TITLE (SHORT, 200 CHARACTERS MAX.):

THE ASSOCIATION OF TARGET TEMPERATURE ON OUTCOME AND HEMODYNAMICS IN OUT-OF-HOSPITAL CARDIAC ARREST PATIENTS WITH SHOCK ON ADMISSION

MAIN HYPOTHESES TESTED (2 MAX)

1. Treatment at 33°C improves outcome in patients with circulatory shock on admission
2. Treatment at 33°C improves hemodynamic parameters

SINGLE CENTER [ ] , MULTICENTER [X]

<Site 2>

PICO

Patients: Patients with shock on admission (moderate and severe).

Intervention/Exposure/Prognostic factor: Targeted hypothermia

Comparison: Targeted normothermia/avoidance of fever

Outcome: Primary outcome 180-day mortality. Secondary outcomes ICU and 30-day mortality, severity of shock assessed by heart rate (HR), mean arterial pressure (MAP), vasopressor doses, and lactate during the intervention and extended circulatory sequential organ assessment score (SOFA), peak lactate, and fluid balance daily during the first 7 days in the ICU.

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

Outcome data – ICU-, 30- and 180-day mortality

Cause of death, presumed

Patient- and cardiac arrest demographics

HR, MAP and lactate at 0, 2, 4, 12, 20, 28, 32, 36 and 40 hours

Type of vasopressor- and sedative agent/s and total dose during 0-40 hours

Daily extended circulatory SOFA score (0-8) in the ICU during day 1-7

Daily peak lactate and daily fluid balance in the ICU during day 1-7

Reason for transfer from the ICU (improved/ready for ward, palliation, move to other ICU, death)

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

Not applicable

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

Total 1900 patients enrolled in study. In TTM 1 14,8% of included patients had moderate chock on admission and patients with severe chock (systolic blood pressue < 80 mm Hg) were excluded. Estimated 20 % or 380 patients of included patients will have shock giving <mark>adequate power</mark> to detect difference in primary outcome.

PRELIMINARY TABLES AND FIGURES:

Table 1

Utstein style table stratified according to patients with severe chock, moderate shock (and aggregated) compared to no shock including: demographics (Y/N; age, male sex, chronic heart failure, myocardial infarction, arrhythmia, hypertension, renal impairment, previous PCI, previous CABG), arrest witnessed (Y/N), shockable rhythm (Y/N), time to ROSC, primary rhythm, bystander CPR (Y/N), total dose epinephrine, number of defibrillations, use of mechanical compression-decompression device (Y/N), Acute ST segment elevation or LBBB on first ECG, PCI (Y/N), success of PCI (Y/N), median time to revascularization, cooling method, time to target temperature, UCG finding on admission, lactate concentration on admission, and all-cause mortality ICU, 30- or 180-day.

Table 2

Clinical events in patients with severe chock, moderate shock (and aggregated) stratified to TTM-33 or normothermia: Acute ST segment elevation or LBBB on first ECG, PCI (Y/N),PCI, success of PCI (Y/N), median time to revascularization, use of mechanical compression-decompression device (Y/N), arryhtmia (bradycardia, AF, VF/VT), urine output, blood products at day 1-7; length of stay (ICU and hospital), SOFA-score day 2,4, and 6, total type of vasopressor and vasopressor dose during intervention, total dose of sedatives and type of sedative during intervention, mortality (ICU, hospital, 30 and 180 days), presumed cause of death (cerebral, cardiac, multiple organ failure and other)

Table 3

Multivariate model with age, initial rhythm, time to ROSC, successful PCI, previous cardiac disease and targeted temperature management.

Fig 1

Consort statement style flow diagram depicting enrollment, allocation, follow-up and analysis.

Fig 2 a

MAP, HR, lactate during the first 40 hours for patients with early moderate and severe shock stratified to TTM-33 vs. normothermia (boxplot).

Fig 2 b

Circulation extended SOFA score and peak lactate/day for day 1-7 for moderate and severe shock stratified to TTM 33 vs. normothermia (box plots).

Fig 3

Kaplan Meier plot of circulatory shock, moderate and severe stratified according to TTM 33 vs. normothermia with mortality as effect, 0-180 days

FUNDING (IF APPLICBABLE)

Not applicable

CORRESPONDING AUTHORS NAME, INSTITUTION & E-MAIL ADDRESS:

<Name>, <institution>, <e-mail>

CO-WORKERS:

<Name>, <Name>, <Name>,…..