Post-cardiac arrest syndrome: update on brain injury management and prognostication

An Essay
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Contents

List of Figures

List of tables

Introduction

Following successful resuscitation from cardiac arrest, neurological impairment as well as other types of organ dysfunction still cause significant morbidity and mortality. The whole-body ischemia-reperfution response that occurs during cardiac arrest and subsequent restoration of systemic circulation results in a series of pathophysiological processes that have been termed the post-cardiac arrest syndrome. The components of the post cardiac arrest syndrome comprise post-cardiac arrest brain injury, post-cardiac arrest myocardial dysfunction, the systemic ischemia-reperfusion response and precipitating pathology. **(Kamarainen A, et al, ٢٠٠٩)**

Management of the post-cardiac arrest syndrome involves intensive care support with input from various other medical specialties in a coordinated fashion. Management of ventilation aims for normal carbon dioxide values and normoxia rather than hyperoxia. Management of the circulation commonly requires vasoactive support to overcome (often transient) myocardial dysfunction. **(O'Driscoll BR, et al, ٢٠٠٨)**

Particular attention should be given to evidence of cardiac ischemia and referral for urgent angiography and

percutaneous coronary intervention, if appropriate, should be available to all. Optimizing neurological recovery will involve seizure control, management of hyperglycemia and therapeutic hypothermia. Prognostication following cardiac arrest remains difficult, but there are diagnostic tests that may be used with some degree of accuracy. **(Garot P, et al, ٢٠٠٧),**

Aim of the work

The aim of this study is to evaluate and minimize the effect of cardiac arrest on vital organs.

Epidemiology of the post-cardiac arrest Syndrome

The tradition in cardiac arrest epidemiology, based largely on the Utstein consensus guidelines, has been to report percentages of patients who survive to sequential end points such as return of spontaneous circulation (ROSC), hospital admission, hospital discharge, and various points thereafter. Once ROSC is achieved, however, the patient is technically alive **(Langhelle A, Nolan J, Herlitz J, et al, ٢٠٠٥).**

A more useful approach to studying post-cardiac arrest syndrome is to report deaths during various phases of post-cardiac arrest care. In fact, this approach reveals that rates of early mortality in patients achieving ROSC after cardiac arrest vary dramatically between studies, countries, regions, and hospitals. The cause of these differences is multifactorial but includes variability in patient populations, reporting methods, and potentially post-cardiac arrest care **(Jacobs I, Nadkarni V, Bahr J, et al., ٢٠٠٤).**

Epidemiological data on patients who regain spontaneous circulation after out-of-hospital cardiac arrest suggest regional and institutional variation in in-hospital mortality rates. During the ALS phase of the Ontario

Prehospital Advanced Life Support Trial (OPALS), ٧٦٦ patients achieved ROSC after out-of-hospital cardiac arrest. In-hospital mortality rates were ٧٢٪ for patients with ROSC and ٦٥٪ for patients admitted to the hospital **(Stiell IG, Wells GA, Field B, et al. ٢٠٠٤)**.

Data from the Canadian Critical Care Research Network indicates a ٦٥٪ in-hospital mortality rate for ١٤٨٣ patients admitted to the intensive care unit (ICU) after out-of-hospital arrest. In the United Kingdom, ٧١,٤٪ of ٨٩٨٧ patients admitted to the ICU after,out-of-hospital cardiac arrest died before being discharged from the hospital **(Nolan JP, Laver SR, et al., ٢٠٠٧).**

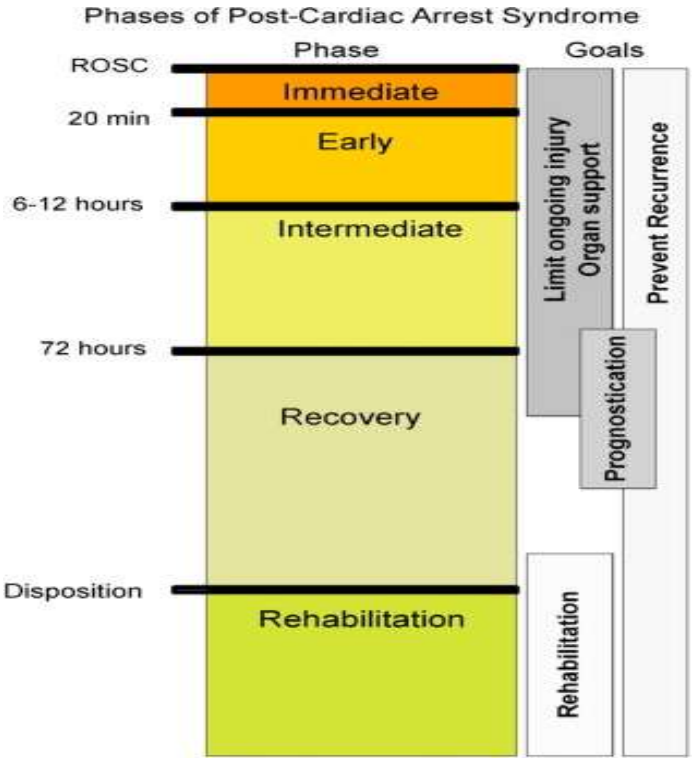
The largest published in-hospital cardiac arrest database (NRCPR) includes data from >٣٦،٠٠٠ cardiac arrests. Recalculation of the results of this report reveals that the in-hospital mortality rate was ٦٧٪ for the ١٩،٨١٩ adults with any documented ROSC, ٦٢٪ for the ١٧،١٨٣ adults with ROSC > ٢٠ min, ٥٥٪ for the ٥٢٤ children with any documented ROSC, and ٤٩٪ for the ٤٦٠ children with ROSC > ٢٠ min. It seems intuitive to expect that advances in critical care over the past ٥ decades would result in improvements in rates of hospital discharge after initial ROSC. However, epidemiological data to

date fail to support this view.**(Mashiko K, Otsuka T, Shimazaki S, et al. ٢٠٠٢).**

The choice of denominator has some relationship to the site of post-cardiac arrest care. Patients with fleeting ROSC are affected by interventions that are administered within seconds or minutes, usually at the site of initial collapse. Patients with ROSC that is sustained for >٢٠ min receive care during transport or in the ED before hospital admission **(Keenan SP, Dodek P.et al., ٢٠٠٧).**

A more physiological approach would be to define the phases of post-cardiac arrest care by time rather than location. The immediate postarrest phase could be defined as the first ٢٠ min after ROSC. The early postarrest phase could be defined as the period between ٢٠ min and ٦—١٢ h after ROSC when early interventions might be most effective. An intermediate phase might be between ٦—١٢ and ٧٢ h when injury pathways are still active and aggressive treatment is typically instituted **(Nadkarni VM, Larkin GL, Peberdy MA, et al.٢٠٠٦).**

Figure (١): Phases of post-cardiac arrest syndrome **(Nadkarni VM, Larkin GL, Peberdy MA, et al.٢٠٠٦).**



Beyond reporting post-cardiac arrest mortality rates, epidemiological data should define the neurological and functional outcomes of survivors. The updated Utstein reporting guidelines list Cerebral Performance Category (CPC) as a core data element. For example, examination of the latest NRCPR database report reveals that ٦٨٪ of ٦٤٨٥ adults and ٥٨٪ of ٢٣٦

children who survived to hospital discharge had a good outcome **(Nolan JP, Laver SR,.et al., ٢٠٠٧)**

Despite variability in reporting techniques, there is surprisingly little evidence to suggest that the in-hospital mortality rate of patients who achieve ROSC after cardiac arrest has changed significantly in the past half-century. To minimise artefactual variability, epidemiological and interventional post-cardiac arrest studies should incorporate well-defined standardised methods to calculate and report mortality rates at various stages of post-cardiac arrest care, as well as long-term neurological outcome. Overriding these issues is a growing body of evidence that post-cardiac arrest care impacts mortality rate and functional outcome **(Young KD, Gausche-Hill M,et al., ٢٠٠٤).**

Pathophysiology of the post-cardiac arrest Syndrome

The high mortality rate of patients who initially achieve ROSC after cardiac arrest can be attributed to a unique pathophysiological process involving multiple organs. Although prolonged whole-body ischaemia initially causes global tissue and organ injury, additional damage occurs during and after reperfusion **(Moers C, Leuvenink HGet al, ٢٠٠٧).**

The unique features of post-cardiac arrest pathophysiology are often superimposed on the disease or injury that caused the cardiac arrest as well as underlying co-morbidities. Therapies that focus on individual organs may compromise other injured organ systems. The four key components of post-cardiac arrest syndrome are post-cardiac arrest brain injury, post-cardiac arrest myocardial dysfunction, systemic ischaemia/reperfusion response, and persistent precipitating pathology **(Sanchez-Fructuoso AI, Marques M,et al.,٢٠٠٧).**

The severity of these disorders after ROSC is not uniform and will vary in individual patients, based on the severity of the ischaemic insult, the cause of cardiac arrest, and the patient's prearrest state of health. If ROSC is rapidly achieved after onset

of cardiac arrest, the post-cardiac arrest syndrome will not occur **(Wilson DJ, Fisher A, Das K, et al, ٢٠٠٣).**

Post-cardiac arrest brain injury:

Post-cardiac arrest brain injury is a common cause of morbidity and mortality. In one study of patients who survived to ICU admission but subsequently died in the hospital, brain injury was the cause of death in ٦٨٪ after out-of hospital cardiac arrest and in ٢٣٪ after in-hospital cardiac arrest **(Laver S, Farrow C, Turner D, et al, ٢٠٠٤).**

The unique vulnerability of the brain is attributed to its limited tolerance of ischaemia as well as its unique response to reperfusion. The mechanisms of brain injury triggered by cardiac arrest and resuscitation are complex and include excitotoxicity, disrupted calcium homeostasis, free radical formation, pathological protease cascades, and activation of cell death signaling pathways. Many of these pathways are executed over hours to days after ROSC **(Bano D& Nicotera, ٢٠٠٧).**

Prolonged cardiac arrest can also be followed by fixed and/or dynamic failure of cerebral microcirculatory reperfusion despite adequate cerebral perfusion pressure (CPP). This impaired reflow can cause persistent ischaemia and small infarctions in some brain regions. The cerebral microvascular

occlusion that causes no-reflow has been attributed to intravascular thrombosis during cardiac arrest and has been shown to be responsive to thrombolytic therapy in preclinical studies.**(Blomgren K, Zhu C,et al, ٢٠٠٣).**

Despite cerebral microcirculatory failure, macroscopic reperfusion is often hyperaemic in the first few minutes after cardiac arrest because of elevated CPP and impaired cerebrovascular autoregulation. These high initial perfusion pressures can theoretically minimise impaired reflow Yet, hyperaemic reperfusion can potentially exacerbate brain oedema and reperfusion injury. In one human study, hypertension (mean arterial pressure (MAP) >١٠٠ mmHg) in the first ٥ min after ROSC was not associated with improved neurological outcome, but MAP during the first ٢ h after ROSC was positively correlated with neurological outcome.Although resumption of oxygen and metabolic substrate delivery a the microcirculatory level is essential **(Sundgreen C, Larsen FS,et al ٢٠٠١).**

Beyond the initial reperfusion phase, several factors can potentially compromise cerebral oxygen delivery and possibly secondary injury in the hours to days after cardiac arrest. These include hypotension, hypoxaemia, impaired cerebrovascular