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Post resuscitation support

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1. Introduction

The goal of cardiopulmonary-cerebral resuscitation (CPCR) is to save "hearts and brains too good to die". Long term prognosis following cardiac arrest is poor. As a result post resuscitation support has become a critical component of CPCR. It aims to maximise CVS resuscitation and support recovery of the post ischaemic brain.

2. History

In the mid-1500s, Vesalius described in experimental animals with thoracotomy, the motion of heart and arteries fading away under asphyxiation from lung collapse, and showed resuscitation by intratracheal mouth to tube intermittent positive-pressure ventilation (IPPV). No one pursued this.[1]

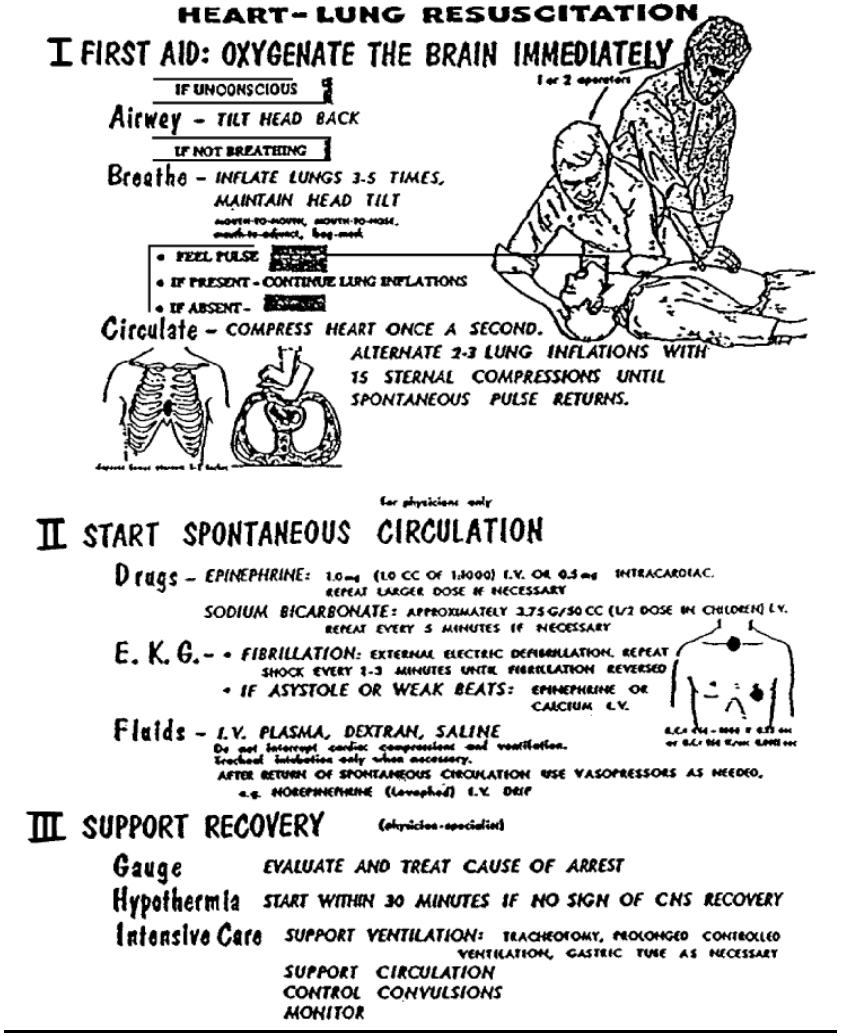
"Before the Renaissance, death was to be accepted as an act of God. From then on, there was a will to attempt resuscitation. The ability to reverse coma-induced airway obstruction, apnoea, and pulselessness began in response to accidents caused by general anaesthesia in the late 1800s. Around 1900, knowledge existed about the majority of CPR steps. This knowledge, however, was then not assembled into an effective system because of lack of communication between laboratory researchers, clinicians, and rescuers."[2]

In the operating room open chest CPR was successfully practised since the 1900's. Since 1961 closed chest CPR has been widely accepted. In 1966 the National Academy of Sciences National Research Council Conference published consensus standards for CPR. Today the American Health Associations BLS and ACLS training programmes and materials are popular worldwide.

CPCR as developed by Safar consists of BLS, ALS and PLS (prolonged life support). BLS is the stopgap providing borderline oxygenation until ALS can be instituted. ALS should be as rapid as possible to restore spontaneous circulation. Once out of immediate danger a patient requires prolonged life support.

In the early 1950's, intensive care for prolonged life support became a reality during a poliomyelitis epidemic in Copenhagen. In 1958, at Baltimore City Hospital, Safar inititiated the first medical-surgical ICU used for multi-organ failure life support. Mobile ICU's were initiated in Prague and Moscow around 1960, followed by Safar in the USA. Since the 1970's there has been modifications of CPCR and research in post arrest support continues to this day.

Fig.1 The first assembly of cardiopulmonary cerebral resuscitation system in 1960



3. Morbidity and Mortality

The first large multicentre report on patients treated for cardiac arrest was published in 1953.[3] A review of 1200 in-hospital cardiac arrests reported that despite only 11% ventricular fibrillation, only 28% were resuscitated to survival. In-hospital mortality was 50 percent. Since then, our understanding of the causes of cardiac arrest and resuscitation techniques has advanced. Despite this, overall prognosis following return of spontaneous circulation (ROSC) has not improved. The prognosis following out of hospital cardiac arrest is poor – only 10% of the 20-40% that have ROSC survive to hospital discharge. Despite having a better prognosis, only 25% of the inpatient population admitted to ICU following ROSC, had good to moderate recovery.

Table 1: Predictors of poor long term outcome following cardiac arrest.[4]

Out of Hospital Arrest	Intra-Operative Arrest
Pre-arrest hypotension	Pre-arrest hypotension
Pre-arrest poor functional status	Pre-arrest uncontrolled haemorrhage
Arrest duration > 15 minutes	Arrest duration > 15 minutes
Metastatic Disease	Post arrest pressure/inotropic support
Pneumonia	

4. Post Resuscitation Status

A person who has sustained dying, cardiac arrest and resuscitation enters a specific pathological state.[5] "Post resuscitation disease" describes the period following ROSC and it is caused by the combination of ischaemia, re-oxygenation and recirculation. When tissue is injured by ischaemia/anoxia the ability to control oxygen metabolism is compromised. Reperfusion/re-oxygenation may generate free radical production that can lead to lipid peroxidation and cellular dysfunction. This sequence of events plays an important role in post resuscitation myocardial, cerebral and systemic dysfunction.

Four key components of post resuscitation disease are brain injury, myocardial dysfunction, systemic ischaemia/reperfusion response and persistent precipitating pathology.

4.1 Brain Injury

Cardiopulmonary arrest results in global cerebral ischaemia. As a result of its high energy utilization but limited energy storage capacity, any interruption in oxygen or glucose supply makes the brain very vulnerable. Calcium is probably central to this process. Present in the cytosol of normal neurons, calcium gains access to the cytosol via neurotransmitter gated and voltage dependant channels and is also released from intracellular storage sites in endoplasmic reticulum. Its normal concentration range is tightly regulated by energy consuming processes that extrude it from the cell, resequester it in the mitochondria or ER and inactivate factors that liberate it from the storage sites (Fig.2).

Two simultaneous impacts on these processes occur during cerebral ischaemia.

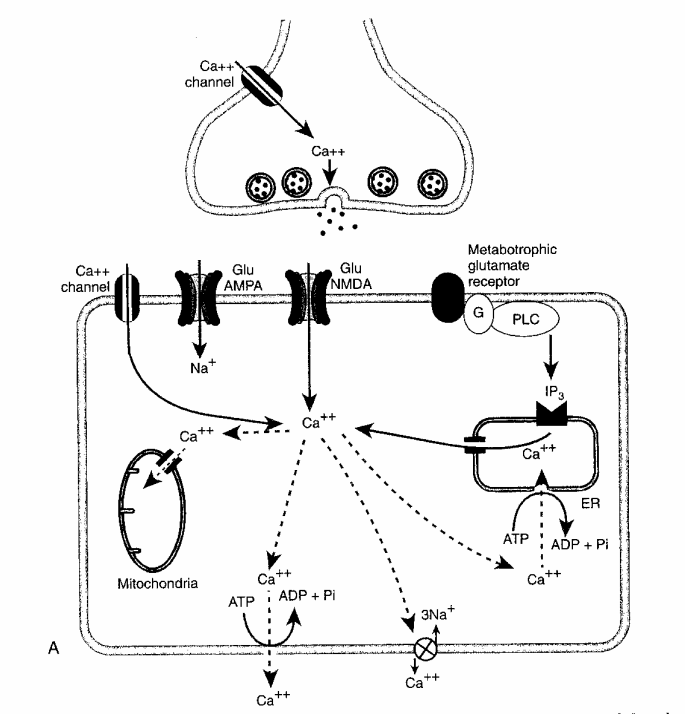
1. Excess release of neurotransmitters that activate the various calcium influx processes
2. Failure of supply of ATP

One of calcium's functions intracellularly is the activation of lipases, nucleases and proteases. Ischaemia results in elevated calcium levels therefore causing sustained activation of these and other enzymes. Among the free fatty acids is arachidonic acid – the substrate for prostaglandin and leukotriene generation. They have numerous effects, all of which can contribute to the evolution of the ischaemic neuronal insult.

During re-oxygenation increased levels of free radical species are formed further contributing to degeneration of membrane lipids and structural elements and worsening of microcirculatory failure. Re-oxygenation restores ATP which may result in massive uptake of calcium into mitochondria. Mitochondria loaded with calcium may be destroyed; increased calcium levels and via triggering of free oxygen radical results in lipid peroxidation, membrane leak and cell death (Fig.3).

Factors that can compromise oxygen delivery and worsen brain injury in the hours to days following cardiac arrest include hypotension, hypoxaemia, impaired cerebro-vascular auto- regulation, brain oedema, pyrexia, hypoglycaemia and seizures. Clinical manifestations include coma, seizures, myoclonus, various degrees of neurocognitive dysfunction and brain death.

Fig 2. Neuronal calcium homeostasis[6]



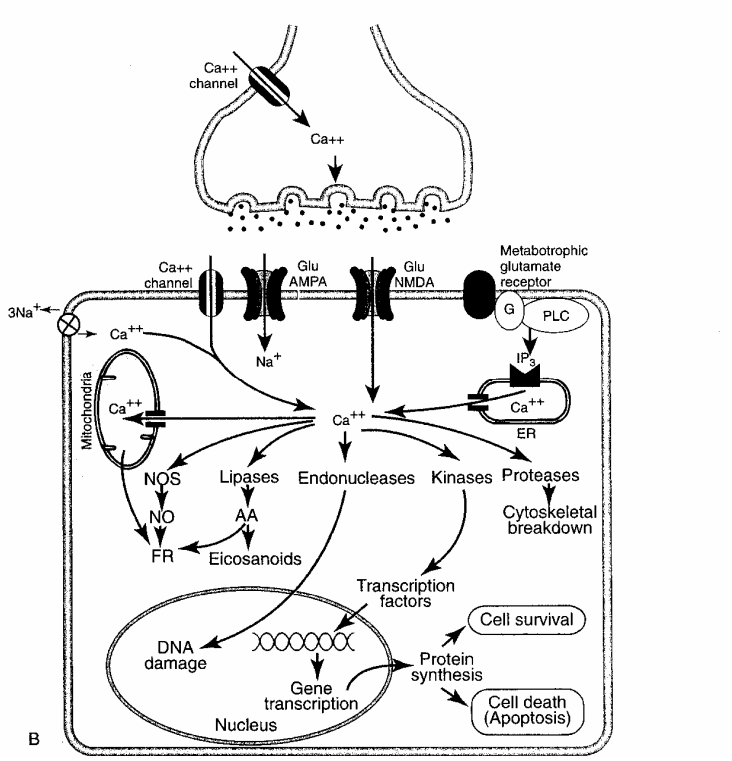
Intracellular calcium can be increased by three mechanisms.

1. Depolarisation of neurons open voltage gated calcium channels
2. Neurotransmitter agonists activate ligand-gated channels i.e. NMDA subtype of glutamate receptor.
3. Neurotransmitters may activate surface receptor leading to generation of IP3 which release calcium from endoplasmatic reticulum and mitochondria

Removal of calcium from cytosol

1. Calcium-ATPase pump and re-sequestration within ER/mitochondria
2. Ca++/Na+ exchanger

Fig 3. Changes occurring during ischaemia[6]



ATP depletion leads to neuronal depolarisation. This results in the release of large quantities of neurotransmitters especially glutamate. This results in a rapid entry of calcium into neurons by:

1. Excessive stimulation of ligand-gated channels
2. Opening of voltage dependant calcium channels

Stimulation of metabotropic glutamate receptors generate IP3, causing release from ER/mitochondria. Activation of AMPA-gated subset of glutamate receptors permits excessive entry of sodium. Lack of ATP will inhibit calcium extrusion re-sequestration processes and high intracellular sodium levels may result in reversal of Ca++/Na+ exchanger. All of the above results in excessive free calcium.

This results in activation of numerous enzymes:

1. Proteases – breakdown of cytoskeleton of neurons
2. Lipases – damage plasma membrane lipids and release arachidonic acid
3. Arachidonic acid is metabolised to yield free radicals
4. Nitric Oxide synthase result in release of NO, generating
5. Peroxynitrate which is a highly reactive free-radical (FR)
6. Activated endonucleases break down DNA
7. Activation of certain protein kinases lead to synthesis of transcription factors that initiate gene transcription and protein synthesis. Some of these new proteins contribute to restorative functions while others can initiate processes to apoptosis.

4.2 Myocardial Dysfunction

Myocardial dysfunction contributes to low survival rate after in- and out of hospital cardiac arrest following ROSC. Heart rate and blood pressure are extremely vulnerable. This can be a result of an increase in circulating and local catecholamine levels. Appropriate monitoring can detect myocardial dysfunction within minutes of ROSC. Swine studies show a decrease in EF and increases in LVEDP as early as 30 minutes following ROSC. During the period of significant dysfunction coronary blood flow is not reduced indicating a true stunning phenomena rather than permanent injury.

This global dysfunction is transient and full recovery can occur. In a swine model with no previous coronary or other left ventricular dysfunction features, the time to recovery appears to be between 24 and 48 h. Several case series have described transient myocardial dysfunction after human cardiac arrest. Cardiac index values reached their nadir at 8 h after resuscitation, improved substantially by 24 h, and almost uniformly returned to normal by 72 h in patients who survived out of hospital cardiac arrest. More sustained depression of ejection fraction among in- and out of hospital post-cardiac arrest patients has been reported with continued recovery over weeks to months.[3]

4.3 Systemic Ischaemia/Re-perfusion response

Cardiac arrest represents the most severe shock state. CPR only partially reverses this. During CPR a compensatory increase in systemic oxygen extraction occurs. This can lead to significant decrease in central and mixed venous oxygen saturation. Inadequate tissue oxygenation persists owing to myocardial dysfunction, haemodynamic instability and microcirculatory failure.

Post cardiac arrest, whole body ischaemia/reperfusion has many features in common with sepsis. Blood concentrations of various cytokines and endotoxins can increase as early as 3 h post arrest. Activation of blood coagulation without adequate activation of endogenous fibrinolysis may contribute to microcirculatory reperfusion disorders. Intravascular fibrin formation and microthrombi are distributed throughout the entire microcirculation.

Adrenal function is affected by the stress of total body ischaemia/ reperfusion. Relative adrenal insufficiency is common.

Clinical manifestations include intravascular volume depletion, impaired oxygen delivery and utilization and increased susceptibility to infection.

4.4 Persistent Precipitating Pathology

Persisting pathology, which includes acute coronary syndromes, pulmonary disease, haemorrhage and sepsis, can both cause and contribute to cardiac arrest.

Acute coronary artery occlusion is frequent in survivors of out of hospital cardiac arrest and is predicted poorly by clinical and ECG findings. 48% of patients, who had no obvious non-cardiac aetiology but had undergone coronary angiography after resuscitation from out of hospital cardiac arrest, had an acute coronary occlusion.[7]

Elevations in troponin T measured during treatment of cardiac arrest suggest that an ACS precedes out-of-hospital cardiac arrest in 40% of patients. Injury to the heart during initial resuscitation however reduces the sensitivity of cardiac biomarkers for identifying ACS after ROSC. At 12 h after ROSC from out-of-hospital cardiac arrest, troponin T has been reported to be 96% sensitive and 80% specific for diagnosis of AMI, whereas Creatine Kinase MB (CK-MB) is 96% sensitive and 73% specific.[3]

Pulmonary thromboembolic disease should also be considered. PE has been reported in 2-10% of sudden deaths. No reliable data are available to estimate the likelihood of pulmonary embolism among patients who achieve ROSC after either in or out-of-hospital cardiac arrest.[3]

Pulmonary physiology may be worsened in a patient with pulmonary disease in a patient with ROSC. This may be as a result of redistribution of blood into the pulmonary vasculature leading to pulmonary oedema or increased alveolar-arterial oxygen gradient.

Sepsis is a cause of cardiac arrest, ARDS and multi-organ failure. When cardiac arrest occurs in this setting it predisposes to exacerbation of the pre-arrest disease.

Table 2: Reference 3

Table 1 Post-cardiac arrest syndrome: pathophysiology, clinical manifestations, and potential treatments.

Syndrome	Pathophysiology	Clinical manifestation	Potential treatments
Post-cardiac arrest brain injury	• Impaired cerebrovascular autoregulation • Cerebral oedema (limited) • Postischaemic neurodegeneration	• Coma • Seizures • Myoclonus • Cognitive dysfunction • Persistent vegetative state • Secondary Parkinsonism • Cortical stroke • Spinal stroke • Brain death	• Therapeutic hypothermia[177] • Early haemodynamic optimization • Airway protection and mechanical ventilation • Seizure control • Controlled reoxygenation (SaO_2 94%-96%) • Supportive care
Post-cardiac arrest myocardial dysfunction	• Global hypokinesis (myocardial stunning) • Reduced cardiac output • ACS	• Early revascularization of AMI[171,373] • Hypotension • Dysrhythmias • Cardiovascular collapse	• Early haemodynamic optimization • Intravenous fluid[97] • Inotropes[97] • IABP[13,160] • LVAD[161] • ECMO[361]
Systemic ischaemia/ reperfusion response	• Systemic inflammatory response syndrome • Impaired vasoregulation • Increased coagulation • Adrenal suppression • Impaired tissue oxygen delivery and utilisation • Impaired resistance to infection	• Ongoing tissue hypoxia/ischaemia • Hypotension • Cardiovascular collapse • Pyrexia (fever) • Hyperglycaemia • Multiorgan failure • Infection	• Early haemodynamic optimization • Intravenous fluid • Vasopressors • High-volume haemofiltration[374] • Temperature control • Glucose control[220] • Antibiotics for documented infection
Persistent precipitating pathology	• Cardiovascular disease (AMI/ACS, cardiomyopathy) • Pulmonary disease (COPD, asthma) • CNS disease (CVA) • Thromoboembolic disease (PE) • Toxicologic (overdose, poisoning) • Infection (sepsis, pneumonia) • Hypovolaemia (haemorrhage, dehydration)	• Specific to aetiology, but complicated by concomitant PCAS	• Disease-specific interventions guided by patient condition concomitant PCAS

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; EMCO, extracorporeal membrane oxygenation; COPD, chronic obstructive pulmonary disease; CNS, central nervous system; CVA, cerebrovascular accident PE, pulmonary embolism; and PCAS, post-cardiac arrest syndrome.

5. Therapeutic Strategies

The pathway to best hospital post resuscitation care is not completely known. There is however, an increasing interest in identifying and optimizing practises that can improve outcome.

5.1 General Measures

Both pre-hospital and post-admission post resuscitation care may significantly influence outcome. This care is provided by multiple, diverse teams of health care workers. The first goal of post resuscitation care is having an optimal multidisciplinary team. Treatment plans need to accommodate a spectrum of patients, focus on reversing the manifestations of post resuscitation disease and be tailored to available resources. General management should follow standard of care for critically ill patients in the ICU setting.

5.2 Monitoring

Post-cardiac arrest syndrome: Monitoring Options
1.General intensive care monitoring
Invasive blood pressure monitoring
Pulse Oximetry
Continuous ECG
SvO_2
Temperature (bladder/oesophagus)
Urine output
Serum Lactate
Arterial Blood Gases
FBC, U&E, Glucose
CXR
2. Advanced Haemodynamic Monitoring
Echocardiography
Cardiac output monitoring
3. Cerebral Monitoring
EEG (on indication or continuous): early detection and treatment of seizure activity
CT/MRI

Minimal requirements include general intensive care monitoring and depending on patient status and availability, additional monitoring should be added. There is insufficient data to validate the impact of specific monitoring techniques on outcome following cardiac arrest.

5.3 Early haemodynamic optimisation

This is otherwise known as early goal directed therapy(EGDT). The aim is to initiate monitoring and treatment as early as possible in order to restore the balance between oxygen delivery and demand. EGDT has been studied in randomised prospective clinical studies of post-op patients and patient with severe sepsis. The benefits of EGDT include modulation of inflammation, reduction of organ dysfunction, and reduction of healthcare resource consumption. In severe sepsis EGDT also has been shown to reduce mortality.[8] It has been hypothesised that early haemodynamic optimisation may improve outcome of post cardiac arrest survivors since the systemic ischaemia/reperfusion response and myocardial dysfunction have similarities with sepsis.

What is unique to the post arrest patient is a need to adequately perfuse the post-ischaemic brain without putting unnecessary strain on the post-ischaemic heart. The optimal MAP for post cardiac arrest patients has not been defined. Cerebral autoregulation is lost. Cerebral perfusion is dependant on CPP. Sustained elevation of ICP during the early post cardiac arrest phase is uncommon. Cerebral perfusion is therefore predominantly dependant on MAP. A MAP of 65 to 100 mm Hg is an acceptable goal. Good outcomes have been achieved in published studies in which MAP target was as low as 65 to 75 mm Hg to as high as 90-100 mm Hg for patients admitted after out of hospital cardiac arrest.[3]The target MAP may be dependant on patients' normal blood pressure, cardiac arrest duration, severity of myocardial dysfunction and cause of arrest e.g. myocardial infarction.

The optimal CVP goal has also not been defined. It is important to remember that an elevated CVP independent of volume status can be caused by persistent precipitating pathology e.g. cardiac tamponade, tension pneumothorax and pulmonary embolism. Post cardiac arrest ischaemia/reperfusion response cause intravascular volume depletion and volume expansion is usually required. There is no evidence to support the advantage of one fluid type over another.[3]

Mixed Venous Oxygen Saturation is an indirect measure of the balance between oxygen delivery and consumption. However, the optimal SVO_2 goal and value of continuous SVO_2 monitoring in the post cardiac arrest patient is yet to be defined by any clinical trial. The down side of using it as a monitoring tool in the post cardiac arrest patient is that a subset may have "venous hyperoxia"
- elevated SVO_2 due to impaired tissue oxygen utilisation caused by microcirculatory/ mitochondrial failure.

Additional surrogates for oxygen delivery include urine output and lactate clearance. However there are limitations to their use. Urine output could be misleading in the presence of acute or chronic renal insufficiency. Lactate clearance can be impaired by seizures, excessive motor activity, hepatic insufficiency and hypothermia. Reasonable goals for post cardiac arrest care are urine output > 1ml/kg/hr and a normal or decreasing serum blood lactate level. A goal for haemoglobin concentration has yet to be defined.

5.4 Oxygenation

"Keeping red blood moving" seems obvious and existing CPR guidelines advocate the use of 100% oxygen during CPR and clinicians usually maintain this for variable periods after return of spontaneous circulation.

A growing body of preclinical evidence suggest that hyperoxia during the early stages of reperfusion could harm post-ischaemic neurons by potentiating free radical formation and tissue injury. Benefits/risks of hyperoxia seem to be related to the type of ischaemic insult and on timing of therapy. During or after a focal ischaemic insult, it has been shown that rats exposed to 100% oxygen had reduced infarct size. However, hyperoxia has been shown to have adverse effects in newborn babies and dogs following cardiac arrest – they had more severe injury in the selectively vulnerable hippocampus.[9]

Further research is required regarding the role of hyperoxia in post-resuscitation period.

5.5 Ventilation

One of the brain's most primitive mechanisms of blood flow regulation is its response to arterial CO_2 concentration. It has been common practice to treat intracranial hypertension with hypocapnia because reduced CO_2 is associated with reduced cerebral blood flow and subsequent reduced intracranial pressure. Although cerebral autoregulation may be dysfunctional/absent in the acute phase post cardiac arrest, changes in cerebro-vascular reaction to CO_2 changes is preserved. Cerebro-vascular resistance may be elevated for at least 24 h in comatose survivors following cardiac arrest.[3]

Studies in brain injured patients have shown that cerebral vasoconstriction caused by hypoventilation may cause potentially harmful cerebral ischaemia. The Brain Trauma Foundation has advised that the use of hyperventilation "be avoided during the first five days after severe TBI and particularly during the first 24 h.[9]" Use of hyperventilation both during and

after cardiopulmonary resuscitation increases intrathoracic pressure which will decrease cardiac output.[10] Hypoventilation may also be harmful because hypoxia and hypercarbia could increase intracranial pressure and compound metabolic acidosis.

There is no data to support targeting a specific $PaCO_2$ after resuscitation from cardiac arrest; however, extrapolating data from other studies suggest ventilation to normocarbia is appropriate.

5.6 Circulatory Support

Haemodynamic instability is common following ROSC. This includes dysrhythmias, hypotension and low cardiac index. Underlying mechanisms include volume depletion, impaired vasoregulation and myocardial dysfunction. There is no evidence to support the use of anti-arrhythmics following cardiac arrest. However, it is important to maintain normal electrolyte concentrations and if cardiac arrest is due to primary dysrhythmias these patients should be evaluated for placement of a pacemaker or ICD.

Intravenous fluids are the first line of intervention for treatment of hypotension. Consider vasopressors and Inotropes if the haemodynamic goals are not achieved. Post arrest myocardial dysfunction is generally reversible and responsive to inotropes but severity and duration may impact survival. Early echocardiography can quantify extent. Impaired vaso-regulation is also common but reversible with vasopressors. The dependency on vasopressors has been reported for up to 72 h despite adequate preload and reversible global myocardial dysfunction.

5.7 Therapeutic Hypothermia

References to using hypothermia as a way of preserving living tissue date back to Hippocrates who advocated packing bleeding patients in snow.[11] The use of moderate hypothermia after cardiac arrest was initially reported in the late 1950's and early 1960's. Findings were inconclusive and rate of complications high. There were no further investigations for hypothermia as a resuscitative measure, until the early 1990's, when laboratory studies indicated the benefit of mild hypothermia. These studies lead to preliminary clinical studies of mild hypothermia.

Two randomized clinical trials have shown that therapeutic hypothermia should be part of a standardized treatment strategy for comatose survivors of cardiac arrest. Working independently on two continents both research groups found that lowering the body temperature to 33˚C for 12-24h in comatose survivors of out of hospital cardiac arrest resulted in improvement

in neurological outcome. Methods used for cooling were simple – placing icepacks over a patient's torso or use of a device that circulates cool air over a patient.[12 13]

The simplest biological explanation of how hypothermia may provide protection against anoxic brain injury is that it reduces cerebral oxygen requirement. However, the mechanism involved may be more complex than that. Hypothermia may prevent free radical injury, membrane damage and injury due to the release of neurotransmitters, by interrupting one or more of the pathways participating in the anoxic ischaemic brain insult.

Therapeutic hypothermia is associated with several complications. Shivering is common, and should be treated by ensuring adequate sedation or neuromuscular blockade with sedation. Other complications include arrhythmias, decreased insulin sensitivity and secretion, impaired coagulation, impaired immunity with increased infection and drug clearance may be reduced by up to 30%. However, in the Hypothermia After Cardiac Arrest study group (HACA) trial complication rates for the first seven days did not differ significantly between the two groups although there was an increased risk of sepsis and bleeding in the hypothermia group. Although previous studies have shown adverse effects on platelet and white cell counts when hypothermia is used for more prolonged periods the Australian study found no statistically significant differences between the two groups. Furthermore no clinically significant infections were noted.

Prospective Randomized Human Trials of Induced Hypothermia

	Bernard (Australia)[11]	HACA (Europe)[12]
Number of subjects	77	275
Hypothermic method	Ice packs	Cool air over entire body
Time ROSC to initiate cooling	Ambulance	105 minutes
Target temperature achieved after ROSC	2 hrs	8hrs
Minimum duration of hypothermia	12hrs	24 hrs

Outcome Induced Hypothermia (HACA)[12]

Outcome	Normothermia	Hypothermia	P-value
Favourable neurological outcome*	54/137 (39%)	75/136 (55%)	0.009
Death	76/138 (55%)	56/137 (41%)	0.02

* Defined as good recovery or moderate disability.

Outcome for Induced Hypothermia (Bernard – Australia)[11]

Outcome	Hypothermia (N=43)	Normothermia (N=34)	P-value
Normal or minimal disability (able to care for self at home)	15	7	0.046*
Moderate disability (discharged to a rehabilitation facility)	6	2	
Severe disability, awake but completely dependant (long term nursing facility)	0	1	
Severe disability, unconscious (long term nursing facility)	0	1	
Death	22 (51%)	23 (68%)	0.145

* 21/43 patients in the hypothermia group (49%) were considered to have a good outcome (discharged to home or to a rehab facility) as compared with 9/34 in the normothermia group (26%), p=0.046

If therapeutic hypothermia is not feasible or contra-indicated then at a minimum pyrexia must be prevented. There is considerable evidence that hyperthermia is adverse to the post-ischaemic brain. The risk of poor neurological outcome increases for each degree of body temperature above 37 degrees Celsius. Pyrexia during the first 72 h after cardiac arrest should be aggressively treated with anti-pyretics or active cooling.

Further studies are needed to elucidate benefit for other initial cardiac rhythms, stroke, TBI, spinal cord injury and haemorrhagic shock. Temperature monitoring is essential for those patients with, or those at risk for, cerebral injury.

5.8 Glucose Control

In the face of oxygen deprivation the brain converts to aerobic glycolysis. Despite it being a critical substrate for aerobic glycolysis the brain does not maintain a meaningful reserve of glucose.

Retrospective studies of patients successfully resuscitated from out of hospital cardiac arrest have suggested that hyperglycaemia is common during the post resuscitation period and may be associated with worse outcomes.

In a recent study hyperglycaemia has been commonly found in both diabetic and non-diabetic patients during the immediate post-ROSC period after in-hospital cardiac arrest. Furthermore derangements in blood glucose are associated with increased mortality following in-hospital cardiac arrest.[14]

The impact of elevated blood glucose levels at the time of ischaemia on neuronal injury has been well investigated in animal models; impairing recovery of the cerebral energy state, cerebral perfusion and electrophysiology as well as increasing cerebral morphological damage, seizures and mortality. High glucose levels lead to increased brain lactate accumulation and patients are known to become more acidotic during hyperglycaemia and global ischaemia. In humans both in focal ischaemic stroke and global ischaemia (as seen in cardiac arrest patients) elevated admission blood glucose levels are related to neurological deterioration. Furthermore there has been an association between blood glucose levels in a 24 h post ischaemic period and functional neurological outcome irrespective of duration of cardiac arrest.[15]

Recent studies indicate that post-arrest patients may be treated optimally with target range of blood glucose concentration of up to 8 mmol/l. In a recent study, comatose survivors of out of hospital VF cardiac arrest were randomized into two treatment groups. A strict glucose control (SGC) group with blood glucose target of 4-6 mmol/L and a moderate glucose control (MGC) group with a target of 6-8 mmol/L. Episodes of moderate hypoglycaemia occurred in 18% of the SGC group and 2% of the MGC group (p=0.008). There was no difference in mortality. The lower value of glucose control may not reduce mortality but can expose patients to potentially harmful effects of hypoglycaemia.

Regardless of target range, blood glucose should be measured frequently.

5.9 Seizure Control

Post cardiac arrest, especially if prolonged, seizures and myoclonus are a common occurrence. Seizures increase cerebral metabolism up to three fold. No study directly addresses the use of prophylactic anti-convulsants. However, if seizures are present they should be treated rapidly. Prolonged seizure duration (>30-60 minutes) following ROSC after CPR is associated with poor outcome. Prolonged seizures cause cerebral injury and should be promptly treated with benzodiazepines, phenytoin, propofol or barbiturates. Thereafter maintenance therapy should be instituted once precipitating causes are excluded. Myoclonus should also be controlled with appropriate sedative agents since it is also associated with worse outcome. Muscle relaxants should be avoided since they would preclude clinical diagnosis of ongoing seizure activity.

6. Conclusion

Post-resuscitation care is an important part of advanced life support. Patient mortality remains high after ROSC. During the post-resuscitation period every organ system is at risk with eventual multi-organ failure.

Objectives of post-resuscitation care:

1. Optimize haemodynamic, respiratory and neurological support
2. Identify and treat reversible causes of arrest
3. Monitor temperature and consider treatment for disturbances of temperature regulation.
4. Monitor glucose especially during insulin therapy, cooling and rewarming
5. Control seizures and myoclonus

The challenge for resuscitation medicine is to maximise long term neurological survival by supporting organ system function.

7. References

1. Safar P. On the future of Reanimatology, Academic Emergency Medicine Jan 2000, Vol.7, Nr.1
2. Safar P. International Congress Series 1242 (2002) 215-227
3. Nolan JP et al. Post cardiac arrest syndrome. Resuscitation (2008) 79, 350—379
4. Fahy BG. Raising the dead: Management of the post arrest patient. ASA annual meeting refresher course lectures October 2006
5. Negovsky VA, Gurvitch AM. Resuscitation Aug 1995, Volume 30 Issue 1, p.23-27
6. Miller D. Anaesthesia 5th edition, 2000, Chapter 19, p. 715-716
7. Spaulding CM et al. Immediate Coronary angiography in survivors of out of hospital cardiac arrest. NEJM Volume 336, Nr 23
8. Rivers et al. Early Goal Directed Therapy in the treatment of Severe Sepsis and Septic Shock. NEJM 2001; 345: 1368-77
9. Warner DS. Managing Brain Ischaemia. ASA annual meeting refresher course lectures October 2006
10. Aufderheide TP. Hyperventilation induced hypotension during cardiopulmonary resuscitation. Circulation 2004, 109, 1960-1965.
11. Cooper AJ. CPR History, current practice and future direction. Circulation 2006, 114, 2839-2849
12. Bernard SA et al. Treatment of comatose survivors of out of hospital cardiac arrest with induced hypothermia. NEJM Vol. 346 p. 557-563
13. The hypothermia after cardiac arrest study group. Mild therapeutic hypothermia to improve the neurological outcome after cardiac arrest. NEJM 2002 Vol. 346 p. 549-556
14. Beiser DG et al – Derangements in blood glucose following initial cardiac arrest. Resuscitation 80 (2009) 624-630
15. Mullner M et al – Blood glucose concentration after CPR influences functional neurological recovery in human cardiac arrest survivors. Journal of Cerebral Blood Flow and Metabolism 1997