

Editorial

Withdrawal of treatment after devastating brain injury: post-cardiac arrest pathways lead in best practice

Every year in England, cardiopulmonary resuscitation (CPR) is attempted on about 30,000 people suffering an out of hospital cardiac arrest (OHCA) [1]. Return of spontaneous circulation (ROSC) is achieved in approximately 25%, and 7-8% of those in whom resuscitation is attempted will leave hospital alive. This figure is below the survival rates achieved in other countries, but if it could be increased to 10-11%, a further 1,000 lives a year could be saved in England [2]. The OHCA steering group aims to achieve this by addressing all aspects of the chain of survival pathway for victims of OHCA, and to this end has published its national framework “Resuscitation to Recovery” in March 2017 [1]. This single consensus document outlines a pathway based on best scientific evidence, national and international guidance, and expert opinion [3, 4]. Key elements of the framework are: to increase the number of patients who receive bystander CPR to more than the current 30-40% of all OHCA by increasing recognition of cardiac arrest; increasing the number of people trained in resuscitation; increasing the availability and use of public access defibrillators; transfer of patients who have achieved ROSC to recognised centres of care that provide immediate access to echocardiography, CT scanning, a cardiac catheterisation laboratory and advanced circulatory support techniques; management of post-resuscitation care in a general or cardiothoracic intensive care unit (ICU); and addressing the shortage of appropriate facilities for neurological and physical rehabilitation.

One of the key recommendations made by the OHCA steering group is that neurological prognostication should not be made in the first 72 hours after ROSC, and for longer if hypothermia has been used as part of the intensive care management of the patient. This is already routine practice in UK ICUs; data from the Intensive Care National Audit and Research Centres (ICNARC) shows that

between 2004 and 2014 the proportion of patients admitted to UK ICUs after OHCA increased from 9% to 12%, and that over this time both the length of stay in ICU and the time to the withdrawal of life-sustaining treatments (WLST) have also increased [5]. However, it is not that long ago that early neurological prognostication followed by withdrawal was common practice in patients admitted after OHCA. Over the past twenty years, the imprecision and inaccuracy of early prognostication after OHCA has been recognised, and this key recommendation to delay the WLST is supported by international resuscitation professional bodies [6-8]. The cardiac arrest community arguably leads the way in prognosticating after a severe neurological insult, in this case a hypoxic brain injury. If a patient remains comatose after allowing 72 hours for observation and physiological stabilisation, then using a combination of clinical examination (pupillary reactions, cough reflex, motor responses), radiology (CT or MRI brain), neurophysiology (electroencephalogram, somatosensory evoked potentials) and biomarkers (neurone specific enolase) may more precisely identify patients who will die or have a poor neurological outcome. While the ideal combination of tests needed for optimal prognostication remains unknown, cumulative experience with using these tools, coupled with careful audit, could lead to progressive refinement in the way we make decisions about WLST using objective scientific criteria. The importance of delaying prognostication and decisions to withdraw treatment is further emphasised by reports of 2.5% of OHCA survivors becoming responsive more than 7 days after rewarming [9]. The OHCA steering group stresses the importance of full discussions about withdrawal and its timing with the family, acknowledging the range of opinion about what constitutes an acceptable quality of life, and that some individuals or their families may be willing to accept survival with neurological disability. These opinions should be taken into consideration alongside the assessment of medical prognosis. The patient's preferences and values should be elicited in discussions with the family and a shared decision-making approach used to develop a bespoke end-of-life care plan for the patient [10]. Finally, the steering group also made the point that when a decision to withdraw is made, it is important to consider organ donation and to offer this option to the family when it is a possibility. In 2014, 10% of patients dying after admission to UK ICUs following OHCA became solid organ donors compared with 3% in 2004. [5]

Is the approach to prognosticating after OHCA applicable to other areas of ICU practice? The Danish Nobel prize winning physicist Niels Bohr reputedly said that “prediction is very difficult, especially about the future”. This difficulty is clear when it comes to predicting the outcome of an individual patient receiving intensive care. When an individual member of the ICU team predicts that an ICU patient would not survive to hospital discharge, 50% of those predicted to die will nonetheless survive. When the ICU team unanimously predicts that the patient would not survive to hospital discharge, 15% survive; and 12% survive even when the same prediction was made unanimously on 3 or more separate days of the patient’s ICU stay. [11]. These data underline the fact that individual assessments of outcome are less dependable than those that are shared across several members of the clinical team, but suggest that even assessments that are concordant across clinicians and over time have a finite error. These difficulties are likely to be exacerbated when trying to make early treatment limitation decisions based on predictions not just of mortality, but also on the anticipated future quality of life, which is a major consideration in patients with devastating brain injury and in as many as 50% of decisions to proceed to WLST in ICU [12].

There is concern that early withdrawal in the critically ill, especially those at the extreme end of the spectrum, such as comatose survivors of cardiac arrest, tend to be a self-fulfilling prophecy [13, 14]. Similar concerns have also been raised by the Neurocritical Care Society and neuro-intensive care opinion leaders about the early withdrawal in patients with devastating brain injury [15, 16]. Devastating brain injury can be defined as any neurological condition that is assessed at the time of hospital admission as an immediate threat to life or incompatible with good functional recovery and where early limitation or withdrawal of therapy is being considered. The Neurocritical Care Society strongly recommends using a 72-h period of physiological stabilisation and observation to determine the clinical response and delaying decisions regarding withdrawal in the meantime. This recommendation is gaining support from within both the UK ICU and Emergency Medicine communities [17, 18]. It is further supported by reports of unexpected survivors with good functional outcomes in patients admitted to ICU for a period of stabilisation and observation rather than undergoing early withdrawal [19] and by the observation that withdrawal is the most common cause of death in patients with DBI [15]. A forthcoming joint

statement on the management of DBI from the Faculty of Intensive Care Medicine, the Intensive Care Society, the Society of British Neurological surgeons, the Royal College of Emergency Medicine and the Neuro Anaesthesia and Critical Care Society of Great Britain is also expected to recommend an approach that includes delaying withdrawal, physiological stabilisation, clinical observation and exclusion of confounding factors.

Outcome studies, and the prediction models that are developed from them, only allow clinicians to provide a statistical likelihood of outcome, which can be applied to groups of devastating brain injury patients, but cannot provide satisfactory accuracy in individual cases [16]. Further, in relying on previously validated models of outcome prognostication, it should also be remembered that many patients in the studies underpinning these models would have died following treatment limitation decisions or the withdrawal. Including these data to predict outcome or to develop predictive models is flawed because they introduce a powerful bias and make prediction of mortality a self-fulfilling prophecy [20, 21]. Most prediction models are based on physiological data and radiological appearances at the time of hospital admission. Assessment of the patient's response to stabilisation and active therapy not only increases the precision of prognostication, but also ensures that potential survivors do not undergo withdrawal inappropriately, and that the clinical outcome of any survivor is maximised [22]. Current outcomes may be better than those predicted by established prognostic schemes or by past experience might suggest, even for conditions that might be perceived to be devastating [23, 24]. For example, in one case series, favourable outcomes were obtained with intra-arterial therapy in 70% of patients with basilar artery occlusion treated more than 6 hours post-ictus [24], and patients with severe TBI who undergo decompressive craniectomy for intractable intracranial hypertension may experience late outcomes that are better than that predicted by well recognised prognostic schemes.[23] Finally, most prognostic schemes only provide a prediction of mortality, rather than functional outcome, a substantial failing when the quality of survival is considered more important than the duration of life by patients and their families [25].

Delaying the decision to withdrawal to determine the clinical response will usually prove the initial prognosis correct, and can be undertaken as planned at this

later stage after discussion within the multidisciplinary team. Other patients will continue to deteriorate and may fulfil the criteria to diagnose death using neurological criteria [26], which provides families with a conclusive diagnosis of death rather than a prognosis of a poor outcome. Finally, a few will improve [19], and the treatment plan can be reviewed by the multidisciplinary team. In most cases the clinical course of the patient becomes clear well before 72 hours, and the decision to withdraw, to test for the neurological determination of death, or to reverse the treatment limitations can be made at an earlier time [17, 19].

The delay in withdrawal will not only increase prognostic accuracy but will also allow better shared decision making with the family, improve end of life care for the patient and their relatives, enable the incorporation of palliative care into the patient's ICU management, and facilitate the adoption of best practice in organ donation [10, 16, 17, 27-29]. These are all good reasons for adopting pathways for the management of devastating brain injury that follow the principles of those for OHCA, but unfortunately there are no robust outcome studies for devastating brain injury pathways as there are for OHCA. It is essential that proper national audit of patients with devastating brain injury admitted to ICU are undertaken. National audit (for example, through ICNARC) is best placed to identify such patients and provide the data required for the development of rational protocols. Such audits must collect data that allows us to explore whether the pathways for non-OHCA devastating brain injury patients may require different details compared to those developed for OHCA. One key issue in this context includes decision making around time sensitive interventions such as evacuation of a space-occupying lesion, or thrombolysis/thrombectomy for occlusive cerebrovascular disease. Supporting systemic physiology while not attending to such primary pathology may fail to maximise the quality of outcome. Developing robust protocols to address this issue will not be easy, but where significant uncertainty of outcome exists in otherwise retrievable patients, there is a case for proceeding with definitive interventions as soon as systemic physiology is stabilised, and reassessing prognostic potential subsequently. A second issue will be the duration of observation that is needed for non-OHCA cases. While the current recommendation for OHCA is for a 72-hour window, this duration of observation may not be required in individuals where initial

or follow up neuroimaging provides clear objective evidence of the extent and progress of neurological injury.

Until such protocols are developed, it is not unreasonable that some ICU clinicians will continue to have reservations about devastating brain injury pathways. Some will be concerned that their use will increase the number of patients surviving with severe disability. This outcome is always a possibility when treating patients with severe brain injuries, even when they are being treated fully and aggressively. However, it must be remembered that the pathway does not remove the option to withdraw if a patient does not improve or continues to deteriorate; it simply delays that decision. Others will argue that good end of life care can be provided in many locations other than in the ICU. While this is true, tracheal extubation in patients with devastating brain injury in the emergency department not only removes any small hope of improvement, but gives families very little time to understand and come to terms with the situation. This does not mean that all patients with critical illness should be admitted to ICU for end of life care. Devastating brain injury is by its nature an unexpected and sudden onset illness, and unlike the families of patients known to have terminal illnesses such as metastatic malignancy or advanced dementia, families of patients admitted to the emergency department with devastating brain injury will have had little time for preparation for the potential death of a loved one.

Perhaps the greatest concern is that we have inadequate ICU resources, and that admitting patients with devastating brain injury will potentially deny these resources to patients with a better chance of survival. The pressure on ICU beds in the UK is relentless, and the practical, moral and financial impacts of increasingly using scarce ICU resources at the end of life are recognised [30]. These are concerns that have arisen previously with many patient populations, such as those with haematological malignancy, HIV, and neutropenic sepsis. These patients are now admitted routinely, with much improved outcomes. This argument would not sit comfortably with our current practice of routinely admitting patients after an OHCA despite only 7-8% of those receiving CPR surviving to hospital discharge [1]. Yet few would think that admitting these patients to ICU is an inappropriate use of ICU resources. Finally, the argument about resources goes beyond the individual ICU admitting the patient with devastating brain injury; the effect on wider NHS resources

should also be considered. Clearly, where devastating brain injury occurs in a patient in whom severe comorbidities limit quality of life before the acute event, admission to ICU and further prolongation of clinical course would be inappropriate. Again, the collection of high-quality audit data would allow us to address implementations of different pathways for different contexts, based on clinical and community consensus.

There will be views expressed that devastating brain injury pathways are being created simply to increase the potential for organ donation. The OHCA community already accept that organ donation is a positive secondary outcome of their pathways [5, 31]. Any increased organ donation potential following the introduction of these pathways should be viewed similarly. Indeed, one could question the equity of a situation where patients with devastating brain injury are only admitted to ICU, and in effect given a small chance of survival, if their relatives agree to organ donation, whereas patients whose family decline donation undergo withdrawal in the emergency department and are not given the same opportunity. Admitting a patient to the ICU for end-of-life care, and possibly organ donation, has been shown to yield on average seven times the quality-adjusted life years in transplant recipients per ICU bed-day compared with the average benefit for the admission of an ICU patient expected to survive [32]. Further, although an analysis of the relevant issues is complex [33], it is likely that the act of donation may provide some bereaved families benefit, especially when they feel that they are fulfilling the wishes of the potential donor, and when they feel that they have not been hurried into making a decision on donation.

In conclusion, we believe that the time has come to develop rational pathways of care for the management of non-OHCA patients with devastating brain injury, which can draw on the considerable experience of managing these patients following OHCA. This would, in many cases, involve admitting patients with devastating brain injury to the ICU, stabilising systemic physiology and implementing time-sensitive definitive interventions where appropriate, and delaying withdrawal until the prognosis is clearer. This would ensure survival of retrievable patients, permit families time to come to terms with a catastrophic event, allow informed withdrawal after an appropriate interval, offer families the opportunity for carefully considered

organ donation, and support development of the evidence base for clearer prognostication and decision making in the management of these patients. It is likely that uptake of these management principles is likely to vary between centres. Audit of such variations in practice could provide a substrate for observational comparative effectiveness research [34] in a context where formal randomised clinical trials may not currently be possible, and allow assessment of the benefits and costs of implementing these recommendations.

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