

# Sudden Cardiac Death and Post Cardiac Arrest Syndrome. An Overview

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## ABSTRACT

A satisfactory neurologic outcome is the key factor for survival in patients with sudden cardiac death (SCD), however this is highly dependent on the haemodynamic status. Short term cardiopulmonary resuscitation and regained consciousness on the return of spontaneous circulation (ROSC) is indicative of a better prognosis. The evaluation and treatment of SCD triggering factors and of underlying acute and chronic diseases will facilitate prevention and lower the risk of cardiac arrest. Long term CPR and a prolonged unconscious status after ROSC, in the Intensive Care Units or Coronary Care Units, indicates the need for specific treatment and supportive therapy including efforts to prevent hyperthermia. The prognosis of these patients is unpredictable within the first seventy two hours, due to unknown responses to therapeutic management and the lack of specific prognostic factors. Patients in these circumstances require the highest level of intensive care and aetiology driven treatment without any delay, independently of their coma state. Current guidelines suggest the use of multiple procedures in arriving at a diagnosis and prognosis of these critical cases.

**Keywords:** cardiac arrest, therapeutic hypothermia, cardiopulmonary resuscitation

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## ■ DEFINITION OF SUDDEN CARDIAC DEATH, INCIDENCE AND TREATMENT

Based on data given in *Morbidity and Mortality Weekly Report*, sudden cardiac death (SCD) is responsible for 63% of deaths of cardiac origin in the US [1].

The incidence of SCD is 450.000 per year in the US, 400.000 per year in Western European countries and 3.000.000 per year worldwide. After admission to a hospital, and on the resumption of spontaneous circulation (ROSC), the survival rate is very poor, being in the range of about 5% in the US, between 5% and 7.9% in the EU, and below 1% worldwide [2,3].

A large number of deaths result as a consequence of permanent severe neurological damage due to prolonged “no-flow anaesthesia” and “low-flow anaesthesia” from SCD to ROSC associated with complex resuscitation procedures [4].

The Seattle-study reported on over 12,000 SCD patients over a period of twenty four years, who had been treated by emergency medical services (EMS). An improvement in survival rates from 15.7%, during the period between 1998 and 2001, to 17.5%, between

the period between 1977 and 1981 was recorded. The long term outcome among patients who survived until discharged from hospital, also improved during this period [5,6].

The analysis of data obtained from a nationwide cohort of 547.153 Japanese patients who presented with SCD between 2005 and 2009, showed that survival with a concomitant favourable neurologic status improved nearly two-fold. The survival to hospital discharge improved from 1.6% to 2.8% among all out-of hospital cardiac arrest (OHCA) patients, from 2.1 to 4.3% in confirmed SCD, and from 9.8% to 20.6% among confirmed SCA with initial ventricular fibrillation (VF) [7].

The Canada registry, pooling the data of a population of more than 34.000 patients who presented with OHCA between 2002 and 2011, showed a significant improvement from 7.7% in 2002 to 11.8%, in one-year survival rates [8].

The CARES registry, included 70.027 OHCA US patients, prospectively enrolled from 2000 to 2012, showed that survival to hospital-discharge improved significantly from 5.7% to 8.3%, with an accompanying significant improvement in neurological function [9].

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The main causes of SCD are lethal ventricular arrhythmias. Eighty three percent were either ventricular tachycardia (VT) or ventricular fibrillation (VF), of which 62% were recorded as VT and 8% as VF. In patients with cardiac arrest, the key elements in the “chain of survival” are early recognition of SCD, early “call for help” and the immediate start of high quality advanced life support, including chest compression, ventilation, early defibrillation and advanced post cardiac arrest (PCA) care. Treatment options for patients who have survived an episode of SCD, or who are at high risk of SCD, are antiarrhythmic drugs, implantable cardioverter-defibrillator (ICD) devices or both [10].

### ■ ADVANCED CARE IN THE CHAIN OF SURVIVAL AND POST CARDIAC ARREST MANAGEMENT

Post-cardiac arrest syndrome (PCAS) has been well documented over the last three decades in emergency, intensive care and acute cardiac care units. Cardiac arrest accompanied by „no-flow”, successive cardiopulmonary resuscitation (CPR) and the concomitant „low-flow” haemodynamic state, results in a time- and CPR-quality-dependent reversible or irreversible hypoxic injury of organs. PCAS treatment starts immediately after ROSC, and is tailored to the physiologic needs of the patient’s haemodynamic state. The aim of the therapeutic measures is to restore the normal cerebral function. The basics of the latter is a stable rhythm and an optimal cardiac output, in order to avoid neurological impairment and generalised ischaemic-reperfusion injury. Part of the systemic ischaemia reperfusion injury reaction causes a multi-organ pathophysiology, with cardiac, cardiovascular, neurologic, pulmonary, renal metabolic disorders, and a „sepsis-like” syndrome with specific complement activations. The survival limiting factor is the ischaemia tolerance and metabolic reserve of the brain. Ischaemia and ischaemia reperfusion injury, cause intense stress in the brain, including oxidative stress, microvascular injury, excitotoxicity, blood–brain barrier dysfunction and postischaemic inflammation initiated by neuronal, glial and endothelial cell death, or apoptosis [11,12].

All the pathophysiologic disorders are dependent on the duration and quality of CPR. The main determinants of survival are the reversibility of post-cardiac arrest (PCA) brain injury, PCA myocardial dysfunc-

tion and the aetiology and recurrency of SCD. All the factors involved in the genesis of cardiac arrhythmia need to be ruled out and treated. Such factors may include structural diseases, e.g. acute or chronic coronary artery disease, cardiomyopathies, trigger mechanisms such as abnormal automaticity, premature beats or modulating factors such as ischaemia, electrolyte-disorders, sympathicotonia, drug effects modulating repolarisation. One of the most important diagnostic and therapeutic methods is urgent coronary angiography and revascularisation, since at least seventy percent of the SCD patients have been proven to have a significant coronary lesion [13].

Neurologic injury is the most common cause of death in OHCA patients. Preventing hyperthermia during the first few hours after CA reduces the risk of neurologic injury. Therapeutic hypothermia (TH), and since 2015, forced normothermia, are part of the advanced PCAS care intended to save brain and vital organs from ischaemic-reperfusion injury [14].

Randomised clinical trials have shown improved outcome using TH. Those adults remaining comatose after CPR for OHCA, with initial rhythm of VF, a temperature reduced within minutes to hours after ROSC to 32–34°C for twelve to twenty four hours, had a significantly better survival. [15]

The Hachimi-Idrissi trial reported improved lactate and O<sub>2</sub> extraction in comatose adult patients who were cooled after ROSC [16]. Other studies showed a benefit after therapeutic hypothermia in comatose survivors of SCD caused by non-shockable rhythm [17].

Janata et al [2009] conducted a meta-analysis of thirty seven non-randomized trials and fifteen controlled studies and showed that the pooled absolute risk reduction gained with this new treatment modality is approximately twenty five percent, with a number needed to treat of 5 [18].

The 2010 ERC Guidelines did not agree with the opinion that all unconscious adult patients with spontaneous circulation after VF associated to OHCA should be cooled to 32–34°C starting as soon as possible and continuing for twelve to twenty four hours. However, 2015 guidelines accept normothermia as an option, suggesting that the patient’s temperature be reduced to 32-36 °C. It is suggested that the maintenance of normothermia or hypothermia be facilitated by sedatives and neuromuscular blocking agents to prevent shivering [19].

The technique of therapeutic hypothermia has three phases, the induction of cooling, maintenance and re-warming. External cooling is performed using traditional icepacks placed on the groin, axilla, and sides of neck together with surface temperature devices to monitor temperature changes. Internal cooling may be started by infusion of 30 mg/kg of 4°C saline. This is capable of decreasing core temperature by a maximum of 1.5°C. Intravascular cooling enables more precise temperature control than external methods and endovascular heat-exchange catheters enable a fast induction and rewarming. However this is associated with a higher cost due to the expensive equipment which is required.

The basic intensive support of the comatose PCAS patient includes mechanical ventilation, sedation with short acting agents, e.g. propofol and opioids and neuromuscular blockade. Invasive haemodynamic monitoring, urine output, core temperature and neurologic function monitoring is strongly recommended. Supportive intensive care includes balanced K, Ca and Mg electrolyte-supply, volume therapy based on volumetric monitoring, parenteral or enteral feeding, antibiotics based on microbiological cultures and prophylaxis of decubitus lesions.

## ■ WHAT IS THE PROGNOSIS AFTER SUCCESSFUL CPR AND PCAS TREATMENT?

Unfortunately it is frequently difficult to arrive at an exact prognosis in a comatose PCAS patients. It has been suggested that after seventy two hours of treatment, the absence of cornea or pupil reflex and the presence of continuous convulsion and myoclonus, is indicative of a poor outcome. The recommendations of the European Resuscitation Council [2014] aimed to clarify all the prognostic factors and give exact perspectives that could help in the continuation of maximal intensive care or withdrawal of supportive therapy, based on the recognition of adverse neurologic events [20].

There are several limited but robust points for prognosis. During examination of neurologic function, account of the residual effects of sedatives, opioids and neuromuscular blocking agents must be taken into account. It is important to appreciate that at ROSC, bilateral absence of pupillary light reflex has very limited value in predicting a poor outcome, while myoclonus within seventy two hours from ROSC is not consistently associated with a poor outcome. At seventy two

hours from ROSC, a bilaterally absent pupillary light reflex predicts poor outcome independently of therapeutic hypothermia usage. Moreover, a bilaterally absent corneal reflex is slightly less specific than a pupillary reflex, in predicting a poor outcome. At the same time, an absent motor response or extensor response to pain and a Glasgow Coma Scale of one to two, has a seventy four percent sensitivity in predicting a poor outcome as was a status myoclonus, starting within forty eight hours from ROSC. Additionally, the absence of EEG reactivity to external stimuli and the presence of status epilepticus in comatose PCAS patients at seventy two hours after ROSC, is indicative of a poor outcome. Bilateral absence of the N20 wave in short-latency somatosensory evoked potentials (SSEPs) predicts brain death or a vegetative status. Recommendations point to the use of these criteria only in combination with other predictors, since there is no standardised technique or hard evidence as the recommendations are based on few studies.

The availability of biomarkers is limited though they can be useful if combined with other prognostic factors, if used at 48–72 hours from ROSC and measured repeatedly for at least twenty four hours after ROSC. Imaging techniques such as brain CT or MRI are useful to exclude the causes of coma or subarachnoid haemorrhage and may help to detect cerebral oedema and anoxic-ischaemic cerebral injury. Since the methodology is inconsistent, current recommendations indicate that the use of brain CT and MRI is made only in combination with other predictors [20].

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