Post-Cardiac Arrest Syndrome
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Introduction
Advanced cardiac life support training focuses on restoration of circulation. While if this is often accomplished, the vast majority of patients still die of damage to the brain and other vital organs. This is true both in and out of the hospital. On average, approximately 6.4% of out-of-hospital cardiac arrest victims survive to hospital discharge. Patients that experience cardiac arrest in the hospital have a 24% survival rate.

These statistics had not changed in half a century. In the last few years, a prompt, comprehensive approach to these patients has been shown to significantly improve the prognosis. The following recommendations are based on widely accepted guidelines.

One should always attempt to determine the disorder that precipitated the cardiac arrest, as it may be reversible. The commonest causes include acute coronary syndrome, cardiac tamponade, pulmonary embolism, toxins, tension pneumothorax, hypovolemia, hypoxia, acidosis, electrolyte imbalance, and hypothermia.

Problems following return of spontaneous circulation
- Brain injury (impaired autoregulation, cerebral edema, neurodegeneration, coma, seizures, myoclonus, cognitive dysfunction, stroke, brain death)
- Myocardial stunning, acute coronary syndrome
- Damage to other vital organs (systemic ischemia, reperfusion injury, impaired vasoregulation, increased coagulability)
- Adrenal dysfunction
- Hyperglycemia
- Renal Failure
- Infection, particularly pneumonia
- Impaired oxygen delivery
- Persistence of the precipitating pathology (e.g. cardiovascular disease, pulmonary disease, stroke, pulmonary embolism, infection, poisoning or drug overdose, hemorrhage, dehydration)

Recovery phases after resuscitation
Early post-arrest phase: 20 minutes to 6-12 hours - early interventions are more apt to be effective at this time.
Intermediate phase: 6-12 hours to 72 hours - Injury pathways are still active. Aggressive treatment is indicated.
Recovery phase: 3 days and beyond
Contributing factors to poor prognosis

- Fever – for every 1° C above 37° mortality increases 2.3 fold
- Hyperglycemia
- Seizures
- Inappropriate ventilation
- Hypotension or hypertension
- Old age

Recommendations

Ventilation
If patient is not awakening within 5-10 minutes he should be intubated. While administration of 100% oxygen may be appropriate during resuscitation, subsequent hyperoxia causes oxidative stress, which results in a worse neurologic outcome and reduced survival. Therefore routine administration of 100% oxygen is not recommended following the initial resuscitation, unless it is required to provide a physiologic arterial oxygen saturation. A starting rate of 10-12 breaths per minute has been recommended. Hypoxemia should also be avoided. Titrating to an SaO2 of 94-96% is advised. Shortly after resuscitation vasoconstriction makes pulse oximetry unreliable. Hyperventilation is also detrimental. A normal pCO2 should be maintained by regular measurement of arterial blood gases. Hyperventilation lowers cardiac output which in turn reduces cerebral perfusion. Lowering the PaCO2 also causes cerebral vasoconstriction.

In general, it is not advised to treat acidosis with hyperventilation. It usually resolves with adequate perfusion.

Hypotension
Hypotension should be treated aggressively. Third-spacing tends to occur following cardiac arrest, so fluid administration is the first line. This may require 3.5-6.5 liters of crystalloid in the first 24 hours to optimize the hemodynamic parameters. Inotropes and vasopressors are the second choice, as they often induce focal ischemia and arrhythmias. Epinephrine, dopamine or norepinephrine are appropriate choices. Blood pressure should be sufficient to provide adequate brain perfusion, yet not so high as to overload the damaged heart. The balance between systemic oxygen delivery and consumption can be monitored indirectly with mixed venous oxygen saturation (SvO2) or ScvO2.

Pulmonary artery catheterization has not been shown to improve the outcome.

Circulatory assist devices may be considered. Percutaneous cardiopulmonary bypass and other invasive measures are also options.

Hypothermia
There is strong evidence that hypothermia is neuroprotective. It reduces cerebral glucose and oxygen consumption, intracellular acidosis, calcium influx and oxygen free radical production. It also reduces brain edema and lessens the risk of thrombosis and seizures. It is probably also cardioprotective. It is indicated in most patients who, after return of spontaneous circulation, do not respond meaningfully to verbal commands (even if they are not unconscious).
number needed to treat for one additional patient to be discharged with improved neurologic function is six. While the evidence favoring it is less robust in patients with non-shockable rhythms, it is recommended both for ventricular fibrillation-induced cardiac arrest, and non-ventricular fibrillation arrest. The latter patients, however, have a worse prognosis. It is not necessarily contraindicated in patients with shock (Delhaye).

Therapeutic hypothermia should be initiated as soon as possible. Mortality increases by 20% for every hour of delay. However, it may still be beneficial after 6-12 hours. Temperature fluctuations should be kept below 0.5°C.

There are three phases:

*Induction* is easily initiated by one of the following methods:

- Giving ice cold intravenous saline or Ringer’s lactate at 30 ml/kg. This needs to be combined with other methods, as soon as they are available. Prehospital treatment with cold fluids is not recommended.
- Placing ice packs at the groin and axillae and around the head and neck
- Use of a cooling blanket or cold air tent
- Insertion of an intravascular cooling catheter

Other techniques include iced saline gastric lavage, cooling helmets, and trans-nasal cooling device.

Core temperature must be monitored, ideally with an esophageal probe or a pulmonary artery catheter. Shivering is counterproductive, and can be managed with neuromuscular blockade and sedation. Magnesium sulfate 5 g can be infused over 5 hours. It reduces shivering and is a vasodilator (thus increasing cooling rate). It also has antiarrhythmic properties. Animal studies suggest that it is also neuroprotective. Scirica routinely gives 4 g. over 4 hours to all patients undergoing hypothermia. Warming the skin helps to reduce shivering. This can be done with a forced-air rewarming blanket, at the same time lowering the core temperature with a cooling catheter. Sedation with propofol or midazolam can be helpful. Administration of fentanyl, hydromorphone, or meperidine with or without buspirone may be used in conjunction with skin warming if the patient is awake. Pain control should be continued if the patient has been paralyzed.

*Maintenance phase*

Hypothermia should be maintained at 32-36°C for at least 12-24 hours. Most advise 24 hours. The higher range might be more appropriate for patients with bleeding complications, and lower ones for those with seizures or cerebral edema. Temperature must be monitored continuously.

*Rewarming phase*

Body temperature is controlled with the above devices. After 24 hours of hypothermia, one should rewarm the patient at approximately 0.25-0.5°C per hour. It is especially important to monitor electrolytes and hemodynamic parameters during this phase. A higher urine output
goal of >1 mL/kg/h is reasonable in post-arrest patients treated with therapeutic hypothermia. There are devices (e.g. Arctic Sun pads) that automatically control the rate of rewarming.

**Complications of hypothermia**
- Systemic vascular resistance is increased, which reduces cardiac output.
- Bradycardia and other arrhythmias may occur, particularly if the temperature had been reduced below 32° F, or if there is electrolyte imbalance. It should only be treated if there is associated hypotension.
- Hypothermia induces diuresis, which can cause electrolyte abnormalities.
- Decreased insulin sensitivity and secretion resulting in hyperglycemia.
- Impaired coagulation, bleeding
- Immune system impairment, increasing susceptibility to infection.
- Impaired clearance of drugs, including sedatives and neuromuscular blockers

If instability persists and appears to be related to the hypothermia, the body temperature can be increased to 34-35˚C at a rate of 0.25˚ per hour. In any case, after rewarming, care should be taken to maintain the temperature at 37˚C. If hypothermia is not being used, then at the very least, fever should be treated aggressively.

**Contraindications to hypothermia**

*Absolute contraindications:*
- Hemorrhagic stroke
- Major head trauma
- Major surgery within prior 14 days
- Sepsis
- Cardiac arrest due to trauma
- Glasgow coma scale > 8 on arrival of EMS
- Preexisting hypothermia (< 34° C.)
- Uncontrolled active bleeding or significant risk of bleeding
- Uncontrolled hemodynamically unstable arrhythmias

*Relative contraindications:*
- Prolonged cardiac arrest (> 60 minutes)
- Terminal condition or poor prexisting status
- Baseline coagulopathy
- Hypotension refractory to fluid and pressor support
- Pregnancy

**Revascularization**
Coronary artery disease is the commonest precipitating factor of cardiac arrest. Prompt revascularization should always be considered, preferably within 90 minutes. The absence of ST elevation on the electrocardiogram should not influence the decision, although the data is less robust for these individuals. Patients can be transferred to the catheterization laboratory while hypothermia is being initiated. The prognosis is greatly improved with this intervention. When
both reperfusion and hypothermia were employed, the in-hospital mortality was reduced from 72% to 44%, and over 90% of the survivors were neurologically normal. If no facilities are available for immediate PCI, thrombolysis is recommended for those patients with ST elevation myocardial infarctions.

**Sedation**
Neumar et al recommend the use of both opioids and hypnotics (propofol, benzodiazepines, etc). Guidelines advise daily interruptions of sedation to allow neurologic assessment. Observe closely for shivering, including such subtle signs as jaw quivering. If it occurs in spite of deep sedation, neuromuscular blocking drugs can be given either as a bolus or infusion. Frequent, or preferably continuous electroencephalographic monitoring should be used if neuromuscular blockade is employed, so that seizures can be detected. The degree of blockade must be monitored, and its duration kept to a minimum.

**Seizures**
An EEG should be performed as soon as possible in these patients. It should be repeated frequently or monitored continuously. Prolonged seizures may cause cerebral injury and should be treated promptly. The preferred drugs are benzodiazepines, phenytoin, sodium valproate, propofol or a barbiturate, all of which cause hypotension. Myoclonus should also be treated, as it contributes to a poor outcome. The drug of choice at present is clonazepam. Intracranial hemorrhage, electrolyte imbalance and other causes should be ruled out.

**Hyperglycemia**
Blood glucose concentrations must be monitored at least hourly, and hyperglycemia treated with an insulin infusion. The target level of glucose is 144 mg/dl. Scirica recommends not treating hyperglycemia unless the glucose level exceeds 200 mg/mL. Hypoglycemia is obviously also detrimental.

**Renal failure**
Management in these patients follows the usual guidelines.

**Infection**
Patients who experience cardiac arrest are very prone to infections, mainly pulmonary, bloodstream and catheter-related. Surveillance cultures are indicated. Prompt treatment is required, according to the usual guidelines.

**Electrolyte imbalance**
Hypothermia often causes mild hypokalemia. Oomen advises that levels of 3.0-3.5 not be corrected, since this can result in hyperkalemia during rewarming. Scirica recommends checking electrolytes every 4-6 hours and maintaining a potassium level above 3.5 mEq/L. During rewarming, the potassium tends to rise, so potassium administration should be stopped 4 hours before rewarming is started.
Treatment goals

CVP 8-12 mm Hg
Hct >30% or Hgb >8
Urine output ≥ 0.5 ml/kg/hr
MAP 65-90
Glucose 144-180 mg/dl
Lactate ≤ 2 mmol/ml
ScvO2 ≥70%
Oxygen delivery index > 600 ml/min/m²

Prognostication

The optimal approach to prediction of recovery is controversial. No test that directly evaluates cortical function. There is no predictor of adverse neurologic outcome that is 100% specific.

The majority of patients who recover do so after within 72-96 hours after return of spontaneous circulation. Prolonged coma, even as long as 3 months, can occasionally be followed by recovery. Most patients who do recover continue to improve in the months that follow. By 6 months, many are independent. Those that do not improve usually die within 3-6 months. Age alone should not deter one from attempting resuscitation. For example, Chan et al report that half of their patients aged 85 or more were still alive a year after resuscitation.

O’Riordan cautions against premature abandonment of efforts. This is especially true when hypothermia is employed; about a third of them do not regain alertness until day seven. Scirica advises delaying termination of efforts until at least the fifth day after cardiac arrest. Prophesying futility because of early lack of response is self-fulfilling.

Retention of any neurological function during or immediately after CPR predicts a good neurological outcome, but the reverse is not always true. Shock, metabolic derangements, hypothermia and drug interventions may adversely influence neurologic findings and lead to errors in interpretation. Specifically, the absence of eye movements in response to caloric testing may be blunted by sedation. Seizures and myoclonus also may compromise the neurologic examination.

In general, decreased survival is associated with advanced age, poor fitness and major medical comorbidities. Delayed initiation of CPR or poor quality CPR portends a poor outcome. The pre-arrest APACHE score has not proved helpful. The occurrence of seizures does not preclude a favorable outcome. Withdrawal of life support should not be based on clinical judgment alone.

A Glasgow Coma Scale motor score of ≤ 2, or lack of motor response to painful stimuli at 72 hours indicates a poor prognosis. Decerebrate extensor posturing should not be considered a meaningful response. Absence of brain stem reflexes, such as pupillary light reflex or corneal reflex at 72 hours are unfavorable signs.

Electroencephalography alone is insufficient to prognosticate futility. The most reliable of indication of a poor outcome appears to be generalized suppression to <20 microvolts, burst-suppression pattern with generalized epileptiform activity, and generalized periodic complexes on a flat background.

Neuroimaging techniques, especially CT scans, are only helpful to exclude intracranial pathologies such as brain edema, hemorrhage or stroke. MRI shows promise, but studies are
limited. Metabolic abnormalities (such as lactate accumulation) can be detected by PET scan and other modalities, and are associated with a poor outcome.

Somatosensory-evoked potential testing is probably the single most reliable investigation. This is performed by electrical stimulation of the median nerve at the wrist while monitoring the electroencephalogram. If it is absent bilaterally after 24 hours, the prognosis for neurologic recovery is poor in patients who are not treated with hypothermia.

Neuron-specific enolase and S-100B are blood markers that assist prognostication. However, they should not be used as the sole criteria.

Results
Using a multifaceted approach, the overall in-hospital mortality rate can be reduced from 72% to 44%. Over 90% of survivors were neurologically normal. In their study of 125 patients who had suffered cardiac arrest outside of the hospital, Stub et al found that this tactic nearly doubled survival and neurologic outcome.

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