CORRESPONDENCE

Assessing Prognosis Following Cardiopulmonary Resuscitation and Therapeutic Hypothermia—a Critical Discussion of Recent Studies

by Prof. Dr. med. Frank Thömke in volume 9/13

Dr. med. Christoph Leithner
Prof. Dr. med. Christoph J. Ploner
Klinik für Neurologie, Charité Universitätsmedizin, Berlin

christoph.leithner@charite.de

PD Dr. med. Christian Storm
Klinik für Innere Medizin mit Schwerpunkt Nephrologie und internistische Intensivmedizin, Charite Universitätsmedizin, Campus Virchow Klinikum, Berlin

Conflict of interest statement
PD Storm has received consultancy fees and travel expenses from BARD, Zoll,, Covidien, and Philips.
Dr Leithner and Professor Plotner declare that no conflict of interest exists.

Prognostic Assessment Always Requires Several Parameters

An important point of criticism regarding the cited studies is the fact that the prognostic parameters under investigation are further used in decisions about stopping therapy. This entails the possibility of a self-fulfilling prophecy. In the study by Bouwes et al., for example, therapy was immediately ended or limited in 40 out of 42 patients with lacking somatosensory evoked potentials (SEP) (1).

We have repeatedly cared for patients who woke up again in spite of concentrations of neuron-specific enolase (NSE) >97 µg/L. The biggest impression was left by the case of a patient with a neuroendocrine tumor, whose NSE rose to >1000 µg/L. In assessing the NSE, malignant tumors should be regarded as confounders. In our opinion, the key message "Elevated serum concentrations of neuron-specific enolase have to be above 97 µg/L to serve as a safe indicator of an unfavorable prognosis" is therefore problematic in this abbreviated form. We think that the factually equating the bilateral absence of the pupillary light response or the corneal reflex with reliable indicators of a poor prognosis is equally problematic, because of possible examiner bias. Especially absent corneal reflexes should be assessed with a great deal of caution. Bouwes and Samaniego described 2 of 23, and 2 of 22, patients whose outcome was good in spite of absent corneal reflexes (1, 3).

A high degree of certainty in the prognostic assessment is possible only by basing it on several parameters, rather than a single one. We treat most patients for seven days before we limit their treatment according to an interdisciplinary prognostic algorithm, on the basis of several consistent parameters for a poor prognosis (2).

DOI: 10.3238/arztebl.2013.0421a

REFERENCES

1. Bouwes A, Binnekade JM, Kuiper MA, et al.: Prognosis of coma after therapeutic hypothermia: a prospective cohort study. Ann Neurol 2012; 71: 206–12.
2. Leithner C, Storm C, Hasper D, Ploner CJ: Prognose der Hirnfunktion nach kardiopulmonaler Reanimation und therapeutischer Hypothermie. Akt Neurol 2012; 39: 145–54.
3. Samaniego EA, Mlynash M, Caulfield AF, et al.: Sedation confounds outcome prediction in cardiac arrest survivors treated with hypothermia. Neurocrit Care 2011; 15: 113–19.
4. Thömke F: Assessing prognosis following cardiopulmonary resuscitation and therapeutic hypothermia—a critical discussion of recent studies. Dtsch Arztebl Int 2013; 110(9): 137–43.

A Word of Warning

In the past we investigated the development of biomarkers (for example, neuron-specific enolase [NSE]) and the neurological outcome in patients who had been treated with therapeutic hypothermia after CPR in a retrospective as well as in a prospective manner. For this reason we wish to express a warning against the NSE cutoff value that was attributed 100% specificity in the article.

According to our data, it is absolutely not the case that a poor prognosis can be assumed in patients whose NSE concentration is higher than 97 µg/L after therapeutic hypothermia following CPR. It should be noted, however, that in our prospective data collection none of the survivors had a concentration > 80 µg/L. Outside the study setting, we have repeatedly seen patients who survived fully intact neurologically with concentrations that were above the mentioned 97 µg/L NSE cutoff value (1).

As a matter of medical principle, we recommend clinical symptoms and presentation of the patient to be considered first and foremost when measuring neurological function. Individual biomarkers (which can be prone to failure) and imaging studies may be important for treatment options but should never be used solely in life and death decision making (2, 3).

DOI: 10.3238/arztebl.2013.0421b

REFERENCES

1. Schummer W, Schummer C, Wiegand J: High levels of neuron-specific enolase after CPR and good clinical outcome. Resuscitation 2010; 81: 365.
2. Pfeifer R, Börner A, Krack A, Sigusch HH, Surber R, Figulla HR: Outcome after cardiac arrest: predictive values and limitations of the neuroproteins neuron-specific enolase and protein S-100 and the Glasgow Coma Scale. Resuscitation 2005; 65: 49–55.
3. Pfeifer R, Ferrari M, Börner A, Deufel T, Figulla HR: Serum concentration of NSE and S-100b during LVAD in non-resuscitated patients. Resuscitation 2008; 79: 46–53.
4. Thömke F: Assessing prognosis following cardiopulmonary resuscitation and therapeutic hypothermia—a critical discussion of recent studies. Dtsch Arztebl Int 2013; 110(9): 137–43.

PD Dr. med. Wolfram Schummer
cand. med. Sebastian Hottenrott
Klinik für Anästhesie und Intensivtherapie
SRH Zentralklinikum Suhl und
Friedrich Schiller Universität Jena
cwsm.schummer@gmx.de

Conflict of interest statement
The authors declare that no conflict of interest exists.

In Reply:

I completely agree with my colleagues, that a prognostic assessment of a resuscitated patient and especially the subsequent therapeutic recommendations should not be based on a single finding. Decisions of such enormity should be made only on the basis of several indicators that consistently point at an unfavorable prognosis. In the case of only one unfavorable indicator or inconsistent findings, such decisions should be postponed, as I emphasized in my article on several occasions.

Leithner et al. quite rightly point out that NSE can also be raised if a patient has a tumor and can therefore be used as a parameter only in the absence of tumors. After cerebral hypoxia, NSE takes a typical course, with a peak mostly between the second and fourth day after resuscitation a and subsequent drop back down to normal values. Schummer and Hottenrott emphasize that they have "repeatedly" seen patients whose values were above the cutoff point and who survived neurologically intact; they explicitly mention two patients whose cases they published (1). In one of them, the NSE concentration was 72 ng/mL, which was notably below, and in the other, 98 ng/mL, which was just above the cutoff value that I am familiar with from the literature and which is generally cited—97 ng/mL. I do not think that this one patient alone raises fundamental doubt in the prognostic importance of NSE concentrations of this magnitude, as long as one is aware of the limited validity of a single parameter.

Leithner et al. critically mention "examiner bias" in the absence of corneal reflex and pupillary light response. In my opinion, we should be able to take it for granted that experienced intensivists and neurologists are able to identify the absence of these brain stem reflexes—and only these specialists should examine such patients and assess their prognosis. They also point out that in some series, patients had a good outcome in spite of the absence of a corneal reflex (2, 3). In one study that rated survival with severe neurological deficit and the need for continuous care as a good outcome (2), the only obvious fact is that both patients were conscious—which does not necessarily equate to a good outcome. This means a rather high rate of false-positive results in one series (3) on the one hand, and, on the other hand, a series of studies in which the prognosis in the absence of the corneal reflex was without exception poor. Does this one study make all other observations worthless or useless? I do not think so, as long as one is aware of the limited value of a single parameter and makes prognostic assessments only if several indicators show consistent results.

DOI: 10.3238/arztebl.2013.0422

REFERENCES

1. Schummer W, Schummer C, Wiegand J: High levels of neuron-specific enolase after CPR and good clinical outcome. Resuscitation 2010; 81: 365.
2. Samaniego EA, Mlynash M, Caulfield AF, et al.: Sedation confounds outcome prediction in cardiac arrest survivors treated with hypothermia. Neurocrit Care 2011; 15: 113–19.
3. Bouwes A, Binnekade JM, Kuiper MA, et al.: Prognosis of coma after therapeutic hypothermia: a prospective cohort study. Ann Neurol 2012; 71: 206–12.
4. Thömke F: Assessing prognosis following cardiopulmonary resuscitation and therapeutic hypothermia—a critical discussion of recent studies. Dtsch Arztebl Int 2013; 110(9): 137–43.

Prof. Dr. med. Frank Thömke
Fachbereich Neurologie, Klinikum Worms GmbH, Worms
frank.thoemke@klinikum-worms.de

Conflict of interest statement
The author declares that no conflict of interest exists.