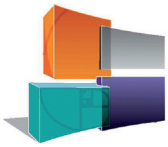
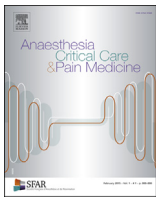
Anaesth Crit Care Pain Med 38 (2019) 415–417



SFAR
Société Française d'Anesthésie et de Réanimation



Editorial

Neuro-prognostication: Don't forget that time is brain!

ARTICLE INFO

Keywords:
NeuroICU
Neuroprognostication
Coma
Consciousness
Advance directives
EEG

"It seems that there is wakefulness without awareness" [1]. More than 45 years ago, Jennett and Plum opened the door to the unknown that many neuroscientists would throw themselves into: the cognitive-motor dissociation [2]; the ability to respond mentally to an order without being able to speak, move or establish contact with the outside world. A variant of the Diving Bell and the Butterfly; that is, the appearance of a coma with consciousness. On the other hand, there are many cases of patients who wake up without consciousness and that can remain in an unresponsive wakefulness syndrome (also known as vegetative state). How to predict the possibility of awakening? And how to assess the possibility of a conscious awakening?

Since the 1960s in the United States and the Leonetti law of 2005 in France, paternalistic medicine has given way to personalised medicine, where the patient becomes an autonomous actor in his care and where practitioners must consider his choices as the main elements in decision-making. Advance directives [3,4], written by the patient or expressed by his or her family, take a fundamental place in the reflection process. Decisions to continue, limit or withdraw the life sustaining treatments (WLST) are no longer determined only by the prognosis of short and medium term survival, but also by the functional, cognitive and emotional quality of life, particularly in brain injured patients. Predicting awakening capacity and quality becomes essential to adapt ICU management to the patient's wishes.

The objective is to reduce the uncertainty of being able to apply the advance directives in the future. Uncertainty is the grey area in which are located unconscious patients who receive care against their will, and those whose care is withdraw although they could have awakening according to their will.

1. How to reduce the grey area?

Currently, society requires the physician to be able to provide the prognostic elements necessary for decision-making that is compatible with the patient's wishes. From the very first moments of intensive care hospitalisation, decisions to limit or withdraw the life sustaining treatments are issues inherent in medical practice and can lead to death quickly. In these situations, robust prognostic tools must assist communication between physicians, as well as with the patient and family (Fig. 1).

With the progress of research and new technologies, new tools are now available and can be used from the earliest stages of ICU management.

For example, neurophysiology is a field in which prognostication has become widespread. In the recently published study in the *New England Journal of Medicine*, Claassen et al. [5] highlight the importance of using early EEG in unconscious and brain-injured patients for the detection of cognitive-motor dissociation (CMD). Machine learning allows electrophysiological detection of brain activation to verbal commands in 15% of unresponsive even in slightly sedated. These early responses are correlated with an additional 30% positive outcome at one year. However, 14% of patients with no CMD also detected progress favourably and 56% of patients with CMD found progress adversely. We can question the heterogeneity of the study population or the impact of the pharmacology of the sedation but in any case, the grey area persists. Each tool seems to be limited and cannot be used to answer all questions. Here, the continuous EEG answers the question of the presence or absence of CMD, but not on the long-term prognosis.

2. One tool for one answer, or several tools for the right answer?

In the context of post-anoxic coma [6] and also globally in brain-injured patients [7], the answer appears to be the utility of multimodal analysis: neurophysiology (electroencephalogram and evoked potentials), biology (NSE and S100B) and imaging (quantified MRI) [8]. These recommendations also highlight the need for neuroscientific expertise in the management of care at the critical phase, and more especially at the prognostic phase. The performance of a multimodal prognostic analysis remains complex both in terms of logistical realisation (e.g. quantitative MRI) and scientific interpretation, and must be carried out taking into account the evolving nature of brain damage. Brain dynamics make it difficult to evaluate the ideal time-window for prognostic

https://doi.org/10.1016/j.accpm.2019.09.002

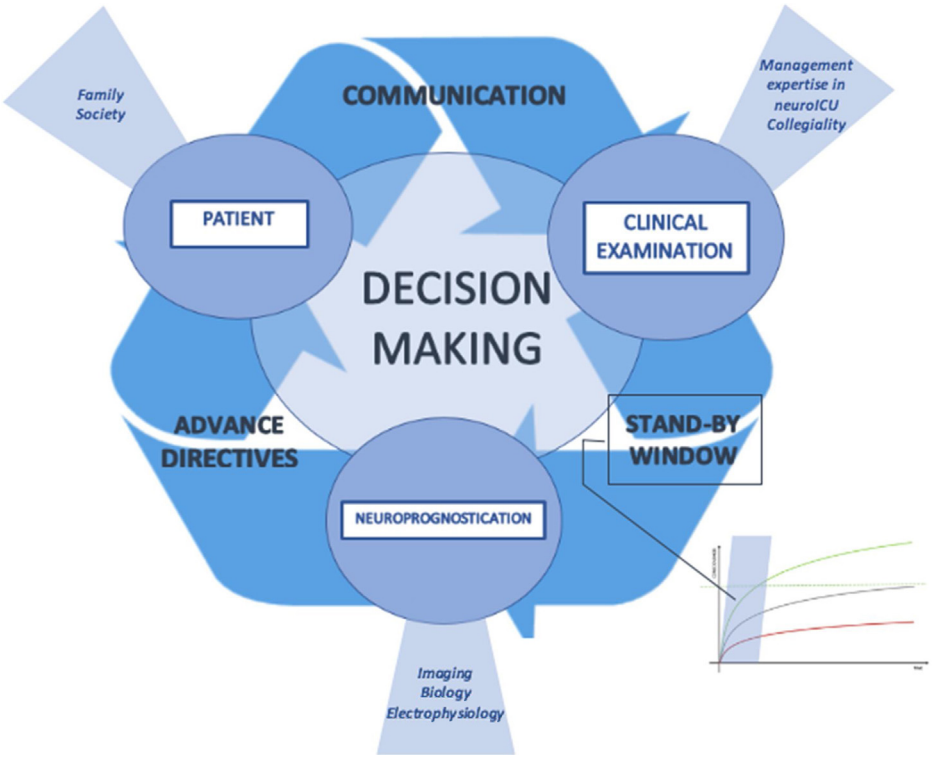


Fig. 1. Tools useful for decision-making in neuroprognostication.

analyses; not too early not to dangerously worsen the patient's clinical condition or be biased by initial therapies, nor too late to avoid therapeutic relentlessness. This notion of ideal time-window is essential and requires the expertise of a team specialised in neuroprognostication [9].

Claassen et al. recall that early examinations may be necessary to quickly identify patients for whom a positive outcome is possible, and especially those for whom a negative outcome is almost on. The better the initial progress, the better the recovery seems. In these cases, it is a matter of making the decision to continue care.

The American and English recommendations refer to an observation period of at least 3 days for patients with "perceived devastated brain injuries" [10]. These deadlines are short and seem to be part of a socio-economic and ethical dimension concerning the ability to access neuro-resuscitation care.

3. Where is the truth?

Each patient and pathology has its own evolution; the challenge lies in the estimation of this initial progression slope and timing of its evaluation. Waiting is essential to understand with certainty; waiting is the art of neuro ICU speciality.

In conclusion, neuro ICU alone makes possible a multimodal, global and multidisciplinary approach [11] to understand the question of the potential future awakening of these patients. The article by Claassen et al. is part of an innovative dynamic with the desire to answer this social question, to remove doubts in the medical answer and insist on the notion of temporality in decision-making.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Jennett B, Plum F. Persistent vegetative state after brain damage. A syndrome in search of a name. Lancet Lond Engl 1972;1(7753):734–7.
[2] Schiff ND. Cognitive motor dissociation following severe brain injuries. JAMA Neurol 2015;72(12):1413–5.
[3] Aubry R, End-of-life. euthanasia, and assisted suicide: an update on the situation in France. Rev Neurol (Paris) 2016;172(12):719–24.
[4] Fins JJ, Bernat JL. Ethical, palliative, and policy considerations in disorders of consciousness. Neurology 2018;91(10):471–5.
[5] Claassen J, Doyle K, Matory A, Couch C, Burger KM, Velazquez A, et al. Detection of brain activation in unresponsive patients with acute brain injury. N Engl J Med 2019;380(26):2497–505.
[6] Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VRM, Deakin CD, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. Resuscitation 2015;95:202–22.
[7] Rohaut B, Eliseyev A, Claassen J. Uncovering consciousness in unresponsive ICU patients: technical, medical and ethical considerations. Crit Care Lond Engl 2019;23(1):78.
[8] Velly L, Perlbarg V, Boulier T, Adam N, Delphine S, Luyt C-E, et al. Use of brain diffusion tensor imaging for the prediction of long-term neurological outcomes in patients after cardiac arrest: a multicentre, international, prospective, observational, cohort study. Lancet Neurol 2018;17(4):317–26.
[9] Rohaut B, Claassen J. Decision making in perceived devastating brain injury: a call to explore the impact of cognitive biases. Br J Anaesth 2018;120(1):5–9.
[10] Harvey D, Butler J, Groves J, Manara A, Menon D, Thomas E, et al. Management of perceived devastating brain injury after hospital admission: a consensus statement from stakeholder professional organizations. Br J Anaesth 2018;120(1):138–45.
[11] Bruder N, Boussen S, Velly L. Development of neurocritical care: enhanced neuromonitoring or better specialists' cooperation? Minerva Anestesiol 2017;83(1):9–11.

E. Bouchereau[a], V. Degos[b,c,*]
[a]*Department of anaesthesiology and intensive care, Sainte-Anne Hospital, 1, rue Cabanis, 75014 Paris, France*
[b]*Department of Anaesthesia and Critical Care, Pitié Salpetrière Hospital, AP–HP-SU, Paris, France*
[c]*Groupe recherche clinique BIOSFAST, Sorbonne University, 47-83, boulevard de l'Hopital, 75013 Paris, France*

*Corresponding author at: Groupe recherche clinique BIOSFAST, Sorbonne University, 47-83, boulevard de l'Hopital, 75013 Paris, France

E-mail address: vincent.degos@inserm.fr (V. Degos).