# Commentary
# Optimizing neurologic prognosis after cardiac arrest
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## Abstract

Neurologic disability is a feared outcome of resuscitation from cardiac arrest. The study by Rech and colleagues in the previous issue of *Critical Care* describes the use of neuron-specific enolase to inform an early prognosis in patients who survived in-hospital cardiac arrest. In their study 'none of the patients had a DNR order and there was no limitation of life support.' As a result, 10% of patients remained in a vegetative state at 6 months, a higher percentage than in other recent studies. The existence of a population of patients in which all are fully supported without withholding care or withdrawal of care may represent an important research opportunity. High neuron-specific enolase levels have been reported in patients that awoke and seem to occur in studies with a higher percentage of patients in a vegetative state at follow-up (more uniform support). If a comprehensive set of clinical, electrophysiological, biochemical and imaging measures could be obtained in a uniform manner in a cohort of patients without limitations in care, a more objective set of comprehensive prognostic indicators could be obtained. A focused international consortium is called for.

Neurologic disability is a feared outcome of resuscitation from cardiac arrest. The study by Rech and colleagues in the previous issue of *Critical Care* describes the use of neuron-specific enolase (NSE) to inform an early prognosis in 43 patients who survived for more than 12 hours after resuscitation from in-hospital cardiac arrest [1]. A reliable early neurologic prognosis can help families make decisions about continuing life-sustaining care, but also to adjust expectations. If the prognosis suggests little chance of awakening, many medical professionals and lay people feel that continuing life unconscious or vegetative can be ethically avoided – others disagree [2,3]. Care practices at the end of life, including the withholding of and withdrawal of life-sustaining food and hydration, vary considerably across Europe, and differ by factors including region and religion of both the physician and the patient [4].

In a recent study of care after resuscitation from cardiac arrest from the United States, 69% of patients had care either withheld or withdrawn after information about prognosis was discussed with the family [5]. Compare this with Rech and colleagues' study, where 'none of the patients had a DNR order and there was no limitation of life support' [1]. It is interesting to note that despite this full support, 70% of patients died by their 6-month follow-up. Did the patients that died have further cardiac problems and eventual unsuccessful cardiopulmonary resuscitation, did they die of respiratory complications, or did they proceed to brain death? We would assume that the lack of limitation of support should increase the number of patients who remained alive but unconscious. In the study of Rech and colleagues, 10% of patients remained in a vegetative state at 6 months – compared with 0.33% (1/300) who remained vegetative at 3 months in a recent randomized trial [6] and compared with 1.7% (7/407) of patients still unconscious at 1 month in a recent multicenter cohort study [7].

In Rech and colleagues' study, a NSE cutoff value of 60 ng/ml was used, set arbitrarily just above the highest level obtained in a patient who awoke, to obtain a specificity of 100%. The highest value observed in a patient who awoke was 55.41 ng/ml [1]. Would that value have been even higher if sampling was done at 48 hours? In a recent prospective cohort study, the NSE cutoff value used was 33 ng/ml, and 241 patients (157 without treatment restrictions) were tested at 48 hours [7]. No patient with a level above the cutoff value regained consciousness, but would there have been an exception if all 241 patients had no treatment restrictions?

Higher NSE levels have been reported in patients that awoke. These include a level of 43 ng/ml on day 2 (then 90.9 ng/ml on day 3) [8], a level of 47 ng/ml at 24 hours [9], the 55.41 ng/ml level from Rech and colleagues' study [1], and just over 65 ng/ml at 3 days [10]. In this latter study, the 19% (18/97) of patients in a vegetative state at 1 month suggests more uniform continued medical support. Thus, the two

NSE = neuron-specific enolase.

studies with a higher percentage of patients in a vegetative state at follow-up also reported the highest cutoff points for NSE levels.

The 2006 Practice Parameter from the American Academy of Neurology, entitled 'Prediction of outcome in comatose survivors after cardiopulmonary resuscitation', suggests that serum NSE >33 ng/ml tested 1–3 days after cardiopulmonary resuscitation can predict poor outcome with a 0% false-positive rate (95% confidence interval, 0–3%) [11]. The above cases show that the true false-positive rate is >0%.

It seems clear that there is a true association between higher levels of NSE, when sampled about 2–3 days after resuscitation from cardiac arrest, and worse neurologic outcomes. As we look to the future, how can we best resolve these issues surrounding the influence of limitations in care on the performance characteristics of prognostic tests?

The existence of a population of patients in which all are supported without withholding care or without withdrawal of care may represent an important research opportunity. In such a population, the continued support would inevitably lead to higher 'cutoff values' for prognostic tests with a continuous measure (for example, the serum NSE level) and would be more likely to identify exceptions to dichotomous prognostic tests (for example, somatosensory evoked potentials). As such, a more reliable estimate of the predictive value of prognostic tests could be obtained.

Research resources could be targeted to settings where limitations of care do not occur. If a comprehensive set of clinical, electrophysiological, biochemical and imaging measures could be obtained in a uniform manner in a cohort of patients without limitations in care, a more objective set of comprehensive prognostic indicators could be obtained. Specificity for any such prognostic test should be forced to 100% to maximally avoid falsely pessimistic prognoses, and the cohort size should be large enough such that the confidence interval should be a few percent or less. A focused international consortium is called for.

## Competing interests

The author declares that they have no competing interests.

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