Predicting neurological outcome and survival after cardiac arrest

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Cardiac arrest is a devastating event. Despite improving resuscitation practices, mortality for those who suffer an out-of-hospital cardiac arrest (OHCA) is >90% with many survivors being left with severe neurological impairment. However, some do make a good recovery and return home to a meaningful quality of life. Accurately predicting those who will achieve a good neurological outcome in post-arrest comatose patients is difficult. Therapeutic hypothermia (TH), now one of the mainstays of intensive care therapy, has perversely improved neurological function but made accurate prognostication more problematic. In addition, clinical signs previously used to assess the likelihood of neurological improvement are thought to no longer act as accurate predictors of outcome. Recently, some progress has been made in reliably predicting patients who will have a poor neurological outcome.

Intensivists and anaesthetists are frequently asked to make decisions regarding the appropriateness of admission to intensive care and the validity of providing an ongoing active treatment for patients who have had a cardiac arrest. This article will examine the methods, both clinical and investigative, that can aid a clinician in making these difficult decisions. Since survivors of cardiac arrest can have good outcomes, it is very important to ensure that the potential for recovery exists while not providing an ongoing treatment in the face of futility. The rationale for identifying poor outcomes is that most people would not desire to continue living in such a disabled state.

Epidemiology

Every year in Britain, ~50,000 people suffer an OHCA. The figures for in-hospital cardiac arrest (IHCA) range from 1 to 5 per 1000 admissions.1

Approximately 6250 people are admitted to intensive care for post-cardiac arrest care every year in the UK. Eighty per cent of those who survive to hospital discharge will return to their normal place of residence, indicating the likelihood of good neurological recovery.1 The most common cause of death depends on where the initial cardiac arrest occurs. For those who have suffered from OHCA, neurological injury accounts for two-thirds of all deaths, compared with only one-third of deaths in those who have suffered from IHCA. This may simply represent the delayed time taken to return of spontaneous circulation (ROSC) in OHCA compared with IHCA.

Mild TH (32–34°C for 12–24 h) has been shown to improve neurological outcome in patients who are comatose after an out-of-hospital ventricular fibrillation (VF) arrest.2,3 The use of cooling for patients who have undergone IHCA or non-VF arrests (i.e. asystole or pulseless electrical activity) has been more contentious. Although the evidence base is less robust, it would seem intuitive that TH would improve neurological outcome, and indeed, the International Liaison Committee on Resuscitation (ILCOR) has suggested that there may be a potential benefit for its use in this group of patients.4 Post-resuscitation management on critical care is now increasingly recognized as making significant improvements to patient outcomes and has led to ILCOR adding post-resuscitation care to the ‘chain of survival’ (Fig. 1).

Aetiology

Cardiac arrest causes a primary and secondary injury. The primary injury occurs at the time of arrest and is non-reversible, and the secondary injury follows ROSC and subsequent cerebral reperfusion and is potentially reversible.

The brain is exquisitely sensitive to hypoxia. Within 20 s of circulatory arrest, neuronal oxygen stores are used up leading to unconsciousness. After 5 min, glucose and...
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The release of pro-inflammatory cytokines leads to this sepsis-like post-cardiac arrest syndrome first described by Negovsky in 1972. Myocardial dysfunction and multiorgan dysfunction defines the ischaemia/reperfusion response coupled with post-cardiac arrest resistance to infection.

These mechanisms and thus can improve neurological outcome. TH is thought to play a role in ‘damping down’ inflammatory processes. TH is very useful in helping us to formulate a decision for those we are reluctant to admit.

In patients with suspected acute myocardial infarction, an urgent cardiological opinion should be sought. Coronary reperfusion should be performed, either pharmacologically or via angiography, if indicated as a priority. TH is not a contraindication to revascularization and can be commenced before and during revascularization techniques.

Predicting patient’s survival immediately after ROSC after cardiac arrest

Ideally, in the post-arrest comatose patient, survival would be predicted accurately from the immediately available clinical and physiological information. Unfortunately, this is not the case with prediction of those who subsequently make a good recovery difficult.

When deciding about the future provision of critical care, the following should be the major factors considered: the underlying physiological and functional status, the presence or absence of severe concurrent disease, and, if known, the patient’s wishes.

Shorter time to cardiopulmonary resuscitation (CPR), shorter duration of CPR, and an initial rhythm of VF or ventricular tachycardia (VT) have all been associated with improved outcome. However, none of these cardiac arrest characteristics guarantees either survival or non-survival. Therefore, prognosis, in individual cases, should not be based on the circumstances of cardiopulmonary resuscitation.

Scoring systems have been developed that aim to predict survival immediately after cardiac arrest. These include the Prognosis After Resuscitation (PAR) score (Table 1) and the OHCA score. The OHCA score is cumbersome and does not lend itself to use on the ward or in the emergency department environment since it can be difficult to estimate accurately the ‘no flow’ and ‘low flow’ times, and the equation is complicated. The PAR score is, comparatively, more straightforward. A PAR score >5 predicts non-survival, but it was originally based on the retrospective analysis of IHCA.5 No scoring system has yet been fully prospectively validated. We have undergone a retrospective review of 225 cardiac arrests admitted to our intensive care over 8 yr and only four patients with a score >5 survived to hospital discharge (all of whom we would still have admitted despite the score). We would not recommend clinicians to use the PAR score as a sole reason to determine admission to intensive care. However, the PAR score is very useful in helping us to formulate a decision for those we are reluctant to admit.

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Predicting neurological outcome after critical care admission

Classifying neurological outcome

Long-term neurological function after cardiac arrest is usually assessed using Cerebral Performance Categories (CPC) and Glasgow Outcome Scoring System (Tables 2 and 3), but these are unhelpful in the immediate hours and days after ROSC. Clinicians however are often required to predict survival immediately after cardiac arrest and several days later.

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During TH, the patient undergoes a period of sedation. Drug clearance is reduced by hypothermia, and it is not yet known how long this can prolong reawakening due to the build up of drugs. Data are limited in predicting the neurological outcome after TH. A recent small study of post-cardiac arrest in patients who had been treated with TH demonstrated that a small number of patients with absent corneal or pupillary reflexes on day 3 or myoclonic status epilepsy regained awareness (defined as an ability to interact with the environment). A persistently low GCS of 4 or less on the fourth day after cessation of sedation suggests a poor neurological outcome with a specificity of 95% in patients undergoing TH.

Further studies are required urgently to fully elucidate the effect TH has on the historical markers of poor neurological function in the post-arrest phase. Currently, an expert consensus view is that extreme caution must now be used when using clinical signs at 72 h post-cardiac arrest to predict neurological function in those who have undergone TH.

Electrophysiological

**Electroencephalogram**

The electroencephalogram (EEG) has been used to attempt to identify early post-arrest patients in whom the neurological recovery is poor. Certain characteristics seen in the post-arrest patient have been associated with a poor outcome. These include generalized suppression, periodic complexes on a flat background, and burst suppression with epileptiform activity. Burst suppression is where high activity on the EEG is interrupted by periods of low activity. An isoelectric EEG in the first week after cardiac arrest is associated with a poor outcome with a specificity of 100%. Furthermore, EEG may unmask subclinical seizure activity amenable to treatment. EEG requires expert interpretation which may limit availability in different hospitals.

**Bispectral index**

A bispectral index (BIS) is more widely available on intensive care and may potentially provide useful prognostic information. A modified EEG is obtained by attaching a specially designed electrode to the head and gives a BIS value between 0 and 100, indicating the level of cerebral activity. In patients cooled therapeutically, a BIS value of $\leq 22$ and a burst suppression ratio of $\geq 48$ (indicating the percentage of the EEG that is isoelectric during a 63 s epoch) immediately after the first dose of neuromuscular block are associated with a poor neurological outcome. However, BIS as a very early marker of poor neurological prognosis is potentially flawed since the prediction may be wrong in up to 10% of the cases. In conclusion, when coupled with clinical and other indicators of poor neurological function, the BIS may provide additive information when attempting to predict a poor neurological outcome, but more research is needed before recommending it as a reliable investigative modality.
Somatosensory evoked potentials

Somatosensory evoked potentials (SSEP) involve monitoring brain response to electrical stimulation of peripheral nerves. The main response, normally seen, is the N20 signal in the primary somatosensory cortex (N20) 20 ms after electrical stimulation of the median nerve (Fig. 2). Bilateral loss of this response indicated cortical cell death, provided that nerve function is intact at the brachial plexus (N9/10) and the high cervical spinal cord (N13) is required to demonstrate that signal absence at N20 after median nerve stimulation only occurs in the presence of intact signals at N9/10 and N13 ensuring an intact peripheral nerve (reproduced with permission from Young GB).

Biochemical markers

Certain biochemical entities are thought to indicate cerebral damage. These include: neurone-specific enolase (NSE) and S-100β. However, biomarkers are still largely research-based and are currently not commercially available in the UK.

NSE is released in cerebral damage and is also a marker for tumours such as neuroblastoma and small cell lung cancers. Raised levels, after cardiac arrest both from the blood and cerebrospinal fluid (CSF), are indicative of a poor neurological outcome. Reduced levels are seen after TH which predict a better neurological outcome.

S-100β is a protein expressed primarily by astrocytes. The elevation of this protein post-cardiac arrest is associated with cerebral damage and may predict a poorer neurological outcome. The evidence for S-100β is less robust than that for NSE but after TH does appear to be a significant prognostic value.

Intracranial pressure

There are limited data to suggest that raised intracranial pressure in the post-arrest period is associated with a poor neurological outcome. At present, there is insufficient evidence to recommend this as a monitoring modality to aid with neurological prognostication.

Scoring systems

These include systems that indicate the physiological chance of survival such as the OHCA score and the PAR score discussed earlier (Table 1). More specifically, the brain arrest neurological outcome scale (BrANOS) was developed to predict mortality and severe neurological dysfunction after cardiac arrest. This system using a combination of duration of arrest, GCS, and CT brain findings predicts mortality and severe disability with an overall diagnostic accuracy of 90%. However, this score was developed on non-cooled patients and has not been validated on patients after TH, so at present until full validation has taken place, it cannot be recommended.

Conclusion

There have been significant advances in the treatment of cardiac arrest over the last few years, and patient’s survival and neurological recovery is steadily improving.

Consequently, it would appear appropriate to err on the side of caution as temporarily prolonging the life of someone destined to a poor neurological outcome is less of a significant error than withdrawing care on someone who could make a good recovery. The
decision to admit to critical care should be primarily based upon a patient’s pre-morbid physiological status and wishes if known. Predicting potential recovery based on factors associated with the cardiac arrest can no longer be recommended. While patients who incur an unwitnessed non-VF/VT arrest generally have a very poor outcome, some do make an excellent recovery.

As experience of the management of these patients improves, so then will neurological prognostication. In the mean time, caution should be used in interpreting clinical signs at 72 h and the investigation of choice, although underused in the UK, is SSEP (Table 4). A multidisciplinary team approach to establishing neurological prognosis and considering treatment withdrawal is vital. In addition, while a neurological deficit can be significant in survivors, many suffer from very subtle deficits such as short-term memory loss and emotional lability. This can often be managed well if recognized and treated early. All patients who survive to critical care discharge should be referred for specialist neurorehabilitation medicine review as a routine.

### Declaration of interest

None declared.

### References


Please see multiple choice questions 5–8.