Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Nielsen N, Wetterslev J, Cronberg T, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med 2013;369:2197-206. DOI: 10.1056/NEJMoa1310519

(PDF updated March 6, 2014.)

Supplementary appendix

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Funding

The TTM-trial was funded by independent research grants from the non-profit or governmental agencies: Swedish Heart Lung Foundation; Arbetsmarknadens försäkringsaktiebolag (AFA)-insurance Foundation; The Swedish Research Council; Regional research support, Region Skåne; Governmental funding of clinical research within the Swedish NHS (National Health Services); Thelma Zoega Foundation; Krapperup Foundation; Thure Carlsson Foundation; Hans-Gabriel and Alice Trolle-Wachtmeister Foundation for Medical Research; Skåne University Hospital; Sweden, TrygFonden, Denmark, and the European Clinical Research Infrastructures Network. There was no commercial funding.

Acknowledgements

We would like to thank patients, relatives and clinical and research staff at all trial sites.
We would also like to thank Björn Biber, Anders Waldenström, Lars Wallentin, Anders Perner, Liz Jergle-Almquist, Anne-Mette Budde, Ingunn Heie Anundskaas, Isabelle Mercier-Konig, Cinzia Baldini, Emma Thomas-Jones, Kerry Hood, Sharon Micallef, Bert Gustavsson, Anders Dessmark, Johan Malm, Lars Hård, Sofia Hörberg, Mattias Paulsson, Bernt Nielsen, Ema Erkocevic.

SUPPLEMENTARY METHODS

Inclusion and exclusion criteria

Inclusion criteria

1. Age ≥18 years.

2. Out of hospital cardiac arrest of presumed cardiac cause.

3. Sustained return of spontaneous circulation (ROSC)[#].

4. Unconsciousness (GCS <8) (patients not able to obey verbal commands) after sustained ROSC.

[#]Sustained ROSC: Sustained ROSC is when chest compressions have been not required for 20 consecutive minutes and signs of circulation persist

Exclusion criteria

1. Obvious or suspected pregnancy

2. Known bleeding diathesis (medically induced coagulopathy (e.g. warfarin, clopidogrel) does not exclude the patient).

3. Suspected or confirmed acute intracranial bleeding

4. Suspected or confirmed acute stroke

5. Unwitnessed cardiac arrest with initial rhythm asystole

6. Known limitations in therapy and Do Not Resuscitate-order

7. Known disease making 180 days survival unlikely

8. Known pre-arrest Cerebral Performance Category 3 or 4

9. >4 hours (240 minutes) from ROSC to screening

10. Systolic blood pressure <80 mm Hg in spite of fluid loading/vasopressor and/or inotropic medication/intra aortic balloon pump[#]

14. Temperature on admission <30°C.

If the systolic blood pressure (SBP) was recovering during the inclusion window (220 minutes) the patient could be included. The standard definition of shock did not preclude inclusion: A systolic blood pressure<90mmHg for >30min or end-organ hypoperfusion (cool extremities, urine output<30ml/hour, heart rate <60 beats/min).

Neurological prognostication

All patients in the trial were actively treated until a minimum 72 hours after the intervention period, i.e. 108 hours after start of treatment (end of phase 3), when neurological evaluation was done on patients not regaining consciousness. Exceptions from this rule were 1) patients with myoclonus status[#] in the first 24 hours after admission and a bilateral absence of N20-peak on median nerve somatosensory evoked potentials (SSEP), 2) patients who became brain dead due to cerebral herniation and 3) because of ethical reasons described below. External blinded physicians evaluated the patient at the end of phase 3 and made a statement on neurological prognosis. At that time-point, limitations in and withdrawal of therapy could be instituted by the treating physicians. The neurological evaluation was based on clinical neurological examination (including Glasgow Coma Scale (GCS), pupillary and corneal reflexes), SSEP and electroencephalogram (EEG). Biomarkers for brain damage were not used for operational prognostication.

Findings allowing for discontinuation of active intensive care:

- Brain death due to cerebral herniation.
- Severe myoclonus status[#] in the first 24 hours after admission and a bilateral absence of N20-peak on median nerve SSEP.
- Minimum 72 hours after the intervention period: persisting coma with a Glasgow Motor Score 1-2 and bilateral absence of N20-peak on median nerve SSEP.
- Minimum 72 hours after the end of the intervention period: persisting coma with a Glasgow Motor Score 1-2 and a treatment refractory status epilepticus*.

Generalized myoclonic convulsions in face and extremities and continuous for a minimum of 30 min.

* Status epilepticus defined by EEG as sequences (>10 sec) of repetitive epileptiform discharges with an amplitude >50μV and a medium frequency ≥1Hz, constituting >50% of a 30 minute period in a patient with or without clinical manifestations. Treatment refractory defined as unresponsive to treatment with propofol, midazolam or pentothal to a slow suppression burst pattern for 24 hours in combination with at least one intravenous antiepileptic substance (including valproate and/or fos-Phenytoin) in adequate dose for at least 24hours. Free use of further antiepileptic substances and combinations at the discretion of the attending physician.

Patients with Glasgow Motor Score 1-2 at 72 hours or later after the end of the intervention period who had retained N20-peak on the SSEP, or patients in hospitals where SSEP was not available, were re-examined daily and the limitations/withdrawal of intensive care considered if GCS-Motor did not improve and metabolic and pharmacological affection was ruled out. Recommendations and decisions on life sustaining treatment were recorded.
Active treatment could be withdrawn prior to 72 hours after the intervention period for ethical reasons (for instance: previously unknown information about disseminated end-stage cancer or refractory shock with end-stage multiorgan failure). However assumptions of a poor neurological function were not allowed be the sole reason for withdrawal of active treatment prior to 72 h after the intervention period (exception: brain death and early myoclonus status including a negative SSEP).

Details of the intervention

The intervention period of 36 hours commenced at the time of randomization. All patients were sedated, with sedation mandated in both groups until the end of the intervention period. The choices of sedatives, analgesics and neuromuscular blocking agents were at the discretion of the treating physician. Core body temperature was measured with a temperature probe in the urinary bladder, or with an esophageal or intravascular probe in patients with low urinary output.

The goal of the intervention was to achieve the allocated temperature as rapidly as possible using ice-cold fluids, ice-packs, and intravascular or surface temperature management devices at the discretion of the site. Patients with an initial body temperature between 30°C and 33°C were actively rewarmed to 33°C at a maximum rate of 0.5°C per hour in both groups. For patients allocated to the 36°C group, passive rewarming to 36°C was mandated in the range from 33°C to 36°C, after which controlled temperature management was commenced and continued throughout the intervention period. After 28 hours gradual rewarming to 37°C by 0.5°C per hour was commenced in both groups.

At 36 hours mandatory sedation was discontinued or tapered. After the intervention period the intention was to maintain the body temperature for unconscious patients below 37.5°C until 72 hours post-cardiac arrest, using fever control measures at the discretion of the sites. Concomitant intensive care, cardiological and neurological treatment followed standard practice.

Data collection and verification

Data for the primary outcome measure were obtained from national- or hospital registries, or from contacting patients, relatives, and general practitioners. Data for the neurological evaluation at 180-day follow up were obtained from an in-hospital visit, a visit of a trial investigator at the patients' residence or from telephone contact with patients, relatives, or general practitioners. The remaining secondary outcomes were obtained from direct observations during the hospital stay or from hospital registries. The primary outcome, temperature data, and eligibility criteria were verified source data in all patients. Pre-randomization characteristics, adverse events, and the secondary outcomes were verified with a random sample of at least 20% of the patients.

SUPPLEMENTARY RESULTS

Shivering and fever

There was no statistically significant difference between the two trial groups in the reported number of patients with shivering: 141 patients (30%) in the 33°C group and 156 (34%) patients in the 36°C group, P=0.20. The number of hours per day with a temperature >38°C on days 3 through 7 was similar in the 33°C group and the 36°C group (median 1, interquartile range 0-4 in both groups; P=0.77). The highest recorded temperature and the hours of temperature above 38°C on days 2 to 4 are depicted in the Supplementary Appendix, Table S6.

Adjusted analyses, specific analysis populations, and subgroup analyses

Similar results were obtained in the unadjusted analyses, and the analyses adjusted for stratification and design covariates (see Supplementary Appendix Tables S10 and S11). The effect of the intervention did not depend significantly on the binary variables defined by sex, age > 65 years, presence of initial shockable rhythm, time from cardiac arrest to return of spontaneous circulation above 25 minutes, and presence of shock at admission (Supplementary Appendix Figure S2).

The results for the primary outcome were also similar for the intention-to-treat and the per-protocol analysis populations. In the intention-to-treat analysis, there were 236 deaths in 475 patients (50%) in the 33°C group and 228 deaths in 471 patients (48%) in the 36°C group. In the per-protocol analysis, there were 235 deaths in 472 patients (50%) in the 33°C group and 224 deaths in 464 patients (48%) in the 36°C group.

SUPPLEMENTARY FIGURES AND TABLES

Figure S1. CONSORT flow chart

Assessment, randomization, analysis populations, and follow-up of the patients in the TTM trial.

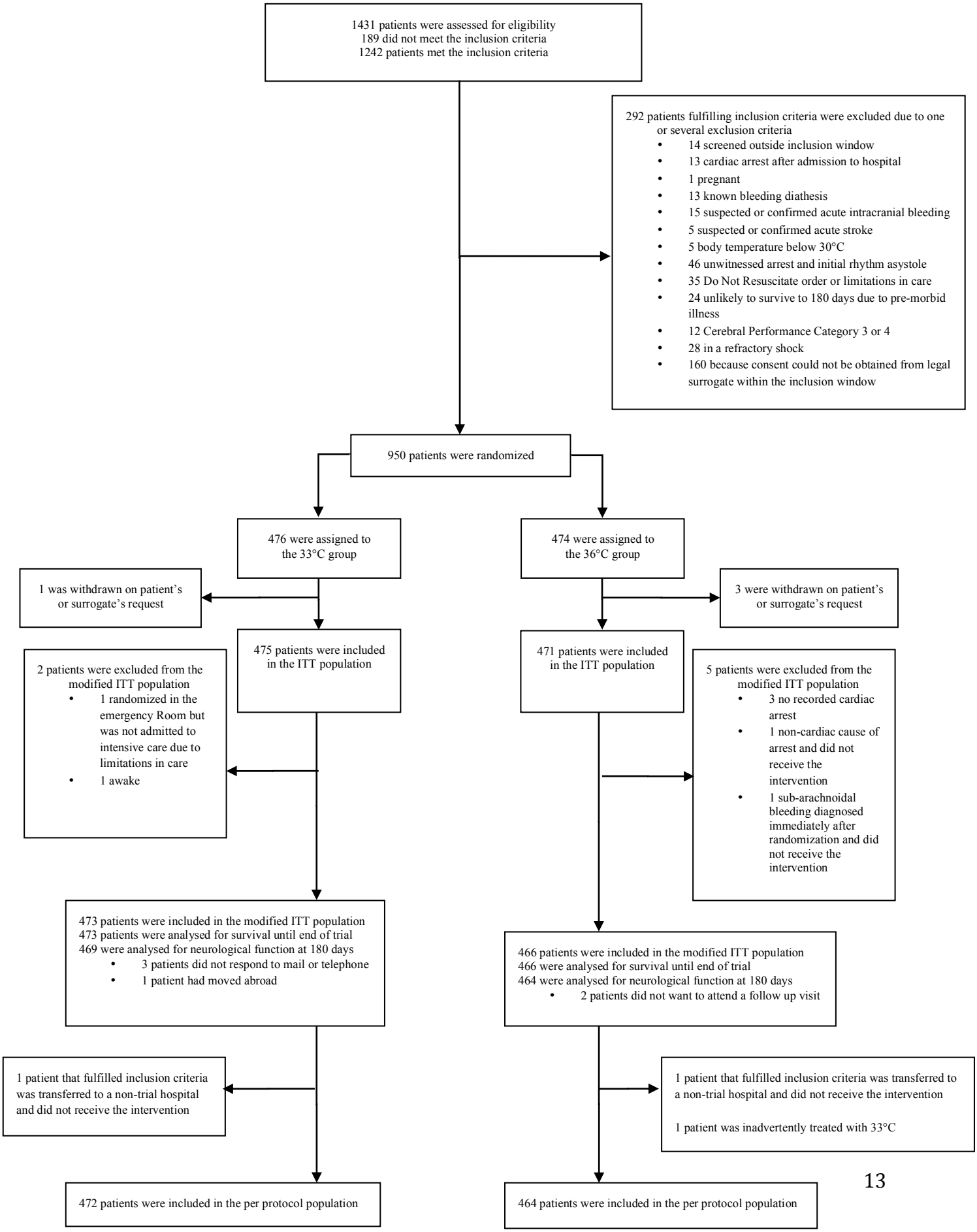

Figure S2. Hazard ratio of death, according to subgroup

The forest plot shows the hazard ratios for six predefined subgroups. The horizontal bars represent 95% confidence intervals. The events are the total events at end of trial. P values are for the tests of subgroup heterogeneity (tests of interactions). ROSC denotes return of spontaneous circulation. For unwitnessed cardiac arrests the time to ROSC was calculated form time of emergency call. Shock at admission was defined as a systolic blood pressure<90mmHg for >30min or end-organ hypoperfusion (cool extremities, urine output<30ml/hour, heart rate <60 beats/min).

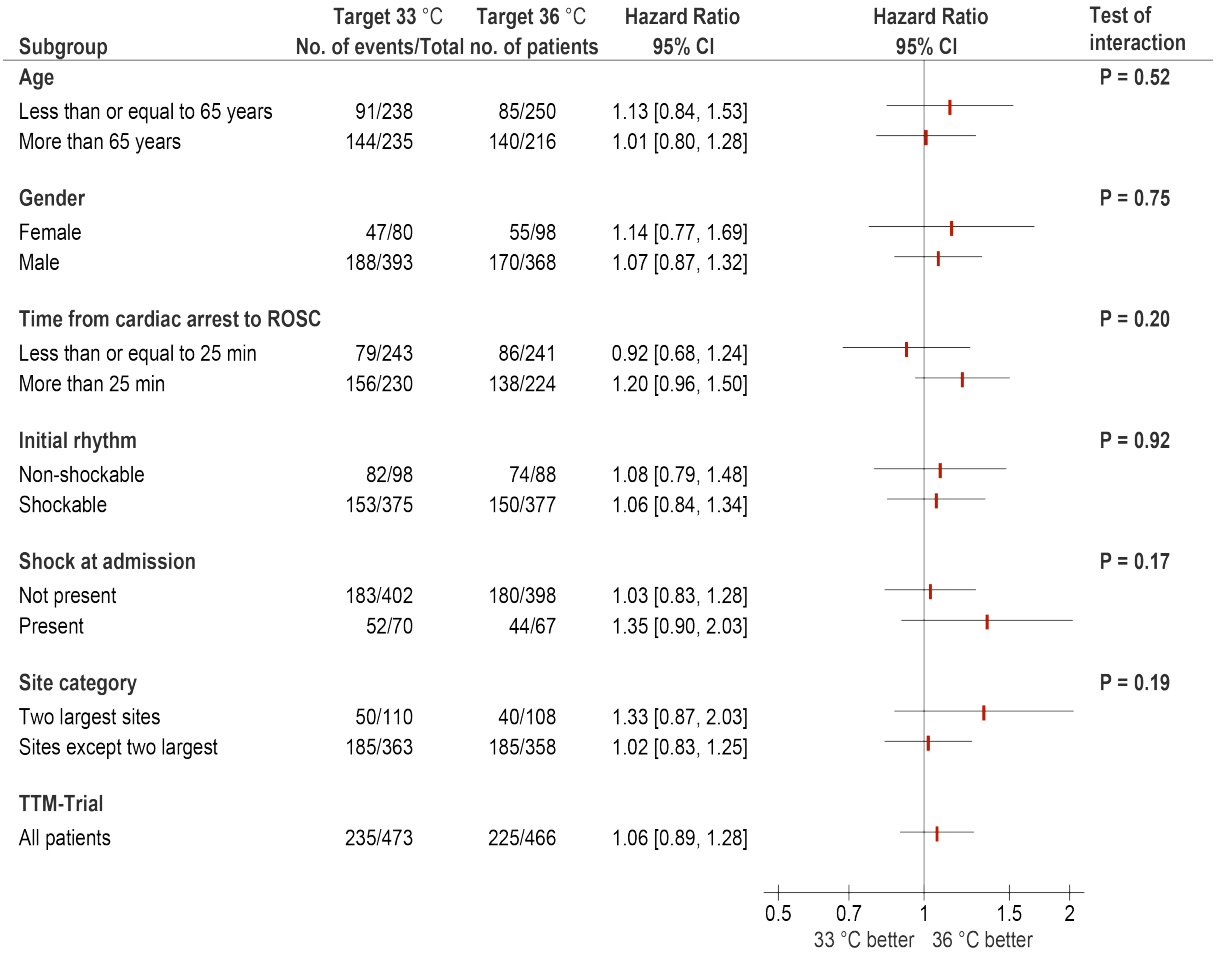

Table S1. Glasgow Coma Scale scores on admission

Table S1. **Glasgow Coma Scale Motor score on admission***			
	33°C	36°C	Total
Total no. patients	473	466	939
GCS-M no. (%)			
GCS-M 1	248 (52)	243 (52)	491
GCS-M 2	23 (5)	16 (3)	39
GCS-M 3	25 (5)	20 (4)	45
GCS-M 4	30 (6)	32 (7)	62
GCS-M 5	12 (3)	12 (3)	23
Sedation affecting GCS evaluation**	130 (27)	139 (30)	269
Missing	5 (1)	4 (1)	9

*GCS denotes Glasgow Coma Scale, GCS-M denotes GCS-motor.
**The patients that were sedated were mainly from tertiary hospitals with extended transfer from the scene of cardiac arrest. The evaluation of unconsciousness for randomization was based on the pre-sedation value (not reported here). The patients that were sedated on admission had similar proportions of initial rhythms and time from cardiac arrest to ROSC as the full cohort.

Table S2. Cardiovascular Sequential Organ Failure Assessment (SOFA) score

Table S2. **Cardiovascular component of Sequential Organ Failure Assessment score Day 1 to 3***						
	Day 1		Day 2		Day 3	
	33°C	36°C	33°C	36°C	33°C	36°C
Observations	466	454	450	434	428	421
SOFA-C						
0	55 (12)	65 (14)	41 (9)	70 (16)	65 (15)	113 (27)
1	47 (10)	41 (9)	11(2)	20 (5)	23 (5)	33 (8)
2	59 (13)	45 (10)	52 (12)	43 (10)	53 (12)	45 (11)
3	142 (30)	145 (32)	155 (34)	151 (35)	114 (27)	123 (29)
4	163 (35)	158 (35)	191 (42)	150 (35)	173 (40)	107 (25)

*SOFA denotes Sequential Organ Failure Assessment, SOFA-C denotes the cardiovascular subcomponent of the SOFA score. SOFA-C=0 No need for inotrope or vasopressor, mean arterial pressure (MAP) > 70mmHg, SOFA-C =1 MAP < 70mmHg, SOFA-C=2 any dose of dobutamine or dopamine <5 μg/kg/minute, SOFA-C=3 dopamine 5-15 μg/kg/minute or epinephrine or nor-epinephrine <0.1 μg/kg/minute, SOFA-C=4 dopamine >15 μg/kg/minute or epinephrine or nor-epinephrine >0.1 μg/kg/minute.

Table S3. Diagnostic procedures, interventions and service utilization

Table S3. **Diagnostic procedures, interventions and service utilization***			
	33°C	36°C	Total
	473	466	939
On admission no. (%)			
CT	150 (32)	165 (35)	315 (34)
Diagnostic procedures during ICU-stay no. (%)			
CT	174 (38)	182 (39)	356 (38)
MRI	18 (4)	17 (4)	35 (4)
EEG	205 (43)	184 (39)	389 (41)
SSEP	107 (23)	91 (19)	198 (21)
Interventions during ICU-stay no. (%)			
Coronary angiography	299 (63)	289 (62)	588 (63)
PCI	198 (42)	212 (45)	410 (44)
CABG	5 (1)	5 (1)	10 (1)
Thrombolysis	10 (2)	10 (2)	20 (2)
Time to intervention			
Hours from CA to angiography median [IQR]	2 [2-3]	2 [2-3]	2 [2-3]
Hours from CA to PCI median [IQR]	2 [2-3]	2 [2-3]	2 [2-3]
Mechanical ventilation** Days receiving mechanical ventilation/days in ICU median [IQR]	0.83 [0.67-1.00]	0.76 [0.60-1.00]	0.80 [0.60-1.00]
Sedation Days with sedation affecting neurological evaluation median [IQR]	2 [2-3]	2 [1-3]	2 [1-3]
Mechanical circulatory assist IABP no. (%)	78 (16)	62 (13)	140 (15)
Length of stay Hours from CA to ICU discharge median [IQR]	124 [71-201]	117 [74-190]	120 [73-195]
Days from CA to hospital discharge, median [IQR]	14 [8-24]	13 [8-24]	14 [8-24]

* CT denotes computed tomography of the head, MRI-magnetic resonance imaging of the head, EEG-electroencephalogram, SSEP-somatosensory evoked potentials, PCI-percutaneous coronary intervention, CABG-coronary artery bypass grafting, CA-cardiac arrest, ICU-intensive care unit, IABP-intra aortic balloon pump, IQR-interquartile range.
**There were no significant differences between the groups except for days receiving mechanical ventilation/days in ICU (P=0.006).

Table S4. Protocol violations and no intervention received

Table S4. **Protocol violations and no intervention received**		
	33°C	36°C
Transfer to another hospital*	1	1
Received the wrong intervention*	0	1
Died before start of intervention**,†	1	1
Fulfilled inclusion criteria but never received intervention†	1	1

*Excluded from the modified intention to treat population; included in the per protocol population.
**Died immediately after randomization.
†Included in the modified intention to treat population and in the per protocol population.

Table S5. Reasons for early rewarming

Table S5. **Reasons for early rewarming in the 33°C-group**	
Reason	**No.**
Arrhythmia (severe bradycardia, recurrent ventricular fibrillation, brady-tachy arrhythmia)	6
Severe circulatory instability	4
Bleeding	2
Uncontrolled lactate rise	2
Urgent coronary artery bypass grafting	1
No reason specified	1

Table S6. Development of fever

Table S6. **Development of fever in the intervention groups day 2-4***						
	Day 2		Day 3		Day 4	
Observations no.	898		865		765	
	33°C	36°C	33°C	36°C	33°C	36°C
Hours of temperature>38°C median [IQR]	0 [0-0]	0 [0-0]	0 [0-1]	0 [0-1]	0 [0-3]	0 [0-3]
Highest recorded temperature °C	36,0 (±1,5)	37,2 (±0.7)	37,7 (±0,5)	37,8 (±0,6)	37,8 (±0,6)	37,9 (±0,7)

*Cumulated hours above a body temperature of 38°C and highest recorded body temperature day 2-4 for patients in the intensive care unit. Trial sites were asked to actively treat fever until at least 72 hours after cardiac arrest. IQR denotes interquartile range. Plus-minus values are mean± standard deviation.

Table S7. Reasons for withdrawal of life sustaining therapy

Table S7. **Withdrawal of life sustaining therapy day 1-7***							
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Total WLST no.	18	27	40	38	40	46	38
Brain dead	1	5	5	4	3	0	0
Neurological reasons	0	4	12	17	22	33	15
MOF and hemodynamic failure	23	32	31	25	13	5	6
Comorbidity	3	6	7	5	4	0	3
Ethical reason	2	5	7	14	10	13	4

*Withdrawal of life sustaining therapy of any reason (WLST) day 1 to 7 in the ICU. More than one reason could be registered for each patient. MOF denotes multi organ failure. Brain death was defined as having fulfilled criteria of brain death as per individual countries legislation. Neurological reasons were as defined in the trial protocol and above in this document. The risk of having a decision of withdrawal within the first 10 days did not differ between the groups: Hazard Ratio = 1.11 95%; CI 0.88-1.40, P=0.38. Median time to WLST of any reason was 5 days (interquartile range (IQR) 2-8) in the 33°C-group and 5 days (IQR 3-7) in the 36°C-group, (P=0.78)

Table S8. Neurological prognostication

Table S8. **Neurological prognostication***			
	33°C	36°C	Total
Total no.	473	466	939
Prognostication performed no. (%)	172 (36)	148 (32)	320 (34)
Recommendation no. (%)			
Continue care	65 (38)	52 (35)	117 (37)
Do not escalate	32 (19)	24 (16)	56 (17)
Withdraw care	73 (42)	71 (48)	144 (45)
Recommendation not recorded	2	1	3
Hours from CA to prognostication median (IQR)	117 (93-137)	119 (94-141)	118 (93-140)
Prognostication not performed no. (%)	16 (3)	15 (3)	31 (3)
Reasons no.			
No reason	2	2	4
Transfer to other hospital	7	10	17
Ongoing sedation	4	2	6
WLST due to ethical reasons	1	1	2
Ongoing multi organ failure	2	0	2
Died before prognostication no. (%)	76 (16)	62 (13)	138 (15)
Presumed cause of death no. (%)			
Cardiac/hemodynamic cause	36 (47)	27 (43)	63 (46)
Multi organ failure	19 (25)	12 (19)	31 (22)
Cerebral cause	21 (28)	23 (37)	44 (32)
WLST of patients who died before reported prognostication no. (%)	48 (63 %)	42 (68 %)	90 (65 %)
Regained consciousness before prognostication no. (%)**	209 (44 %)	241 (52 %)	450 (48 %)

*WLST denotes withdrawal of life sustaining therapy for any reason, CA-cardiac arrest, IQR-interquartile range. Neurological prognostication by a physician blinded to the intervention, was undertaken 72 hours after the end of the intervention period or later, except in cases of brain death and early generalized myoclonic seizures with bilaterally absent N20 waves on somatosensory evoked potentials, when an earlier prognostication could be performed. WLST was allowed in these cases and also due to ethical and medical reasons previously described.[1,2] For more details on reasons for WLST see Table S6.

**There were no statistical differences in the variables in this table between the groups except for the number of patients that regained consciousness before prognostication (P=0.03).

Table S9. Cerebral Performance Category at ICU and hospital discharge

Table S9. **Neurological scores at ICU and hospital discharge***				
Category no. (%)	**CPC ICU discharge**§		**CPC Hospital discharge**§	
	33°C	36°C	33°C	36°C
CPC 1	61 (13)	79 (17)	133 (28)	143 (31)
CPC 2	120 (25)	111 (24)	74 (16)	69 (15)
CPC 3	65 (14)	78 (17)	39 (8)	36 (8)
CPC 4	61 (13)	54 (12)	19 (4)	14 (3)
CPC 5	166 (36)	144 (31)	208 (44)	203 (44)
Total	473	466	473	465

* CPC denotes cerebral performance category
§ CPC 1: Good cerebral performance, may have mild deficits, 2: Moderate cerebral disability, sufficient for independent activities of daily life, 3: Severe cerebral disability, 4: coma or vegetative state, 5: dead.[3,4]

Table S10. Adjusted analyses I

Table S10. **Adjusted analyses I***						
Adjusting covariates	**Mortality end-of-trial**		**CPC score > 2 follow-up†**		**mRS score> 3 follow-up††**	
	HR with 95% CI and n	P value	RR[§§] with 95% CI and n	P value	RR† with 95% CI and n	P value
None	1.08(0.90-1.29) n=939	0.43	1.03 (0.90-1.17) n=933	0.67	1.02 (0.89-1.16) n=933	0.82
Site (primary analyses)	1.06 (0.89-1.28) n=939	0.51	1.02 (0.88-1.16) n=933	0.78	1.01 (0.89 to 1.14) n=933	0.87
Site + design variables[**]	1.14 (0.94-1.37) n=937	0.18	0.97 (0.68-1.27) n=932	0.65	0.96 (0.81-1.11) n=932	0.58
Site category[§]	1.07 (0.89-1.29) n=939	0.45	1.03 (0.90-1.17) n=933	0.67	1.01 (0.89-1.14) n=933	0.82
Site category[§] + design variables[**]	1.13 (0.94-1.35) n=937	0.21	0.99 (0.83-1.15) n=932	0.85	0.97 (0.83 to 1.12) n=932	0.71

*Hazard ratio (HR) and relative risk (RR) of a poor neurological outcome and death between the two intervention groups (36°C-group is reference group) and 95% confidence interval (CI) without and with adjusting covariates

**Effect of intervention (36°C-group is reference group) on survival, on the indicator that the Cerebral Performance Category (CPC) score threshold of 2 has been exceeded, and on the indicator that the modified Rankin Scale (mRS) score threshold of 3 has been exceeded. The design variables include age, gender, shockable first rhythm, duration/min of cardiac arrest, and shock at admission

§The site categories include the category comprising the patients from the two sites with the highest number of patients treated (from the modified intention-to-treat population) and the category comprising the rest of the patients (from the modified intention-to-treat population)

§§In the adjusted analyses logistic regression analyses were used and the odds ratio estimate (OR) and its 95% CI were transformed to estimated relative risk (RR) using the equation RR = OR/((1-P)+OR*P) where P is the observed risk of death in the reference group (36°C)[5]

†CPC 1: Good cerebral performance, may have mild deficits, 2: Moderate cerebral disability, sufficient for independent activities of daily life, 3: Severe cerebral disability, 4: coma or vegetative state, 5: dead.[3,4]

††mRS 0: mRS 0: no symptoms, 1: no significant disability despite symptoms, 2: slight disability, able to look after own affairs without assistance, 3: moderate disability, requires some help, but able to walk unassisted, 4: moderately severe disability, unable to attend own bodily needs, 5: severe disability, bedridden, 6: dead.[6]

Table S11. Adjusted analyses II

Table S11. **Adjusted analyses II***				
	Mortality 180 days		**Best CPC**	
Adjusting covariates	Relative risk (RR) † 95% CI and n	P value	Relative risk (RR) † 95% CI and n	P value
None	1.01 (0.94-1.08) n=939	0.92	1.03 (0.91-1.17) n=938	0.63
Site	1.01 (0.87-1.14) n=939	0.92	1.04 (0.89 to 1.17) n=938	0.67
Site + design covariates**	0.95 (0.79-1.11) n=937	0.74	0.99 (0.83-1.15) n=936	0.89
Site category§	1.01 (0.88-1.15) n=939	0.86	1.04 (0.90-1.17) n=938	0.62
Site category + design covariates§**	0.96 (0.81-1.13) n=938	0.66	0.99 (0.84-1.14)	0.89

*Relative risk (RR) of death and the best reported Cerebral Performance Category (CPC) threshold of 2 has been exceeded between the two intervention groups (36°C-group is reference group) and 95% confidence interval (CI) without and with adjusting covariates

**The design variables include age, gender, shockable first rhythm, duration/min of cardiac arrest, and shock at admission

§The site categories include the category comprising the patients from the two sites with the highest number of patients treated (from the modified intention-to-treat population) and the category comprising the rest of the patients (from the modified intention-to-treat population)

†In the adjusted analyses logistic regression analyses were used and the odds ratio estimate (OR) and its 95% CI were transformed to estimated relative risk (RR) using the equation RR = OR/((1-P)+OR*P) where P is the observed risk of death in the reference group (36°C)[5]

Table S12. Serious adverse events

*Serious adverse events collected during day 1-7 when the patient was in the intensive care unit. CA denotes cardiac arrest, CPR-cardiopulmonary resuscitation

Table S12. **Serious adverse events excluding death***			
Serious adverse event no. (%)	**Occurrence of event during stay in ICU**		
(Denominator 'n=xxx' in parenthesis)	33°C	36°C	P value
Seizures			
Myoclonic seizures (n=923)	128 (28)	101 (23)	0.13
Tonic-clonic seizures (n=934)	36 (7.7)	34 (7.3)	0.85
Bleeding			
Uncontrolled bleeding (n=916)	10 (2.2)	6 (1.3)	0.45
Intracranial bleeding (n=902)	2 (0.4)	7 (1.5)	0.09
Intraspinal bleeding (n=906)	0 (0.0)	1 (0.2)	0.49
Intraocular bleeding (n=904)	0 (0.0)	1 (0.2)	0.49
Intraarticular bleeding (n=902)	0 (0.0)	1 (0.1)	0.49
Pericardial bleeding (n=886)	4 (0.9)	5 (1.1)	0.75
Gastro-intestinal bleeding (n=906)	25 (5.4)	23 (5.1)	0.84
Tracheal bleeding (n=907)	16 (3.5)	16 (3.6)	0.93
Oral cavity bleeding (n=906)	31 (6.8)	30 (6.7)	0.97
Nose bleeding (n=904)	26 (5.7)	25 (5.6)	0.96
Genital bleeding (n=896)	8 (1.8)	6 (1.3)	0.81
Bleeding from insertion sites (n=901)	42 (9.2)	27 (6.1)	0.076
Infection			
Pneumonia (n=932)	245 (52)	214 (46)	0.089
Severe sepsis (n=925)	46 (10)	46 (10)	0.92
Septic shock (n=922)	22 (4.8)	25 (5.4)	0.63
Other serious infection (n=923)	10 (2.2)	13 (2.8)	0.52
Arrhythmia			
Atrial fibrillation (n=929)	123 (26)	130 (28)	0.51
Atrial flutter (n=923)	17 (3.6)	19 (4.2)	0.68
Tachycardia (n=924)	65 (14)	71 (16)	0.49
Bradycardia needing pacing (n=922)	24 (5.2)	29 (6.4)	0.43
Ventricular tachycardia (n=922)	86 (18)	70 (15)	0.21
Ventricular fibrillation (n=921)	39 (8.4)	34 (7.4)	0.59
Recurrent CA mandating CPR (n=913)	42 (9.1)	46 (10)	0.60
Electrolyte and metabolic disorder			
Hypokalemia (n=911)	86 (19)	60 (13)	0.018
Hypomagnesemia (n=674)	73 (22)	60 (18)	0.20
Hypophosphatemia (n=710)	153 (44)	138 (38)	0.13
Hypoglycemia (n=905)	25 (5.5)	22 (4.9)	0.68
Renal replacement therapy (n=917)	49 (11)	42 (9.1)	0.44
Any of the above events (n=936)	439 (93)	417 (90)	0.086

Table S13. Presumed cause of death

Table S13. **Presumed cause of death***		
	33°C	36°C
Total patients no.	473	466
Dead no. (% of dead) (% of total patients no.)	235 (100) (50)	225 (100) (48)
Cause of death		
Cardiovascular	58 (25) (12)	53 (23) (11)
Cerebral	131 (56) (28)	135 (60) (29)
MOF	31 (13) (7)	26 (11) (6)
Other or undetermined	15 (6) (3)	11 (5) (2)

* The cause of death was based on clinical judgment by the investigators and is not based on results from autopsies. MOF denotes multi organ failure.

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