

The post-resuscitation bundle

Anantharaman V

ABSTRACT

Following restoration of pulse after the institution of cardiopulmonary resuscitation, defibrillation and perhaps, the initial resuscitative drugs, there is a greater challenge of maintaining that heartbeat for at least the next 24 hours, which can better ensure a high likelihood of the patient being discharged alive from the hospital. A bundle of procedures, which may need to be administered simultaneously, is required. These include prompt identification and treatment of the cause of cardiac arrest, with early consideration for procedures such as percutaneous coronary interventions and fibrinolytics, and treatment of electrolyte abnormalities. In addition, a definitive airway and normocapnoeic ventilation without causing hyperoxaemia, together with rational management of haemodynamics with intra-arterial and central venous lines and vasoactive agents will be crucial. Additional benefit is possible with appropriate forms of early goal-directed therapy and achieving therapeutic hypothermia within the first few hours, followed by gradual rewarming and ensuring glycaemic control by maintaining blood sugars within a range of 6–10 mmol/L. All these would be important and need to be continued for at least 24 hours, together with a series of measures to control neurological reactions and monitor neurological responses for best effect. Creation of a bundle that incorporates these various aspects of care would more likely ensure that most patients who achieve return of spontaneous circulation may be discharged alive from the hospital with optimal neurological function.

Keywords: cardiac arrest, glycaemic control, neurological recovery, post-resuscitation bundle, therapeutic hypothermia

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INTRODUCTION

Many cardiac arrest outcome studies have demonstrated a significant gap in the rate of patients who attain return of spontaneous circulation (ROSC) and the rate of survival to hospital discharge. While the quality of

resuscitation and the links in the chain of survival play a major role in the ROSC rate, other factors that determine the subsequent outcome come into play once the patient regains spontaneous circulation. It would be a pity if the tremendous efforts made to achieve ROSC for the patient come to naught due to the suboptimal post-ROSC care delivered. Medicine is just beginning to understand the pathophysiology of the post-cardiac arrest syndrome and to determine how best these factors may be managed to produce the best outcome for the patient.

The objective of this paper is to discuss areas where post-ROSC care may be organised and to identify areas that require careful evaluation for potential utilisation in patient care. The National Resuscitation Council Singapore has yet to determine or recommend the optimal strategy for post-resuscitative care of the cardiac arrest patient in Singapore. This paper introduces the concept in Singapore, with the intention of creating multidisciplinary efforts to generate protocols for organised post-ROSC care in the country for best outcomes. It is an area that is evolving in practice and that will require a combined multidisciplinary effort, with the participation of physicians from the disciplines of Emergency Medicine, Critical and Intensive Care, Nursing, Cardiology and Anaesthesiology, at the very least. This situation illustrates clearly the interdependent nature of medical practice, especially the science and practice of resuscitation. The council will evaluate the current efforts in the field and produce some initial guidelines that can be developed further for clinical practitioners here.

EVIDENCE FOR BENEFIT

Evidence for benefit in post-ROSC care is limited. A number of protocols developed for post-cardiac arrest patients in some communities have shown promise of benefit.⁽¹⁻³⁾ These include areas of care such as hypothermia, glucose control, haemodynamic optimisation, myocardial revascularisation procedures. While some of these may have been studied independently, it is the grouping of some of these protocols that have been able to demonstrate a significant measure of benefit. We list some of these areas of intervention and propose grouping these interventions into a bundle, the various components of which may be carried out simultaneously. The areas that will be addressed in this review include the following:

- Identification and treatment of cause of cardiac arrest
- Airway and ventilation management

Department of Emergency Medicine, Singapore General Hospital, Outram Road, Singapore 169608

Anantharaman V, MBBS, FRCPE, FAMS Senior Consultant and Chairman of National Resuscitation Council Singapore

Correspondence to: Prof V Anantharaman
Tel: (65) 6321 4114
Fax: (65) 6226 0294
Email: anantharaman@sgh.com.sg

- Haemodynamic management
- Therapeutic hypothermia
- Glycaemic control
- Neurological enhancement measures and monitoring

CAUSE OF CARDIAC ARREST

It is important to make an initial provisional diagnosis of the cause of the cardiac arrest so that the factors that contribute to the collapse could be identified early for intervention. Common known causes include the following:

Coronary artery disease

A 12-lead electrocardiogram (ECG) would be warranted in the immediate post-cardiac arrest state, and if this indicates an acute coronary syndrome (ST segment elevation myocardial infarction), it would be reasonable to arrange for immediate coronary angiography. There is reasonable evidence of improved myocardial and neurological function after percutaneous coronary intervention (PCI) following cardiac arrest.⁽⁴⁾ PCI may be combined with other acute post-ROSC interventions such as therapeutic hypothermia for maximum benefit. If the patient had received antiarrhythmics during resuscitation, these may be continued during the initial 24 hours post-resuscitation. Further research would still be required in order to determine the measures for optimisation of integrity and function of the reperfused myocardium.

Acute pulmonary embolism

Fibrinolytics may be used in post-cardiac arrest patients suspected to have collapsed from severe pulmonary embolism. Pulmonary embolectomy may also be used, although the morbidity after such a procedure may be high. Indicators of pulmonary embolism as a cause include poor arterial oxygen saturation after ROSC with appropriate ECG changes. One needs to be mindful of the increased risk of severe bleeding after the use of fibrinolytics. Research would be required to determine if either a lower dose of fibrinolytics or a slower rate of infusion would be safer in Asian patients who may have lower body weight. There is also a need for rapid tests that will assist in fine-tuning the rate of infusion of fibrinolytic agents so that severe bleeding tendencies may be minimised during the acute phase of its use, when the bleeding risk may be the highest.

Toxic ingestions

Toxic ingestions that lead to cardiac arrest are usually due to cardiotoxic agents such as tricyclic antidepressants, cardiac glycosides, recreational drugs and others. Initial management includes identifying the drug involved. Most

cardiotoxic drugs are water soluble and may be excreted by the kidney. Therefore, while forced alkaline diuresis may be employed, it is a slow process and the mechanisms of excretion of the drug may not allow rapid clearance through this intervention. Drug overdose resulting in cardiovascular collapse would mostly require rapid removal by haemodialysis. Other interventions that have been suggested in the management of cardiac arrest due to toxic agents include prolonged cardiopulmonary resuscitation, fluids, early use of extracorporeal membrane oxygenation, high-dose insulin euglycaemia, intra-aortic balloon pump, cardiac pacing, use of antidotes and intravenous lipid emulsion.⁽⁵⁾ These may only be considered if the patient has attained ROSC and supportive care is in progress.

Metabolic disorders

Metabolic disorders causing cardiac arrest include hyperkalaemia, hypokalaemia with hypercalcaemia. A 12-lead ECG may throw some light on the initial metabolic insult. Following ROSC, correction of the metabolic disorder needs to proceed in tandem with other supportive care, e.g. hyperkalaemia patients would require glucose and insulin in addition to haemodialysis in order to remove the excessive potassium load, while hypokalaemic patients would require replacement therapy.

Sepsis

Sepsis is a common cause of cardiovascular collapse. Once identified, blood cultures need to be obtained, followed by appropriate intravenous antibiotics in addition to identifying the source of infection and proceeding appropriately. Early goal-directed therapy has been shown to decrease the mortality of patients with acute sepsis.⁽⁶⁾

AIRWAY AND VENTILATORY MANAGEMENT

Airway control is crucial in the initial stages of post-ROSC management. Insertion of a definitive airway (if not done yet) guided by capnography is followed by a chest radiograph for confirmation of tube position. The chest radiograph would also be able to identify any complications of earlier resuscitation such as rib fractures or pneumothorax, or the presence of other comorbidities such as heart failure, pneumonia or pleural effusions.

Arterial blood gas measurements will be valuable in guiding ventilatory management. While mechanical ventilation would be required so as to reduce the work of breathing, the rate of ventilation and tidal volume would need to be adjusted in order to maintain arterial oxyhaemoglobin saturation at $\geq 94\%$. The concern that hyperoxaemia during the reperfusion phase after ROSC with 100% oxygen may lead to increased brain lipid

peroxidation, increased metabolic dysfunction and neurological degeneration, as well as concerns about its impact on short-term functional outcome, have resulted in calls to ventilate with room air or an inspired oxygen fraction titrated to maintain a pulse oximetry reading of 94%–98%.^(7,8) Weaning the patient from 100% oxygen to the FiO₂ required to maintain SpO₂ at the above stated levels should begin once ROSC is achieved.

There is also a concern that the metabolic acidosis occurring in cardiopulmonary arrest will be best treated by continued 100% oxygen and hyperventilation so as to achieve normal pH as early as possible. However, this concern is unwarranted. Once perfusion is established and ventilation is maintained at the abovementioned rate, metabolic acidosis will gradually be reversed. Hyperventilation will drive pCO₂ down, which in turn, will also decrease cerebral blood flow. Lowering cerebral blood flow to subnormal levels during the phase of initial reperfusion and the subsequent reflex decreased flow will result in cerebral vasoconstriction and aggravate brain injury.

The recommendation that must be considered is whether optimal arterial blood gas parameters during the post-ROSC phase^(8,9) should be as follows: PaCO₂ of 35–45 mmHg (5–6 kPa); SaO₂ of 94%–98%; tidal volumes to be maintained in the low range (6–8 ml/kg body weight); PETCO₂ to be maintained at 35–40 mmHg. Since post-ROSC patients are at risk of acute lung injury or acute respiratory distress syndrome, the standard recommendation for ventilation would be normocapnia. Excessive tidal volumes would also not be recommended owing to the risks of increased intrathoracic pressures with attendant reduced venous return and cardiac output.

HAEMODYNAMIC MANAGEMENT

Soon after ROSC, there is a need to maintain adequate coronary perfusion pressure and blood flow to the vital organs. Drugs may be required for these. The following may be considered appropriate for haemodynamic management within the first 24 hours post-ROSC:

- 12-lead ECG soon after ROSC and repeated at eight hours, or whenever needed in order to rule out acute coronary syndrome.
- An arterial line for continuous blood pressure monitoring. This may also be helpful for monitoring blood pressures during therapeutic hypothermia and for accurate measurement of haemodynamic parameters so as to determine the most appropriate combination of medications for maintenance of perfusion. Central venous pressure monitoring would also be useful.
- Intravenous fluid and drug administration should be titrated to optimise blood pressure, cardiac output

and urine output. The target for blood pressure would be a mean arterial pressure \geq 65 mmHg and blood oxygenation at ScvO₂ \geq 70%.^(8,10)

- Drugs that may be used to support the circulation include adrenaline, noradrenaline, dopamine, dobutamine, nitroglycerine and esmolol. Drugs and the dosages used would need to be adjusted based on the parameters monitored.

An echocardiogram at 24–48 hours post-ROSC will be useful to rule out regional wall motion abnormality and to determine ejection fractions.

THERAPEUTIC HYPOTHERMIA

It has been well demonstrated that brain temperatures during the first 24 hours after ROSC have a significant effect on survival and neurological recovery in patients who remain comatose soon after ROSC. Fever during the first 48 hours is usually associated with a lowered chance of optimal neurological recovery.⁽¹¹⁾ Cooling to 32°C–34°C will decrease the chances of death and improve likelihood of neurological recovery, as measured by cerebral performance scores.⁽¹⁾ The benefits of hypothermia are best seen when initiated early. Current usual eligibility criteria⁽¹¹⁾ for hypothermia include the following:

- Comatose after ROSC with a Glasgow Coma Motor Score < 6 pre-sedation;
- No other obvious reasons for coma, e.g. hypoglycaemia;
- No uncontrolled bleeding;
- Haemodynamically stable, with no evidence of uncontrollable arrhythmias, severe cardiogenic shock, or refractory hypotension (blood pressure < 60 mmHg) despite fluids and vasoactive agents;
- No obvious pre-existing multi-organ dysfunction syndrome, severe sepsis or comorbidities, with minimal chance of meaningful survival independent of neurological status.

The common contraindications used for this procedure include the following: prolonged arrest time > 60 minutes; thrombocytopenia or other coagulopathy; and pregnancy (although this may not be an issue with the assistance of an obstetrician/gynaecologist).

The goal is to achieve a target temperature of 32°C–34°C within four hours and maintain it for 24 hours from the time of initiation of cooling. Prior to the start of cooling, sedation is induced with sedative and paralytic medications. Analgesia and sedation are usually achieved with fentanyl and propofol, and these can be titrated using a bispectral index monitor. The patient is then paralysed and cooling is initiated. There are many cooling methods available, either through surface or a combination of surface and active internal cooling.

Temperature monitoring is usually through bladder or oesophageal probes. Sedation, analgesia and paralysis are maintained for 24 hours, even if the patient becomes haemodynamically unstable.

Rewarming is usually carried out over a 12-hour period. During the rewarming phase, vasodilatation may occur, requiring volume loading. Close monitoring of electrolytes, especially potassium, would be needed at four hourly intervals. All patients undergoing therapeutic hypothermia will need to be managed in an intensive care unit setting, with close monitoring of vital parameters. One will also need to carefully watch for potential complications of therapeutic hypothermia, viz coagulopathy, arrhythmias, hyperglycaemia, pneumonia and other infections.

GLYCAEMIC CONTROL

Hyperglycaemia occurring post-ROSC has been associated with increased mortality and worse neurological outcomes.⁽¹³⁾ Similarly, hypoglycaemia is also associated with poor outcomes in critically ill patients.⁽¹⁴⁾ The strategy is to maintain blood sugar levels at 6–10 mmol/L. This may be achieved by frequent blood glucose monitoring and the use of insulin infusions to treat episodes of hyperglycaemia. Hypoglycaemia should be avoided.

NEUROLOGICAL ENHANCEMENT MEASURES

Brain injury is very common in cardiac arrest patients and is also a common cause of morbidity in survivors of cardiac arrest. Post-cardiac arrest brain injury is a result of initial ischaemic injury followed by reperfusion injury occurring within the hours and days after ROSC. Features indicating occurrence of brain injury in post-ROSC patients include coma, seizures, myoclonus and various degrees of neurocognitive dysfunction, ranging from memory deficits to a persistent vegetative state and finally, brain death. Occurrence of seizures is detrimental to brain function and should be treated promptly with benzodiazepines and close monitoring of vital signs. An electroencephalogram diagnosis should be sought promptly, and preferably, continuously in comatose patients after post-ROSC seizures.

To date, no benefit has been reported with a variety of neuroprotective agents in multiple clinical trials. The neurological prognosis in the majority of comatose cardiac arrest survivors cannot be reliably predicted until at least 72 hours after resuscitation. As such, decisions on do-not-resuscitate status or withdrawal of care should not be made before 72 hours after ROSC. Currently, the principal neuroprotective measures recommended include normoventilation with controlled oxygenation to avoid hyperoxaemia and minimise the likelihood of lowering cerebral perfusion or aggravating cerebral ischaemia, achieving normoglycaemia to optimise neuronal recovery,

and therapeutic hypothermia to minimise the cerebral and multi-system metabolic functions until biochemical and cellular parameters are better optimised. Neurological status monitoring measures would also need to be instituted.

CONCLUSION

The potential for narrowing the gap between ROSC rates and survival-to-discharge rates for cardiac arrest patients is tremendous. With more aggressive measures being introduced to improve the rates of ROSC, it becomes all the more urgent to actively implement clearly defined guidelines on the immediate management of the patient whose heart beat has returned after the initial resuscitation so as to maximise the number of patients who survive neurologically intact. This is the essence of the fourth link in the chain of survival and the area where hospitals with their third-line responders can add value to resuscitations.

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