NEUROLOGICAL OUTPUTS IN PATIENTS AFTER THE FIBRILLATION OF CIRCULATORY ARREST

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Abstract

The prognosis in patients after the fibrillation of circulatory arrest, who underwent immediate cardio-pulmonary resuscitation, is uncertain. In order to predict a neurological output, we can use the laboratory parameter of neuron-specific enolase (NSE).

Goal: The goal of this study was to assess the neurological output in 56 patients after a successful cardiopulmonary resuscitation that was carried out during non-traumatic circulatory arrest by Cerebral Performance Categories (CPC) score, and to assess the possible predictive indicators during mild hypothermia at 33 °C or 36 °C.

Results: In 20 patients, the cause was acute myocardial infarction with elevated ST divisions (STEMI). In 36 patients, the cause of the fibrillation of circulatory arrest was different. The NSE value in surviving patients after 72 hours of hospitalization was set at 16.6 (12.9–24.6) μg/l (in the deceased it was set at 161.2 (37.8–180) μg/l), which statistically correlated with the neurological prognosis and mortality in both groups. The strategy of temperature management (33 °C or 36 °C) did not affect the patients' neurological output. During discharge, the CPC score of 1–2 was present in 75% of patients after STEMI fibrillation arrest, and in 39% of patients after a fibrillation arrest from other causes.

Conclusions: Patients after STEMI fibrillation arrest had a better prognosis; a CPC score of 1–2 was present in 75% of patients. The NSE set 72 hours of hospitalization to predict the neurological outcome of patients.

Keywords: *Cerebral Performance Categories (CPC); Fibrillation of circulatory arrest; Neurological output; Neuron-specific enolase*

ORIGINAL ARTICLE

INTRODUCTION

Ventricular fibrillation is a rhythm disorder manifested by circulatory arrest that requires the immediate initiation of cardiopulmonary resuscitation. High-quality telephone-assisted urgent resuscitation (TAUR) including subsequent extended resuscitation have been shown to contribute to a better clinical outcome and reduce the risk of hypoxic brain damage. The most common cause of circulatory fibrillation is acute myocardial infarction. Other causes may be ischemic, dilated, or hypertrophic cardiomyopathy, myocarditis, congenital heart defects, aortic stenosis,

arrhythmogenic right ventricular dysplasia or primary arrhythmias (Kettner, 2018).

Therefore, one of the fundamental problems in these patients is the timely and reliable determination of the prognosis, which is necessary for the selection of the most suitable diagnostic and treatment procedure. However, the current possibilities for early forecasting are very limited. One possibility is the determination of neuron-specific enolase (NSE) (Stammet et al., 2015). NSE is a 433 amino acids-long acidic dimeric protein that includes the two isoenzymes enolase γγ and αγ. NSE is predominantly localized in neurons and neuroendocrine cells. Elevated NSE levels can be detected in the blood, and cerebrospinal fluid in association with brain damage in several pathological conditions – such as hypoxic damage during cardiac arrest, stroke, or brain trauma. Based on the results of the PROPAC (Prognosis in Postanoxic Coma) clinical study of Zandbergen et al. (2006), NSE levels >33 μg/l in the first 72 hours after cardiac arrest were identified as a reliable factor in determining an unfavourable neurological prognosis. After the established mild therapeutic hypothermia, the relationship between NSE and prognosis after cardiac arrest is not clear.

MATERIALS AND METHODS

This study included 56 patients who were hospitalized in the ICU of the Cardiology Department of the Faculty Hospital Pilsen for fibrillation of circulatory arrest between 05/2016 and 01/2018. In 20 patients, the cause of fibrillation arrest was the ongoing STEMI. In 36 patients, the cause was primary arrhythmia, ischemic heart disease, dilatation, and hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and significant aortic stenosis. The patients' age, cause of fibrillation arrest, NSE value 72 hours after admission, NT-pro BNP input value, temperature management strategy, Restoration of Spontaneous Circulation (ROSC) and output CPC scores were analysed. Continuous diagnosis of the neurological prognosis was evaluated by continuous monitoring of EEG, CT of the brain and examination of evoked potentials.

The group of patients with STEMI, which was predominantly male, were younger (Table 1). During discharge, we found a favourable CPC score of 1–2 in 75% of patients after fibrillation arrest in STEMI, and in 39% of patients after fibrillation arrest for other reasons. Patients after fibrillation of circulatory arrest in STEMI had a better neurological outcome than patients after fibrillation arrest for other reasons. In-hospital mortality in STEMI patients was 25%, compared to 42% in patients after fibrillation of circulatory arrest for other reasons.

RESULTS

Neither the NT-pro BNP baseline nor the temperature management strategy had an effect on the outcome of CPC scores in patients (Tables 2, 3). NSE and time to ROSC statistically significantly correlated with the CPC scores and the incidence of exitus letalis (Tables 4, 5). Of the total 56 patients, 25 had exitus letalis, and 17 had NSEs above 100 μg/l with a mean ROSC of 31 min. In patients after fibrillation of circulatory arrest in STEMI and for other reasons, a positive correlation between NSE levels and time to ROSC was confirmed. (Chart 1).

Values are the average (more or less) standard deviation, median (interquartile variance) or number (percentage). The differences between groups were calculated using the Student's *t*-test, Wilcoxon test and χ^2 test.

Multivariate logistic regression, association with exitus letalis or CPC ≥3 cannot be calculated, due to the effect of collinearity (Spearman correlation coefficient between NSE and ROSC is high 0.47, P = 0.0002). Both parameters remained important predictors of poor prognosis. ROSC and exitus letalis (P = 0.077), ROSC and high CPC (P = 0.0082), NSE and exitus letalis (NA), NSE and high CPC (P = 0.0035) – Table 6.

In all patients, Targeted Temperature Management (TTM) was initiated upon admission – with the target body temperature set at 33 °C or 36 °C for 24 hours, and the body temperature maintained at 37 °C for the next 72 hours. The temperature management strategy did not affect neurological output. In 42% of patients, the controlled hypother-

Table 1 – Characteristics of the sample group

	STEMI ***n* = 20**	**Other reasons for arrest** ***n* = 36**	***P***
Women, *n* (%)	2 (10.0)	6 (16.7)	0.49
Men, *n* (%)	18 (90.0)	30 (83.3)	
Age (years)	59.6 ± 11.7	67.4 ± 11.9	0.023
NSE (µg/l)	**16 (12–66)**	**29 (16–161)**	**0.059**
NT-proBNP (ng/l)	265 (83–574)	1,162 (237–3,292)	0.016
CPC score	1.5 (1.0–3.5)	4 (1–5)	0.096
ROSC (min.)	14.9 ± 12.8	19.5 ± 11.5	0.17
Temperature 33 °C, *n* (%)	11 (55.0)	26 (72.2)	0.19
EEG, *n* (%)	16 (80.0)	29 (80.6)	0.96
Evoked potentials, *n* (%)	3 (15.0)	13 (36.1)	0.094
CT of the brain, *n* (%)	5 (25.0)	14 (38.9)	0.29
Exitus letalis, *n* (%)	5 (25.0)	15 (41.7)	0.21

Table 2 – The correlation between ROSC and other parameters

The Spearman correlation coefficient between ROSC, NSE and NT-proBNP	***r***	***P***
NSE	0.47	0.0002
NT-proBNP	0.061	0.66
Another reason for fibrillation arrest		
NSE	0.49	0.0022
NT-proBNP	–0.085	0.62
STEMI		
NSE	0.28	0.24
NT-proBNP	–0.060	0.81

Table 3 – The influence of NT pro BNP on the prognosis (CPC, *Exitus letalis*)

	Exitus letalis ***n* = 15**	**Survivors** ***n* = 21**	***P***
Age (years)	70.1 ± 10,1	65.4 ± 12.9	0.24
NT-proBNP (ng/l)	1,529 (272–3,401)	832 (202–3,184)	0.91
NSE (µg/l)	161.2 (37.8–180.0)	16.6 (12.9–24.6)	<0.0001
ROSC (min.)	24.3 ± 12.0	16.2 ± 10.0	0.035
Temperature 33 °C, *n* (%)	11 (73.3)	15 (71.4)	0.90
	CPC ≥3 ***n* = 22**	**CPC 1 or 2** ***n* = 14**	
Age (years)	69.3 ± 9.8	63.8 ± 14.3	0.15
NT-proBNP (ng/l)	1,470 (272–2,374)	814 (132–5,505)	0.66
NSE (µg/l)	140.2 (31.8–180.0)	15.2 (12.5–18.1)	<0.0001
ROSC (min.)	24.8 ± 11.7	11.4 ± 3.9	<0.0001
Temperature 33 °C, *n* (%)	15 (68.2)	11 (78.6)	0.50

Table 4 – Univariate logistic regression, pathologically increased value of NSE (over 18 µg/l)

	OR	95% CI	*P*
Exitus			NA
CPC ≥3	15.83	2.95–85.07	0.0013

Table 5 – Univariate logistic regression, ROSC >15 min.

	OR	95% CI	*P*
Exitus	5.00	1.19–20.92	0.027
CPC ≥3	27.85	3.02–257.15	0.0034

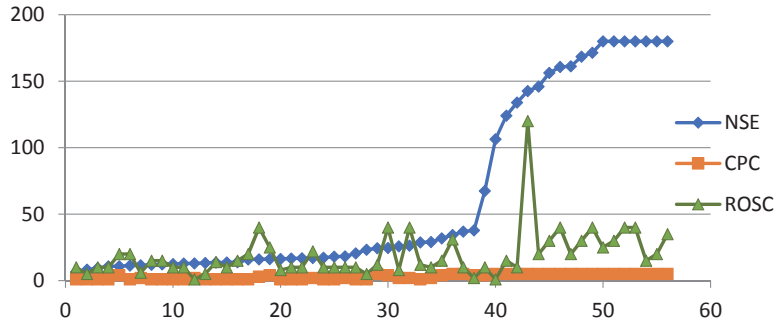

Chart 1 – The correlation between CPC, ROSC and NSE

mia of 33 °C for 24 hours was provided by ArcticSun cooling, 33% with Thermogard, and 25% of patients were only physically cooled. In one patient after fibrillation of circulatory arrest in STEMI, the temperature was regulated by ECMO (extracorporeal membrane oxygenation) – Chart 2.

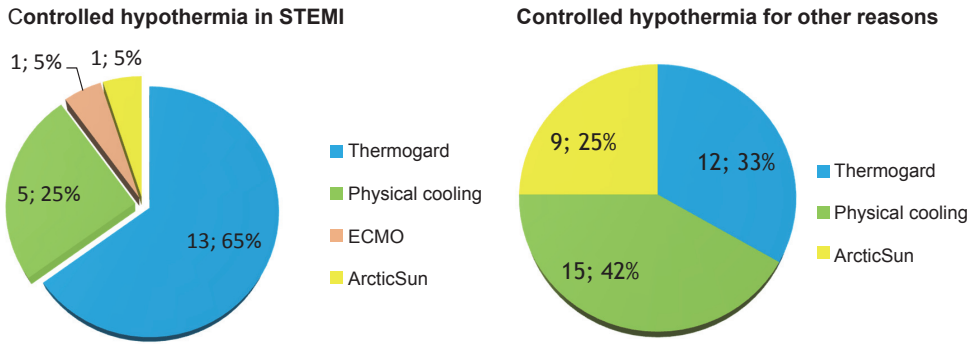

Chart 2 – Temperature management strategy in STEMI and other reasons

Table 6 – The relationship between, NT-proBNP, NSE, ROSC and controlled hypothermia and CPC

	CPC ≥3 *n* = 22	CPC 1 or 2 *n* = 14	
Age (years)	69.3 ± 9.8	63.8 ± 14.3	0.15
NT-proBNP (ng/l)	1,470 (272–2,374)	814 (132–5,505)	0.66
NSE (μg/l)	140.2 (31.8–180.0)	15.2 (12.5–18.1)	<0.0001
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Temperature 33 °C, *n* (%)	15 (68.2)	11 (78.6)	0.50

DISCUSSION

The results of many worldwide studies contribute to the continuous progress of resuscitation care in patients after circulatory arrest. According to Hsu et al. (2014), surviving patients with CPC 1 had the highest long-term survival, but those with CPC 4 had the lowest long-term survival. Of the total 2,417 patients, 24.1% were successfully resuscitated, of which 24.1% received TTM. In conclusion, they confirm better neurological outcome in patients with TTM. Dostálová et al. (2017) conclude that patients after cardiac arrest have significant cognitive (p = 0.016) and neuropsychiatric consequences (p = 0.023), but point to possible long-term changes in life and that CPC 3 is a very broad category. The retrospective observational study of Kim et al. (2016) confirms that the recovery of patients after cardiac arrest with CPC 3–5 was rare. The agreement in the validity of the used CPC score was confirmed by the studies of Nageeb et al. (2020). The study of Wang et al. (2016) shows that 90% of patients after cardiac arrest had CPC on discharge from hospital – even in the following 3 months – with analysis showing the presence of TTM in 3.2% of patients after cardiac arrest. The use of TTM was significantly associated with a favourable neurological outcome, regardless of the rhythm that caused the cardiac arrest. Muller et al. (2019) identified the establishment of NSE as a prognostic method in monitoring neurological output. The results of the multicentre cohort study (Taccone et al. (2019)) show that 4.2% of cardiac arrest survivors who were admitted to the intensive care unit eventually died after regaining consciousness. The most common causes were sepsis and acute respiratory distress syndrome (ARDS). The cross-sectional retrospective observational study of Kim et al. (2016) used the South-Korean national hospital registry to include patients with cardiac arrest who were treated with targeted temperature control. She found that patients who return ROSC after long cardiopulmonary resuscitation have a poor prognosis, and ROSC has a significant impact on their neurological outcome. Recovery of patients after cardiac arrest with CPC 3–5 was rare.

CONCLUSIONS

The establishment of NSE is a suitable parameter in predicting the neurological outcome in patients after fibrillation of cardiac arrest during therapeutic hypothermia. NSE values above 40 μg/l were associated with a poorer neurological outcome. Patients with STEMI had a better neurological outcome.

Conflict of interests

The authors have no conflict of interests to declare.

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