TITLE (SHORT, 200 CHARACTERS MAX.):

TRANSCRANIAL DOPPLER IN PATIENTS AFTER OHCA AND TARGETED TO HYPOTHERMIA OR NORMOTHERMIA: A SUBANALYSIS OF TTM 2

MAIN HYPOTHESES TESTED (2 MAX)

The main aim of this study is to describe and compare the changes in transcranial Doppler, within the first 3 days after OHCA and its relationships with 28-day hospital mortality.
A secondary aim is to investigate the effects of hypothermia and normothermia on transcranial Doppler, as well as relationships between transcranial Doppler during the first 3 days of ICU stay and quality of life (QoL).

SINGLE CENTER [ ] , MULTICENTER [X]

All TTM 2 centres.

PICO

Patients: All patients admitted in ICU after OHCA included in TTM Trial.
Exclusion: ultrasound detectable stenosis of hemodynamic relevance in the common carotid artery, internal carotid artery, or vertebral artery. Patients expected to die within 24 hrs
Intervention/Exposure/Prognostic factor: Cerebral Doppler
Comparison: Transcranial Doppler and outcome in patients after OHCA.
Outcome: in-hospital mortality and length of stay in ICU – QoL

DATA NEEDED FOR THE ANALYSIS
(SPECIFY VARIABLES AND MOTIVATE ANY PROPOSED ADDITIONS TO THE ECRF)

Cerebral Doppler within the first three days after ICU admission.
If possible, measurements of cerebral Doppler should be performed: 1) within 48 hours; 2) between 3-5 days; 3) between 7-10 days
In addition, data collection might be the following: 1) at ICU admission, before target management; 2) during hypothermia on normothermia (12 - 14 hrs after randomization); 3) when rewarming is complete (40 hrs after randomization); 4) at 96 hrs after randomization, when neurological prognostication will be performed; 5) at discharge from ICU

Technique: the blood volume flow in ICAs and Vas analysed using a linear array transducer and a colour coded ultrasound system. For BVF measurements the ICA is assessed approximately 1 cm above the carotid bulb and the VA in the vertebral segment (between C4-C5 or C5-C&). The angle corrected time averaged flow velocity (Vavg) over two cardiac cycles and the vessel diameter measured in the longitudinal plane. The cross sectional area (CSA) of the vessel is calculated from diameter assuming a circular vessel shape. BVF is calculated as the product of the CSA and the time averaged flow velocity. BVF is assessed at least twice for every vessel and the mean value is used for further analysis. CBF is determined as the sum of the BVF of both ICAs ad Vas. Additional data are assessed using a transcranial pulsed probe of the same ultrasound system: blood flow velocity (Vmean) of the middle artery index (MCA) and the BVR as well as the pulsatility index (PI) of the MCA, in each case in both sides.

Medical staff involved in patients' clinical treatment and therapeutic decisions must be unaware of the ultrasonic data.
Additional recording: 1) mean arterial blood pressure; 2) heart rate; 3) oxygen saturation; 4) partial pressure of oxygen and carbon dioxide; 4) blood levels of glucose, haemoglobin and sodium; 5) pH value; 6) treatment of sedatives and amines.
Neurologic outcome as assessed in TTM2.

LOGISTICS – HOW WILL ADDITIONAL DATA BE GATHERED?

Data will be gathered by individual participants to the study. Each centre interested in this study, should nominate a responsible – coordinator.
Centres will be provided with an extra CRF for transcranial Doppler measurement variables.

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

From previous studies (Nielsen N et al., NEJM 2013; Sustherasan Y et al., Critical Care 2015) we expect a 28-days mortality of around 50%. The analysis should then include at least 300 patients in order to observe at least 150 death events, allowing us to enter up to 15 covariates in a multivariable logistic regression, to identify if Doppler parameters are associated with mortality.

FUNDING (IF APPLICBABLE)

None.

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