## **British Society for Clinical Neurophysiology**

## Medical Student Essay Prize 2015

# Clinical Audit on prognostication and neurophysiological testing in cardiac arrest at the Bristol Royal Infirmary

A review against current guidelines
(An advisory statement from European Resuscitation
Council and the European Society of Intensive Care
Medicine, August 2014),



A literature review of Neurophysiological assessment in the management of comatose patients post-cardiac arrest.

Alexander Goodliff, University of Bristol

July 2015

Word count: 2979 (excluding tables, acknowledgements, appendices and references)

#### Introduction/Background

In the UK there are approximately 60,000 out of hospital cardiac arrests (OOHCA) per year, with a survival rate of less than 10%¹. Hypoxic Ischaemic Encephalopathy (HIE) occurs when the brain is completely starved of oxygen, and frequently causes severe neurological deficits in resuscitated survivors². Subsequently many patients are left indefinitely comatose, whilst their potential for recovery is difficult to predict. Both clinicians and families are left with tough decisions regarding continuation of care, and therefore it is necessary to accurately predict the prognosis of such patients. Neurological outcome of survivors has classically been determined through clinical observation, with a meta-analysis³ of 11 studies involving 1,194 patients demonstrating five clinical signs that are strongly predictive of death: absent corneal reflexes, absent pupillary reflexes, absent withdrawal response to pain, no motor response at 24 hours and no motor response at 72 hours. However it is stressed that prognostication cannot be made on clinical examination alone, and that there are no defined good or bad prognostic criteria that can be used uniformly.

Further complicating the issue, recent advances in management including sedatives, neuromuscular blockers and therapeutic hypothermia (TH) potentially interfere with traditional prognostic markers, including the crucial clinical examination<sup>4</sup>. The previous guidelines were based on studies performed before the introduction of these therapeutic measures, casting doubt on the validity of old prognostic markers. This uncertainty has paved the way for ventures into biochemical and neurophysiological prognostic testing, which are not confounded in this way.

Neurophysiological testing in cardiac arrest involves assessing the integrity of the nervous system through a variety of measures, namely electroencephalography (EEG) and somatosensory evoked potentials (SSEPs). Encephalograms are non-invasive measures of cortical electrical activity through electrodes placed on the scalp<sup>5</sup>. There is a role however for determining changes in cerebral function when the brain is damaged by a variety of causes, known as an encephalopathy, including HIE<sup>6</sup>. SSEPs assess the function of the cerebral neuronal pathways, as opposed to brainstem function in clinical signs, by measuring the transmission of an electrical impulse from

<sup>&</sup>lt;sup>1</sup> NHS England Ambulance Quality Indicators. 2015 [Internet]. Last accessed 20 July 2015. Available from: www.england.nhs.uk/statistics/statistical-work-areas/ambulance-quality-indicators/

 $<sup>^2</sup>$  Stiell et al. Early versus later rhythm analysis in patients with out- of-hospital cardiac arrest. (2011) N Engl J Med 365:787–797

<sup>&</sup>lt;sup>3</sup> Booth CM, Boone RH, Tomlinson G, Detsky AS. Is this patient dead, vegetative, or severely neurologically impaired? JAMA 2004;291:870-9.

<sup>&</sup>lt;sup>4</sup> Samaniego EA, Mlynash M, Caulfield AF, Eyngorn I, Wijman CA (2011) Sedation confounds outcome prediction in cardiac arrest survivors treated with hypothermia. Neurocrit Care 15:113–119

<sup>&</sup>lt;sup>5</sup> NHS Choices. Health A-Z. EEG (electroencephalogram) Overview. [Internet]. Last accessed 20 July 2015. Available from: http://www.nhs.uk/Conditions/EEG/Pages/Introduction.aspx

<sup>&</sup>lt;sup>6</sup> S J M Smith. EEG in neurological conditions other than epilepsy: when does it help, what does it add? J Neurol Neurosurg Psychiatry 2005;76:ii8-ii12 doi:10.1136/jnnp.2005.068486 2005;76:ii8-ii12 doi:10.1136/jnnp.2005.068486

a peripheral nerve through to the cortex<sup>7</sup>. They are widely used for intra-operative monitoring and diagnosis of Multiple Sclerosis, however their role in assessing prognosis in comatose patients has proved more controversial.

The Bristol Royal Infirmary (BRI) is one of only 5 centres<sup>8</sup> in the UK using these methods of assessing neurological outcome, despite recent recommendations from the European Resuscitation Council<sup>9</sup> and the American Academy of Neurology<sup>10</sup> advocating their use. These expert panel advisory statements make clear the proper sequence of events that are recommended, whilst failure to correctly follow procedure could potentially provide false information on prognosis. The BRI is pioneering the use of SSEPs in the UK, so therefore the purpose of this audit is to assess whether proper protocol has been followed.

<sup>7</sup> P Walsh, N Kane, S Butler. The clinical role of evoked potentials. J Neurol Neurosurg Psychiatry 2005;76:ii16-ii22 doi:10.1136/jnnp.2005.068130

2006;67:203-10.

 <sup>8</sup> Thomas, M. Prognostication and neurophysiology following cardiac arrest. 2015 (Unpublished)
 9 Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: an

advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1816–1831. doi: 10.1007/s00134-014-3470-x. 

<sup>10</sup> Wijdicks EFM, Hijdra A, Young GB, Bassetti CL, Wiebe S. Practice Parameter: Prediction of outcome in comatose survivors of cardiopulmonary resuscitation (an evidence- based review). Neurology

#### Aims

 To evaluate whether comatose patients, post-cardiac arrest on Critical Care in the Bristol Royal Infirmary (BRI), are managed appropriately as per guidance.

#### **Objectives**

- To check whether all comatose patients post-cardiac arrest requiring prognostication received both an electroencephalogram (EEG) and somatosensory evoked potentials (SSEPs).
- Whether prognostication was performed in an appropriate timescale.
- To evaluate reasons why treatment differed from the guidance

#### Methodology

The audit was performed as a retrospective case note review. Through the Critical Care computer system Innovian, the prognostication of comatose cardiac arrest patients at the BRI Intensive Care Unit (ICU) was assessed to evaluate compliance with the most recent advisory statement.

A surrogate marker was used to determine which cardiac arrest patients required neurological prognostication, which was whether either an EEG or SSEP was requested during their stay on ICU. Not all patients who suffered an OOHCA required further testing of their neurological status for a variety of reasons, however a request for either one of these neurophysiological tests indicated uncertainty in their outcome. It was then documented which prognostic tests were performed, the timeframe that they were done and whether the neurophysiological management complied with the prognostication strategy suggested as best practice in the standards.

We searched from May 2012, the date of the first recorded EEG and SSEP for prognostic purposes, through to May 2014. The Innovian computer system was replaced in May 2014, and therefore it was decided to end the audit at that date. A cohort of 46 patients was generated through these means, and further analysis was performed to gather information on age, gender, down time (the estimated amount of time between arrest and return of spontaneous circulation (ROSC)) and cause of cardiac arrest.

#### **Clinical Audit Standards**

| Star | ndards/Criteria   |               |   |  |   |                                     |  |
|------|---|---------------|---|--|---|-------------------------------------|--|
|      | Criteria  | Target<br>(%) | Exceptions  | Source & Strength* of Evidence                             |   | Instructions for where to find data |  |
| 1    | All comatose patients after an out-of-hospital cardiac arrest received neurophysiological testing to assess prognosis as follows:  • Electroencephalography (EEG) undertaken • Somatosensory evoked potentials (SSEP) | 100%          | EEG showed Status Myoclonus < 48 hours after OOHCA, therefore SSEP is not indicated | Advisory statement from the European Resuscitation Council | С | Medical notes                       |  |
| 2    | All Somatosensory evoked potentials were performed >72 hours after return of spontaneous circulation (ROSC)   | 100%          | None  | Advisory statement from the European Resuscitation Council | С | Medical Notes                       |  |

#### \*Strength of Evidence

A At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation

C Expert committee reports or opinions and/or clinical experience of respected authorities. Absence of directly applicable clinical studies of good quality

**D** Recommended good practice based on clinical experience (local consensus)

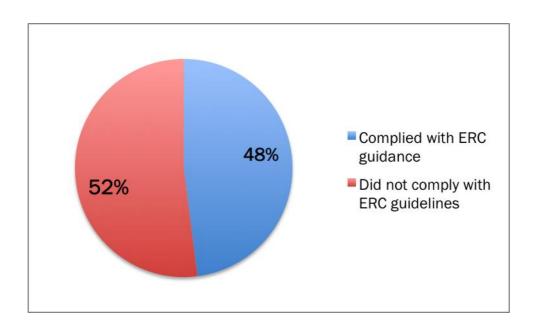
**B** Availability of well-conducted clinical studies but no randomised clinical trials on the topic of the recommendation

|   | Criteria  | Target<br>(%) | Exceptions  | Results        |
|---|---|---------------|---|----------------|
| 1 | All comatose patients after an out-of-hospital cardiac arrest received neurophysiological testing to assess prognosis as follows:  • Electroencephalography (EEG) undertaken • Somatosensory evoked potentials (SSEP) | 100%          | EEG showed Status<br>Myoclonus < 48<br>hours after OOHCA,<br>therefore SSEP is<br>not indicated | 48%<br>(20/42) |
| 2 | All Somatosensory evoked potentials were performed >72 hours after return of spontaneous circulation (ROSC)   | 100%          | None  | 95%<br>(19/20) |

#### **Analysis of Results Against Targets**

#### Standard 1

Figure 1: A pie chart illustrating the percentage of patients that received both an EEG and SSEP, minus stated exclusion criteria, and therefore complying with ERC guidelines.

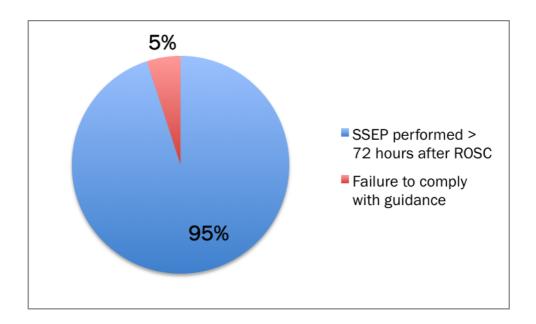


Results showed that 20 patients received an SSEP as well as an EEG during prognostication post-OOHCA, with 4 patients proven to be in Status Myoclonus within 48 hours. Therefore 48% (20/42) of patients were treated with both suggested neurophysiological tests suggested as best practice in Standard 1. However when incorporating the acknowledged exclusion criteria for withholding SSEPs, 52% (24/46) of patients were managed according to the ERC prognostic algorithm.

Therefore, 48% (22/46) of patients had management that differed from the suggested guidance, and only had an EEG performed (that didn't prove myoclonus) with no SSEP.

#### Standard 2

Figure 2: A pie chart illustrating the percentage of SSEPs that were performed >72 hours after ROSC, as per the ERC guidelines.



Results show that 19/20 (95%) of patients who received an SSEP had it performed >72 hours after ROSC, which complies with the ERC prognostic algorithm.

However information on 1 patient (5%) was not conclusive on the exact timing of when the SSEP was performed, as not enough data was entered onto the Innovian system to accurately interpret the outcome. Whilst it wasn't shown to have been performed <72 hours after ROSC, it was deemed to not meet the criteria set by Standard 2.

#### Discussion

#### Audit Results (see Appendix 1)

The advisory statement from the European Resuscitation Council<sup>9</sup> formed the audit standards, dictating the best practice in prognostication for comatose OOHCA survivors in a new era of therapeutic hypothermia and other confounders of the clinical examination. Through the analysis of evidence from 73 separate studies, a prognostic algorithm (see Appendix 2) was developed to aid clinicians. This paper was published in August 2014, after the last recorded patient in the audit population. The BRI pre-empted the recommended use of SSEPs, due to the evidence from Europe and America on its effectiveness. Therefore the purpose of the audit is not to analyse how strictly the department adhered to guidelines before its release, but to evaluate the processes in the BRI compared to what is recommended as best practice and the explanations for differing management.

The prognostic algorithm suggests an initial EEG within 48 hours of cardiac arrest and SSEPs >72 hours after ROSC, which formed the basis of Standard 1. A CT

head within 48 hours and serum NSE levels are also suggested in the algorithm. However the focus of this audit was to assess neurophysiological prognostication, so therefore will be omitted from this discussion. 24/46 (52%) of patients adhered to the protocol suggested by the guidelines. However 22/46 patients only had EEGs performed without an SSEP. SSEPs were available for all 22 patients, so the explanations for not requiring this extra scan were assessed.

Firstly, from the case notes of two patients it was noted that an EEG was initially performed during the rewarming phase of treatment post-arrest, but they eventually made a sufficient neurological recovery that an SSEP was unnecessary. Both these patients survived to be discharged to another ward for continuing medical care, with a good standard of life expected.

Secondly, one patient was deeply comatose post-arrest, with an abnormal EEG but no conclusive evidence to the extent of his neurological damage. However due to advanced Parkinson's disease, and previously expressed opinions of how difficult his life has already become, the family felt it was in his best interests to withdraw care without needing to know the extent of his neurological damage.

Finally, the remaining 19 patients who didn't receive SSEPs in addition to their EEGs had their care determined from clinical judgement and other prognostic methods. Only four of these patients survived their stay in ICU and left with rehabilitation potential, and a further three patients were transferred off ICU for palliative care. The remaining 12 patients died during their stay in ICU.

Aside from one of the surviving patients, every EEG showed abnormal patterns with varying degrees of severity. In all of these cases the EEG was used in conjunction with other methods to confirm HIE. However the extent that it can be used in prognosis, rather than diagnosis, is more difficult to assess. The suggested indication for EEGs in HIE patients is to detect non-convulsive or clinically subtle seizures<sup>11</sup>. Status Epilepticus, Burst-suppression and Isoelectric EEG patterns are strongly associated with poor neurological outcome, however not exclusively so. Great caution must be taken when viewing an EEG in isolation, as many factors including sedatives, core temperature, electrolyte imbalance and systemic complications can affect cerebral function<sup>11</sup>. Analysis of the EEG patterns (Figure 3) proved difficult, with 8/46 reports described only as 'grossly abnormal' on Innovian, and 2/46 not ever having an EEG report filed at all despite it being performed. However of the recorded patterns, only 9/36 (25%) were recorded as showing an Unreactive Burst-Suppression pattern, Status Myoclonus or Status Epilepticus.

These three EEG findings are the only criteria from the ERC algorithm that indicates a poor prognosis. Furthermore 14 patients who demonstrated an unfavourable EEG pattern not included in the ERC prognostic criteria, yet still indicated HIE, did not go on to receive an SSEP. 8 of these patients died as an inpatient, while 6 went on to be discharged. The treatment of these 8 patients, who died without an SSEP and with an EEG pattern not conclusive of poor

\_

<sup>&</sup>lt;sup>11</sup> S J M Smith. EEG in neurological conditions other than epilepsy: when does it help, what does it add? J Neurol Neurosurg Psychiatry 2005;76:ii8-ii12 doi:10.1136/jnnp.2005.068486

prognosis as per ERC guidelines, could possibly have been improved by the addition of an SSEP in assessing the need for withdrawal of treatment.

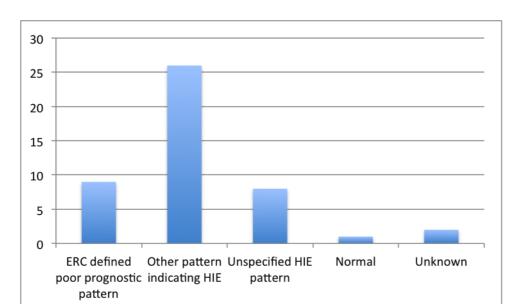


Figure 3: A bar chart illustrating the different recorded EEG patterns for the 46 patients of the audit population.

Standard 2 of the audit necessitated that all SSEPs performed for prognostic purposes on patients treated with therapeutic hypothermia were performed at >72 hours after ROSC, as guidance suggests that the sensitivity is less effective if performed too early9. 19/20 (95%) of SSEPs were performed in an appropriate timescale, whilst 1 patient's (5%) timing went undocumented. There was no evidence it was performed too early, however could not satisfy the criteria set in Standard 2. All SSEPs need to be preceded by an EEG, which was the case in this audit. Whilst arguably considered a prognostic tool as previously discussed, EEGs are important in the discovery of Myoclonic epilepsy or Status Epilepticus, which can confound the interpretation of SSEP results. Myoclonic status can exaggerate cortical potentials by up to as much as 10 times<sup>12</sup>, and this needs factoring into SSEP analysis.

<sup>&</sup>lt;sup>12</sup> Shibasaki H . Electrophysiological studies of myoclonus. Muscle Nerve2000;23:321-35

#### Evidence for EEGs and SSEPs as prognostic tools

A prospective cohort study on 277 consecutive comatose-OOHCA patients demonstrated that EEG within 24 hours of arrest was a robust indicator of both good and poor neurological outcomes, if an unfavourable pattern (burst-suppression, low-voltage or isoelectric) was identified<sup>13</sup>. Other malignant EEG patterns (evolving seizures and generalized epileptiform discharges) indicated a poor neurological outcome, however it was inconsistently associated with death. The relationship between EEG pattern and neurological outcome diminished over time, with this evidence supporting the guidance set in the ERC prognostic algorithm.

Rarely are single tests taken in isolation, however there are three measures that unequivocally predict poor outcome; malignant EEG at 24 hours, absent pupillary light response at 48 hours and absent SSEPs at >72 hours<sup>11</sup>. Due to the complex needs of a patient post-arrest, it could possibly be difficult to gather the appropriate neurological information in such a short time frame. Therefore early EEGs, and to a lesser extent pupillary reflexes, can be difficult to ascertain. This is where the merit of SSEPs is most evident.

The process of recording evoked potentials for prognostication involves a stimulation of the peripheral nervous system (usually the median nerve at the wrist), with bilateral measurements of the progress of the stimulation taken at Erbs point (located over the brachial plexus) and over the CP3 + CP4 locations on the scalp of the contralateral hemisphere<sup>14</sup>. A negative peak from the cortical response normally appears at 20ms, also referred to as the N20 response. The absence bilateral absence of this N20 wave at 72 hours post-arrest predicts death or persistent vegetative state in anoxic-ischaemic patients, with a specificity of >99%15. Conversely, bilaterally present N20 responses have a relatively poor predictive value, with one study<sup>16</sup> demonstrating 66% of patients who demonstrated positive N20 responses died during their stay. SSEPs are less susceptible to confounding from sedation or metabolic changes than clinical signs and pupillary reflexes<sup>7</sup>. Therefore the true clinical value of SSEPs is in allowing early recognition of poor prognosis and subsequently clarity of decision making when withdrawing care, despite the advances in therapeutic hypothermia and other confounding factors.

<sup>&</sup>lt;sup>13</sup> Hofmeijer J, , Beernink TMJ, Bosch FH et al. Early EEG contributes to multimodal outcome prediction of postanoxic coma. Neurology July 14, 2015 vol. 85 no. 2 137-143

<sup>&</sup>lt;sup>14</sup> Anastasian ZH, Komotar RJ et al. Evoked Potential Monitoring Identifies Possible Neurological Injury During Positioning for Craniotomy. Anesth Analg. 2009 Sep; 109(3): 817–821.

 $<sup>^{\</sup>rm 15}$  Young GB, Wang JT, Connolly JF. Prognostic determination in anoxic-ischemic and traumatic encephalopathies. J Clin Neurophysiol2004;21:379–90.

<sup>&</sup>lt;sup>16</sup> Fugate JE, Wijdicks EFM, Mandrekar J et al. Predictors of neurologic outcome in hypothermia after cardiac arrest. Ann Neurol. 2010;68:907 – 14.

#### Additional prognostic data

Whilst this audit covered the two years from May 2012 to May 2014, there was also data available on all SSEPs performed at the BRI up until the present (see Appendix 3). Despite the patients not being eligible to be included in the audit population, the data collected proved relevant to the aims of this project: to evaluate the methods of prognostication in cardiac arrest. The SSEP results of 44 patients were documented, and compared against their eventual outcome. 17 patients (39%) were shown to have bilaterally absent N20 waves, with all 17 (100%) dying as an in-patient. Conversely 24 patients (55%) had bilaterally present N20 waves, with 16/24 (67%) dying as in-patients, 7/24 (29%) surviving to discharge and 1/24 (4%) patient's outcome was undocumented. 2 patients (4%) had unilaterally present SSEPs, who subsequently both died, and 1 patient (2%) had an SSEP that was invalid due to artefacts.

Figure 4: Table comparing SSEP pattern to eventual ICU outcome, using all recorded SSEPs at the BRI regardless of audit inclusion criteria.

| SSEP       | Died | Survived | Unknown<br>outcome |
|------------|------|----------|--------------------|
| Present    | 16   | 7        | 1                  |
| Absent     | 17   | 0        | 0                  |
| Unreadable | 1    | 0        | 0                  |

This data is consistent with the best evidence<sup>9, 14, 15</sup> for the prognostic value of SSEP results, although this data must be interpreted in the context of the 'self fulfilling prophecy' phenomenon. It states that there can be a tendency for early withdrawal of care due to falsely pessimistic interpretation of prognostic information<sup>17</sup>, and therefore retrospective analysis of data regarding poor prognostic markers can be skewed. Whilst data suggests bilaterally negative SSEPs are invariably associated with poor prognosis, future blinded trials would be required to ensure an unquestionably poor prognosis.

<sup>&</sup>lt;sup>17</sup> Geocadin RG, Peberdy MA, Lazar RM: Poor survival after cardiac arrest resuscitation: a self-fulfilling prophecy or biologic destiny? Crit Care Med 2012, 40:979–980.

#### Conclusion

The results of this audit have shown that over the two-year period form May 2012 – May 2014, the BRI ICU team have followed the protocol suggested as best practice by the ERC in 48% of cases. Analysis of data showed that in 52% of patients an SSEP was not ordered due to management decisions being made on clinical signs, multi-system failures, pre-morbid quality of life and EEG as a prognostic tool. Prognostication following cardiac arrest is a rapidly developing field, with further advances into biochemical markers of poor prognosis. Neuron Specific Enolase (NSE) and S100 calcium-binding protein B (S100 B) are biomarkers that are released following neuronal injury, with raised serum levels correlating with HIE and therefore poor neurological outcome<sup>9</sup>. Whilst it is difficult to set a threshold level for poor prognosis, future management of OOHCA will almost certainly incorporate biomarker levels.

Management of OOHCA patients is complex, and sometimes predicting neurological outcome is sometimes only relevant at a later stage during their admission in ICU, so therefore suggested early EEG <24 hours and recording of pupillary response<sup>13</sup> can be logistically difficult. Bilaterally negative SSEPs are valuable in predicting poor outcome, and perhaps the decision making for the 22/46 (48%) of patients who didn't receive an SSEP could have been made with more clarity on their neurological outcome. Anticipating a poor prognosis efficiently would not only prevent unnecessary continuation of care in patients with no rehabilitation potential, but also provide both the family and carers with an absolute confidence that withdrawal of care is the best and most dignified option.

Doctors in ICU, in conjunction with the family, are frequently required to make difficult decisions on continuation of care and therefore want the best information possible. The ERC guidance recommends SSEPs as a prognostic tool in every patient, as well as using all available information on neurological outcome. At the BRI many patients did not receive SSEPs, but by definition these recommendations are only guidelines and clinical acumen has been shown to be important in management. SSEPs can allow this decision to be made with absolute certainty, and here lies the true benefit.

#### Acknowledgements

I would like to thank my supervisor Dr. Matthew Thomas not only for his guidance and knowledge in this project, but also for the work he has put in previously before my involvement in this audit.

In addition, thank you to the audit lead Dr. Jeremy Astin for his help in completing the audit, and also for his teaching on the ICU ward rounds.

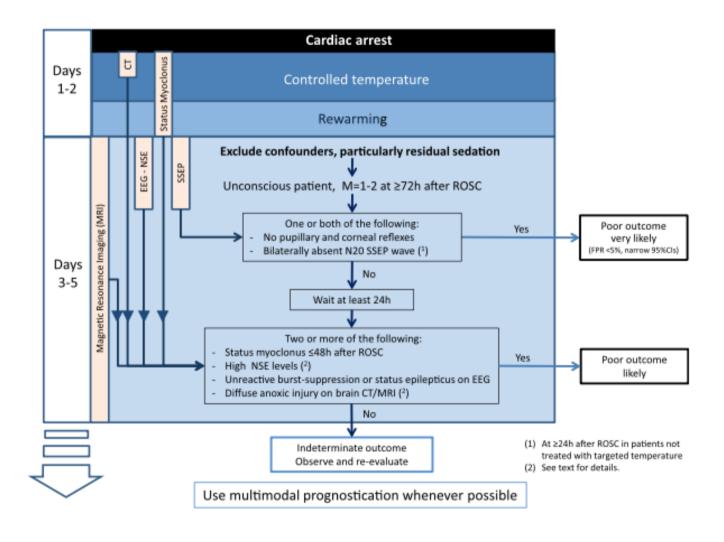
Finally, thank you to Dr. Nick Kane for his expert opinion on neurophysiology and help in data collection.

# Appendix 1 Audit Data Collection

| Audit<br>number | Date of admission | Age | Gender | Cause of arrest                            | Down<br>time | EEG<br>? | SSEP<br>? | Myoclonus<br><48hrs? | Outcome                    |
|-----------------|-------------------|-----|--------|--|--------------|----------|-----------|----------------------|----------------------------|
| 1               | 12.5.12           | 51  | F      | Inferior MI (stent)                        | 15 mins      | Υ        | Υ         | N                    | Survived + discharged      |
| 2               | 13.5.12           | 69  | F      | Inferior MI (no stent)                     | 20 mins      | Υ        | Ν         | N                    | Died                       |
| 3               | 7.6.12            | 56  | F      | HOCM (no stent)                            | 41 mins      | Υ        | Ν         | N                    | Died                       |
| 4               | 8.6.12            | 59  | F      | Inferior MI (no stent)                     | 30 mins      | Υ        | Ν         | N                    | Died                       |
| 5               | 29.6.12           | 62  | M      | Inf/Post MI (stent)<br>Unknown cardiac (no | 53 mins      | Y        | N         | N                    | Discharged for EOLC        |
| 6               | 13.10.12          | 48  | M      | stent)                                     | 30 mins      | Υ        | Ν         | N                    | Discharged for EOLC        |
| 7               | 22.11.12          | 64  | F      | LBBB (no stent)                            | 20 mins      | Υ        | Ν         | N                    | Died                       |
| 8               | 25.11.12          | 63  | F      | RBBB (no stent)                            | 55 mins      | Υ        | Ν         | Υ                    | Died                       |
| 9               | 24.12.12          | 58  | M      | Cardiac (stent)<br>Unknown cardiac (no     | 20 mins      | Y        | Y         | N                    | Discharged for neuro rehab |
| 10              | 16.1.13           | 70  | M      | stent)                                     | 35 mins      | Υ        | Υ         | N                    | Died                       |
| 11              | 22.1.13           | 77  | F      | Cardiac (stent)<br>Unknown cardiac (no     | 3 mins       | Y        | N         | Υ                    | Died                       |
| 12              | 21.2.13           | 87  | M      | stent)                                     | 27 mins      | Υ        | Ν         | N                    | Discharged for EOLC        |
| 13              | 14.2.13           | 63  | M      | Cardiac (stent)                            | 30 mins      | Υ        | Υ         | N                    | Died                       |
| 14              | 15.2.13           | 56  | M      | Cardiac (stent)                            | >15 mins     | Υ        | Ν         | N                    | Died                       |
| 15              | 16.2.13           | 61  | M      | Cardiac (stent)<br>Unknown cardiac (no     | 27 mins      | Y        | N         | Υ                    | Died                       |
| 16              | 27.2.13           | 74  | M      | stent)                                     | 20 mins      | Υ        | Ν         | N                    | Died                       |
| 17              | 9.3.13            | 79  | F      | Cardiac (stent)                            | Unknown      | Υ        | Ν         | N                    | Discharged to CCU          |
| 18              | 26.3.13           | 76  | M      | Cardiac CHB (no stent)                     | 5 mins       | Υ        | N         | Υ                    | Died                       |

|     |          |            |     | Unknown cardiac (no |            |   |   |      |   |
|-----|----------|------------|-----|---------------------|------------|---|---|------|---|
| 19  | 17.4.13  | 39         | F   | stent)              | Unknown    | Υ | Ν | N    | Discharged                                  |
|     |          |            |     | Unknown cardiac (no |            |   |   |      |   |
| 20  | 17.5.13  | 76         | M   | stent)              | Unknown    | Υ | Υ | N    | Died  |
| 21  | 20.5.13  | 59         | M   | Cardiac (stent)     | 20 mins    | Υ | N | N    | Died  |
|     |          |            |     | Unknown cardiac (no |            |   |   |      |   |
| 22  | 8.6.13   | 58         | M   | stent)              | 30 mins    | Υ | Y | N    | Died  |
| 23  | 12.6.13  | 69         | F   | Cardiac (stent)     | 20 mins    | Υ | N | N    | Discharged for neuro rehab                  |
| 24  | 20.6.13  | 67         | M   | Cardiac (no PCI)    | 25 mins    | Υ | N | N    | Died  |
| 25  | 29.6.13  | 58         | F   | Cardiac (stent)     | Unknown    | Υ | Υ | N    | Discharged for neuro rehab                  |
| 26  | 6.7.13   | 33         | M   | Drug overdose       | Unknown    | Υ | Υ | N    | Died  |
|     |          |            |     | Unknown cardiac (no |            |   |   |      |   |
| 27  | 12.7.13  | 62         | F   | stent)              | 31 mins    | Υ | N | N    | Died  |
|     |          |            |     | Unknown cardiac (no |            |   |   |      |   |
| 28  | 19.7.13  | 32         | M   | stent)              | Unknown    | Υ | Y | N    | Died  |
|     |          |            | _   | Unknown cardiac (no |            |   |   |      |   |
| 29  | 28.7.13  | 51         | F   | stent)              | 20 mins    | Y | Y | N    | Died  |
| 00  | 10010    | 70         |     | Unknown cardiac (no |            | V |   | N.1  | D: 1  |
| 30  | 16.8.13  | 72         | M   | stent)              | 20 mins    | Y | N | N    | Died  |
| 31  | 25.8.13  | 47         | F   | Cardiac (stent)     | >25 mins   | Y | Y | N    | Died  |
| 00  | 10010    | <b>7</b> 4 |     | Unknown cardiac (no |            | V |   | N.1  | D: 1  |
| 32  | 16.9.13  | 74         | M   | stent)              | 20 mins    | Y | N | N    | Discharged                                  |
| 33  | 5.11.13  | 64         | M   | Cardiac (stent)     | 30 mins    | Y | Y | N    | Died  |
| 2.4 | 10 10 10 | 40         | N 4 | Unknown cardiac (no | 25         | V | V | N.I. | D: a d                                      |
| 34  | 16.12.13 | 49         | M   | stent)              | 35 mins    | Y | Y | N    | Died  |
| 35  | 27.12.13 | 45         | M   | Drug overdose       | 20 mins    | Y | Y | N    | Died  |
| 20  | 04.4.4   | 04         | _   | Unknown cardiac (no | > CO mains | V | V | NI   | Diad  |
| 36  | 21.1.14  |            | F   | stent)              | >60 mins   | Y | Y | N    | Died<br>Bisslands (Consequence to the bound |
| 37  | 21.1.14  | 91         | M   | Cardiac (stent)     | 13 mins    | Y | N | N    | Discharged for neuro rehab                  |
|     |          |            |     |                     |            |   |   |      |   |

|    |         |    |   | Unknown cardiac (no                    |          |   |   |   |                            |
|----|---------|----|---|--|----------|---|---|---|----------------------------|
| 38 | 4.2.14  | 54 | M | stent)<br>Unknown cardiac (no          | 25 mins  | Y | N | N | Died                       |
| 39 | 7.2.14  | 47 | M | stent)<br>Unknown cardiac (no          | 12 mins  | Y | Y | N | Died                       |
| 40 | 2.3.14  | 64 | F | stent)                                 | 20 mins  | Υ | Υ | N | Died                       |
| 41 | 3.3.14  | 58 | F | Cardiac (stent)<br>Unknown cardiac (no | 50 mins  | Y | Y | N | Died                       |
| 42 | 5.3.14  | 54 | M | stent)<br>Unknown cardiac (no          | 35 mins  | Y | N | N | Died                       |
| 43 | 24.3.14 | 78 | F | stent)                                 | Unknown  | Υ | N | N | Died                       |
| 44 | 3.4.14  | 67 | M | Cardiac (stent)                        | 25 mins  | Υ | Υ | N | Died                       |
| 45 | 28.4.14 | 52 | M | Cardiac (stent)<br>Unknown cardiac (no | 35 mins  | Y | Y | N | Died                       |
| 46 | 18.5.14 | 64 | M | stent)                                 | >15 mins | Υ | N | N | Discharged for neuro rehab |



# Appendix 3 – All SSEPs performed at the Bristol Royal Infirmary for HIE patients (May 2012 – present)

| HIE Patient ID | SSEP results         | Outcome    |
|----------------|----------------------|------------|
| 1              | Present              | Discharged |
| 2              | Absent               | Died       |
| 3              | Present              | Discharged |
| 4              | Present              | Discharged |
| 5              | Absent               | Died       |
| 6              | Absent               | Died       |
| 7              | Absent               | Died       |
| 8              | Present              | Died       |
| 9              | Absent               | Died       |
| 10             | Absent               | Died       |
| 11             | Present              | Died       |
| 12             | Absent               | Died       |
| 13             | Absent               | Died       |
| 14             | Present              | Died       |
| 15             | Present              | Died       |
| 16             | Absent               | Died       |
| 17             | Unilaterally present | Died       |
| 18             | Present              | Died       |
| 19             | Present              | Discharged |
| 20             | Present              | Discharged |
| 21             | Present              | Died       |
| 22             | Absent               | Died       |
| 23             | Present              | Died       |
| 24             | Present              | Died       |
| 25             | Absent               | Died       |
| 26             | Present              | Died       |
|                | Present              | Discharged |
| 28             | Absent               | Died       |
| 29             | Present              | Died       |
| 30             |                      | Died       |
|                | Present              | Unknown    |
| 32             | Present              | Died       |
| 33             | Absent               | Died       |
| 34             | Absent               | Died       |
|                | Absent               | Died       |
| 36             | Unilaterally present | Died       |
| 37             | Present              | Died       |
| 38             |                      | Discharged |
| 39             |                      | Died       |
| 40             | Absent               | Died       |
| 41             | Present              | Died       |

| 42 | Absent  | Died |
|----|---------|------|
| 43 | Absent  | Died |
| 44 | Present | Died |

- 1. NHS England Ambulance Quality Indicators. 2015 [Internet]. Last accessed 20 July 2015. Available from: www.england.nhs.uk/statistics/statistical-work-areas/ambulance-quality-indicators/
- 2. Stiell et al. Early versus later rhythm analysis in patients with out- of-hospital cardiac arrest. (2011) N Engl J Med 365:787–797
- 3. Booth CM, Boone RH, Tomlinson G, Detsky AS. Is this patient dead, vegetative, or severely neurologically impaired? JAMA 2004;291:870-9.
- 4. Samaniego EA, Mlynash M, Caulfield AF, Eyngorn I, Wijman CA (2011) Sedation confounds outcome prediction in cardiac arrest survivors treated with hypothermia. Neurocrit Care 15:113–119
- 5. NHS Choices. Health A-Z. EEG (electroencephalogram) Overview. [Internet]. Last accessed 20 July 2015. Available from: http://www.nhs.uk/Conditions/EEG/Pages/Introduction.aspx
- 6. S J M Smith. EEG in neurological conditions other than epilepsy: when does it help, what does it add? J Neurol Neurosurg Psychiatry 2005;76:ii8-ii12 doi:10.1136/jnnp.2005.068486
- 7. P Walsh, N Kane, S Butler. The clinical role of evoked potentials. J Neurol Neurosurg Psychiatry 2005;76:ii16-ii22 doi:10.1136/jnnp.2005.068130
- 8. Thomas, M. Prognostication and neurophysiology following cardiac arrest. 2015 (Unpublished)
- 9. Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1816–1831. doi: 10.1007/s00134-014-3470-x.
- 10. Wijdicks EFM, Hijdra A, Young GB, Bassetti CL, Wiebe S. Practice Parameter: Prediction of outcome in comatose survivors of cardiopulmonary resuscitation (an evidence- based review). Neurology 2006;67:203-10.
- 11. S J M Smith. EEG in neurological conditions other than epilepsy: when does it help, what does it add? J Neurol Neurosurg Psychiatry 2005;76:ii8-ii12 doi:10.1136/jnnp.2005.068486
- 12. Shibasaki H . Electrophysiological studies of myoclonus. Muscle Nerve2000;23:321–35
- 13. Hofmeijer J, , Beernink TMJ, Bosch FH et al. Early EEG contributes to multimodal outcome prediction of postanoxic coma. Neurology July 14, 2015 vol. 85 no. 2 137-143

- 14. Anastasian ZH, Komotar RJ et al. Evoked Potential Monitoring Identifies Possible Neurological Injury During Positioning for Craniotomy. Anesth Analg. 2009 Sep; 109(3): 817–821.
- 15. Young GB, Wang JT, Connolly JF. Prognostic determination in anoxic-ischemic and traumatic encephalopathies. J Clin Neurophysiol2004;21:379–90.
- 16. Fugate JE, Wijdicks EFM, Mandrekar J et al. Predictors of neurologic outcome in hypothermia after cardiac arrest. Ann Neurol. 2010;68:907–14.
- 17. Geocadin RG, Peberdy MA, Lazar RM: Poor survival after cardiac arrest resuscitation: a self-fulfilling prophecy or biologic destiny? Crit Care Med 2012, 40:979–980.