TITLE (SHORT, 200 CHARACTERS MAX.):

DO PLASMA COPEPTIN LEVELS PREDICT THE RISK OF DEATH AFTER OUT OF HOSPITAL CARDIAC ARREST?

MAIN HYPOTHESES TESTED (2 MAX)

<1. Plasma copeptin. MR-proArenomedullin and CT-pro-Endothelin 1 levels during ICU admission are independently associated with short- and long-mortality

SINGLE CENTER [ ] , MULTICENTER [X]

<Halmstad>

<All Swedish sites participating in TTM2 and contributing with blood samples for the TTM2 biobank.>

PICO

Patients: All patients included in TTM2 study at the relevant sites

Intervention/Exposure/Prognostic factor: Plasma Copeptin. MR-pro-ADM and CT-pro-ET1 (hereafter 'biomarker') concentrations on ICU admission and up to 3 days post-ICU admission or until death/discharge.

Comparison: 1. Highest ICU plasma biomarker concentrations in survivors and non-survivors. 2. Highest ICU plasma biomarker concentrations in patients analysed according to quartiles.

Outcome: Primary 180 day mortality. Secondary: 30-day and 12-month mortality

ICU survival, hospital survival, time on organ support (with predefined criteria 'organ support': VP requirement above 0.05 µg/kg/min norepinephrine or equivalent if patient is on sedation or any dose if not sedated, Vasopresor-Inotrope index during ICU stay.

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

Plasma biomarker levels on ICU admission and Days 1,2,3 or until death/discharge. Day 1 I defined as 12-24 post ICU admission, Day 2 is defined as 25-48 hours post ICU admission, Day 3 is defined at 49-72 hours post ICU admission.

Minimal dataset of prognostic factors to the included in the multivariable analysis based of prior studies (eg. age, tme from CPR to ROSC, witnessed CA, initial shockable rhythm, TTM2 allocation group)

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

<Power calculation and sample size:

There are no data regarding the independent prognostic value of MR-pro-ADM and CT-pro-ET1 in OCHA patients. In a recent study (Geri et al . CCM 2015;43:422.429), and independent prognostic value of admission values of plasma CoPeptin could be demonstrated for 1 year mortality. The sample size in this study was 298 patients.

A ROC analysis will be conducted for each biomarker to define the optimal cut-off concentration fo4 180-day mortality. We will use the biomarker peak value from each study participant for our ROC analyses. The optimal cut-off concentration will be defined according to the corner of the ROC curve defined with the positive likelihood ratio. A convenience sample of 200 patients will be used here (=derivation cohort). To further test the discriminative value of biomarkers, a validation cohort of a further 200 patients will be used.

To test for the association between plasma biomarker levels and the end points, a multivariable analysis will be conducted. The original TTM study demonstrated a 180-day mortality frequency of 50%. Assuming similar frequencies for the current study, one may expect about 200 outcomes in a study population of 400 patients. Conservatively estimated, this allows for the correction of up to 20 dependent variables in a multivariable analysis.

The total sample size will therefore be (200+200)= 400 patients.

FUNDING (IF APPLICBABLE)

<No funding yet. Group will apply for funding 2017 to account for blood sample analysis of endogenous catecholamine levels.>

CORRESPONDING AUTHORS NAME, INSTITUTION & E-MAIL ADDRESS:

<Petter Wilander>, <Hallands hospital Halmstad, Dept. of Operative- and Intensive care medicine, SE-30185 Halmstad>, <petter.wilander@regionhalland.se>

CO-WORKERS:

<Frank Zoerner>, <Michelle Chew>