TITLE (SHORT, 200 CHARACTERS MAX.):

NEUROPSYCHOLOGICAL OUTCOME AFTER CARDIAC ARREST

MAIN HYPOTHESES TESTED (2 MAX)

- The brief neurocognitive screening battery used in the main TTM2-trial will with high sensitivity and adequate specificity identify cardiac arrest patients with neuropsychological decline in five of six examined cognitive domains.
- Cardiac arrest patients will perform significantly worse on neuropsychological tests than a matched control group with myocardial infarction but without cardiac arrest, at both six months and two years time.

SINGLE CENTER [ ] , MULTICENTER [X]

Interested sites will be asked for their participation.

PICO

Patients: All survivors aged 18-80 years at participating sites. Patients with a clinical diagnosis of dementia before the cardiac arrest will be excluded from the substudy.

Intervention/Exposure/Prognostic factor: Detailed neuropsychological assessment six months and two years post-OHCA.

Comparison: Cardiac arrest patients will be compared with matched control patients with myocardial infarction but no cardiac arrest. Comparisons over time, six months compared to two years.

Outcome: Composite scores computed for each of the six cognitive domains; verbal functions, visual/constructive functions, short-term working memory, episodic memory, processing speed, and executive functions.

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

Descriptive background data and results of the MoCA (Montreal Cognitive Assessment) and SDMT (Symbol Digit Modalities Test) collected within the main TTM2-trial will be used. Additionally, neuropsychological assessment variables (raw and scaled scores, when applicable) for the following tests are proposed as a separate eCRF module:

TMT (Trail Making Test); WAIS-IV (Wechsler Adult Intelligence Scale – Fourth Edition) Vocabulary; D-KEFS (Delis-Kaplan Executive Function System) Verbal Fluency; WAIS-IV Block Design; WAIS-IV Matrix Reasoning; WAIS-IV Digit Span; WMS-III (Wechsler Memory Scale – Third Edition) Spatial Span; RAVLT (Rey Auditory Verbal Learning Test); WMS-III Logical Memory; BVMT-R (Brief Visuospatial Memory Test-Revised); D-KEFS Color Word Interference Test; HADS (Hospital Anxiety and Depression Scale); BADS DEX (Behavioural Assessment of Dysexecutive Syndrome – Dysexecutive Questionnaire); MFI-20 (Multidimensional Fatigue Inventory); MISS (Minimal Insomnia Symptom Scale).

LOGISTICS – HOW WILL ADDITIONAL DATA BE GATHERED?

At the regular six month follow-up of the TTM2-trial, patients will be invited to participate in this substudy. The additional data will be gathered at a separate appointment with a standardized neuropsychological assessment, at a time close to the regular TTM2 six months post-OHCA follow-up, and a two years post-OHCA follow-up, respectively. We will recruit neuropsychologists, psychologists and psychology students (with supervision from a psychologist) to administer the assessment. We aim to coordinate this with the substudy of Physical Activity After Cardiac Arrest. Average duration of the main neuropsychological assessment is estimated to 65-85 minutes.

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

Raw scores from all neuropsychological tests will be converted to standardized scores in accordance with normative sample data for each test, and then converted to *z*-scores. Test data will be grouped based on the main cognitive domain measured by the test, and a composite *z*-score will be computed for each cognitive domain. When not included in the *z*-score, covariate adjustments of age, gender, level of education, hypertension, diabetes and depression will be made in between-group comparisons.

Power calculations was based on earlier studies with the subtest TMT A, a test commonly used when assessing processing speed in cardiac arrest patients/patients with myocardial infarction without cardiac arrest. According to these calculations, the sample size is estimated to approximately 150-200 OHCA survivors, and the same amount of matched patients with ST-elevation myocardial infarction without cardiac arrest matched for age, gender and time of event as a control group.

The neuropsychological assessment will be repeated two years post-OHCA to investigate to what extent the long-term cognitive outcome of the survivors is accurately predicted by the six months follow-up. Previous findings on this matter are scarce, which is why this will be examined exploratively.

FUNDING (IF APPLICABLE)

Skane University Hospital, Lions Foundation Skane for study coordination, test licenses, eCRF development and a small reimbursement to sites. Applications for further funding are pending.

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