TITLE (SHORT, 200 CHARACTERS MAX.):

PHYSICAL ACTIVITY AFTER CARDIAC ARREST

MAIN HYPOTHESES TESTED (2 MAX)
Many myocardial infarction patients do not obtain physical activity and physical training to the extent recommended for secondary prevention of cardiovascular disease. Whether this is true also for OHCA-survivors is unknown, but CA-induced cognitive impairment may make this population less prone to physical activity and therefore in more need of specific interventions. The TTM2-trial follow-up protocol includes two questions on physical activity and one objective measure of overall physical function, the Timed-Stands Test (TST). The purpose of this sub-study is to validate these assessments and provide additional information on possible reasons for physical inactivity.

The specific hypotheses for this sub-study are:

1. The self-reported questions of physical activity and physical training and the TST used in the TTM2 main trial follow-up are valid measures and correspond well to objectively measured physical activity (accelerometer Actigraph) at 6 months post-arrest.

2. Physical inactivity is more common among OHCA-survivors compared to matched controls with ST-elevation myocardial infarction (STEMI), and associated with cognitive impairment and emotional problems including anxiety, depression and kinesiophobia at 6 months post-arrest.

SINGLE CENTER [ ], MULTICENTER [X]

PICO
Patients: All surviving patients age 18-80 years at the participating sites will be invited.

Intervention/Exposure/Prognostic factor:
Patients will be provided a hip-placed Actigraph to wear during one week. At the same time they will report their physical activity in a diary.
Patients will report emotional problems through two questionnaires, the Hospital Anxiety and Depression Scale (HADS) and the Tampa Scale for Kinesiophobia Heart (TSK-SV Heart) that assess fear of movement.
Cognitive impairment will be assessed in detail through the neuropsychological sub-study run in parallel. Alternatively, we will use information from the two cognitive tests MoCA and SDMT, performed as part of the main trial.
Self-perceived mobility restrictions will be reported by the patients through the question of mobility included in the EQ-5D-5L^{TM} health survey, also part of the main trial follow-up.

Comparison:
Physical activity, assessed by the two questions (physical activity and physical training) and by the TST in the main trial, will be compared with objectively measured physical activity according to the Actigraph (hypothesis 1).
To test hypothesis 2 patients with different levels of physical activity will be compared for differences in cognitive function, physical function and emotional problems (anxiety, depression and kinesiophobia).

In addition, the OHCA-survivors will be compared with STEMI control patients matched for age, sex and time-of-event regarding potential differences in the level of physical activity, physical function, cognitive impairment and emotional problems.

Outcome:
Hypothesis 1: Correspondence between the simple self-reported questions asked to measure the patients' physical activity and objective testing by Actigraph.
Hypothesis 2: The level of physical activity measured by the simple self-reported questions and the Actigraph will be compared between patients and controls, and associations to variables with assumed importance for physical activity investigated (cognitive impairment, physical function, and emotional stress).

DATA NEEDED FOR THE ANALYSIS
(SPECIFY VARIABLES AND MOTIVATE ANY PROPOSED ADDITIONS TO THE ECRF)
Additional data includes the two instruments HADS and TSK-SV Heart and results of the Actigraph measurement. The HADS consist of two subscales with 7 items each. The TSK-SV Heart includes 17 statements with four different alternatives. Additional information on who, when and how the questionnaire was answered will be collected. We suggest a separate eCRF module for this sub-study.

LOGISTICS – HOW WILL ADDITIONAL DATA BE GATHERED?
Intervention/Exposure/Prognostic factor:
Patients will be asked for participation at the time of their main TTM2 follow-up visit. Patients who are interested in participation will be provided written information about the study, the two additional questionnaires (HADS, TSK-SV Heart) to fill in at home, and an additional appointment, preferably within 2 weeks.
At the appointment patients will be provided a hip-placed Actigraph to wear during one week/10 days. At the same time they will report about their physical activity in a diary. The Actigraph and the diary will be returned by the patients in a prepaid, addressed envelope. They will also be asked to again answer the questions about physical activity and physical training considering an average week/ during the past 4 weeks and rate to what extent the last week has been reflecting an average week.
Control patients with STEMI and matched for age, sex and time-of-event will be recruited at one site in each participating country. They will complete the tests included in the main TTM2 follow-up and this sub-study. Our intention is to coordinate this sub-study with another proposed sub-study investigating neuropsychological outcome.

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE
The aim is to include 150-200 OHCA-survivors. To obtain this number of OHCA-survivors participating sites will need to include 440 patients into the TTM2, with an estimated survival rate of 50%, and an expected missing rate of 10%.

Hypothesis 1: Psychometric properties of the two questions of physical activity used at the second time-point will be evaluated and described by comparison to the chosen criterion standard (Actigraph) by cross tabulation to determine the counts and percentages for combinations of categories (based on established categorization of three different levels of physical activity for secondary prevention). In addition, relationship between the first and second time use of the questions will be compared to investigate stability. All psychometric

evaluations will be performed according to guidelines of reporting accuracy diagnostics by the STARD recommendations.

Hypothesis 2: Descriptive statistics of number and percentage of OHCA-survivors and STEMI-controls that obtain enough physical activity or not will be presented and compared by the Fisher test. Variables with an assumed importance for physical activity (cognitive impairment, physical function, emotional problems) will be presented descriptively and correlations evaluated by Spearmans. Potential differences between the groups for these variables will be tested by Mann Whitney Wilcoxon test or Kruskal Wallis test for continuous data, or Fisher test for categorical data. Due to the explorative design of this study p values<0.05 will be used overall to indicate potential statistical significant results. Effects size will be presented in addition to p-values as absolute differences or effect size measures by the Cohen's *d* for continuous variables. Since this is the first study to evaluate physical activity after OHCA no previous data to perform power calculations is available and all results will be identified as hypothesis generating trends only.

FUNDING (IF APPLICBABLE)
Separate funding for this study is necessary. Current funding is estimated to cover the cost of Actigraphs, study coordination, the additional eCRF module and a small reimbursement to participating sites. Additional funding is being applied for.

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