are not treated with TTM (CoSTR 2015, weak recommendation, very-low quality evidence). [3]

ANZCOR suggests using brain-imaging studies for prognostication only in centers where specific experience is available (CoSTR 2015, weak recommendation, very-low-quality evidence). [3]

5 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. Survivors may however suffer a variety of post-arrest problems that affect quality of life.

Recommendation

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; Expert consensus opinion]

5.1 Organ donation

ANZCOR recommends that all patients who have restoration of circulation after CPR and who subsequently progress to death be evaluated for organ donation (CoSTR 2015, strong recommendation, low-quality evidence).[3]

The Australian and New Zealand Intensive Care Society Death and Organ Donation Committee provides relevant advisory statements at:
http://www.anzics.com.au/Pages/DaOD.aspx

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