TITLE (SHORT, 200 CHARACTERS MAX.):

VASOPRESSOR RESPONSIVENESS IN RELATION TO PLASMA CATECHOLAMINE LEVELS AND EFFECT ON SURVIVAL AFTER CARDIAC ARREST

MAIN HYPOTHESES TESTED (2 MAX)

<1. Plasma catecholamine levels at the time of admission correlate positively with vasopressor requirement

2. Low vasopressor requirement correlates positively with survival>

SINGLE CENTER [ ] , MULTICENTER [X]

<Halmstad>

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

PICO

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

Intervention/Exposure/Prognostic factor: Plasma catecholamine concentrations and vasopressor requirement

Comparison: 1. Plasma catecholamine levels in patients with 'low' and 'high' vasopressor requirement, 2. Plasma catecholamine levels in survivors and non-survivors and 3. Vasopressor requirement in survivors and non-survivors.

Outcome: ICU survival, hospital survival, 30 and 90 day mortality. 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, CRRT and mechanical ventilation) .

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

<Bodyweight, total dose epinephrine until ROSC, total dose norepinephrine/kg bodyweight during first 24 hours in ICU.

Hemodynamics data at baseline (ICU arrival), 4h, 8h, 12h, 16h, 24h, 48h, 72, 96h:

- SBP, DBP, MAP, heart rate, temperature, norepinephrine dose (µg/kg/min), cumulative dose of sedation

Organ support data:

- Time on inotropy (levosimendan, dobutamine), time on CRRT, time on mechanical ventilation, time on sedation, time on norepinephrine (>0.5µg/kg/min)

Plasma norepinephrine concentration in earliest sample taken, preferably at arrival in ER. Plasma epinephrine concentration at ICU arrival. Time of last epinephrine injection and time of ICU samples taken.

Outcome data:

- ICU survival, hospital survival, 30 and 90 day mortality, vasopressor free >24h, incidence of acute kidney injury (AKI), chronic kidney disease with need for dialysis.

Please send this form as a pdf to ttm2@ttm2trial.org

LOGISTICS – HOW WILL ADDITIONAL DATA BE GATHERED?

<outcome data are probably already collected according to TTM2 study protocol?

Epinephrine- and norepinephrine- dosages have to be calculated from patient journals. If possible, the data should be documented on-site and reported electronically in the TTM2 data report.>

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

<Power calculation and sample size:

Normal range for epinephrine serum concentration: up to 900 pg/mL, normal range for serum norepinephrine: up to 600 pg/mL.

Both epinephrine- and norepinephrine-concentrations after cardiac arrest have been shown to increase to supraphysiological levels. While epinephrine plasma levels have been shown to be up to 3000 times as high as baseline levels in healthy individuals, norepinephrine concentration is increased 30- 90 times in humans in cardiac arrest. Serum norepinephrine concentration in non-responders is only increased 30 times or less compared to baseline. We hypothesize therefore a difference of at least 50% between responders and non-responders.

Power calculation for comparison of 2 means: 2-sample, 2-sided equality:

Group A mean 6000 pg/mL, group B 5000 pg/mL, SD 2500 pg/mL, sampling ratio 1.

Sample size 98 patients, 1-beta 0.80 and alpha 5%.

Statistical analysis with ANOVA and non-parametric test

FUNDING (IF APPLICBABLE)

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

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