

# Ventilace, krevní oběh, vnitřní prostředí, kontrola tělesné teploty

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# Ventilace po ROSC

- nestudována specificky u pacientů po srdeční zástavě
- racionální je používat doporučení ze studií s ARDS (*protektivní ventilace*)

***Protektivní ventilace:***  
Vt 6-8 ml/kg, PEEP 4-8 cmH2O,  
Pplat < 30 cmH2O

- ↓incidenci ARDS, plicní infekce, dobu na UPV a mortalitu

CARING FOR THE  
CRITICALLY ILL PATIENT

## Association Between Use of Lung-Protective Ventilation With Lower Tidal Volumes and Clinical Outcomes Among Patients Without Acute Respiratory Distress Syndrome: A Meta-analysis

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**Context** Lung-protective mechanical ventilation with the use of lower tidal volumes has been found to improve outcomes of patients with acute respiratory distress syndrome (ARDS). It has been suggested that use of lower tidal volumes also benefits patients who do not have ARDS.

**Objective** To determine whether use of lower tidal volumes is associated with improved outcomes of patients receiving ventilation who do not have ARDS.

**Data Sources** MEDLINE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up to August 2012.

**Study Selection** Rigorous studies evaluated use of lower vs higher tidal volumes in patients without ARDS at onset of mechanical ventilation and reported lung injury development, overall mortality, pulmonary infection, antibiotic, and biochemical outcomes.

**Data Extraction** Three reviewers extracted data on study characteristics, methods, and outcomes. Disagreement was resolved by consensus.

**M**ECHANICAL VENTILATION is a life-saving strategy in patients with acute respiratory failure. However, epidemiological evidence suggests that mechanical ventilation has the potential to aggravate and precipitate lung injury.<sup>1</sup> In acute respiratory distress syndrome (ARDS), and in a milder form of ARDS formerly known as acute lung injury (ALI),<sup>2</sup> mechanical ventilation can cause ventilator-associated lung injury. Ventilator-associated lung injury is a frequent complication in critically ill patients receiving mechanical ventilation, and its development increases morbidity and mortality.<sup>3</sup>

Higher tidal volume (V<sub>t</sub>) ventilation causes the alveoli to overstretch in a process called volutrauma, and this overstretching is the main cause of ventilator-associated lung injury.<sup>4</sup> The use of a lower V<sub>t</sub> was shown to reduce morbidity and mortality in

ARDS patients.<sup>5</sup> Higher V<sub>t</sub> ventilation was associated with better clinical outcomes. Some of the limitations of the meta-analysis were the mixed setting of mechanical ventilation (intensive care unit or operating room) and the duration of mechanical ventilation.

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**For editorial comment see p 1682.**

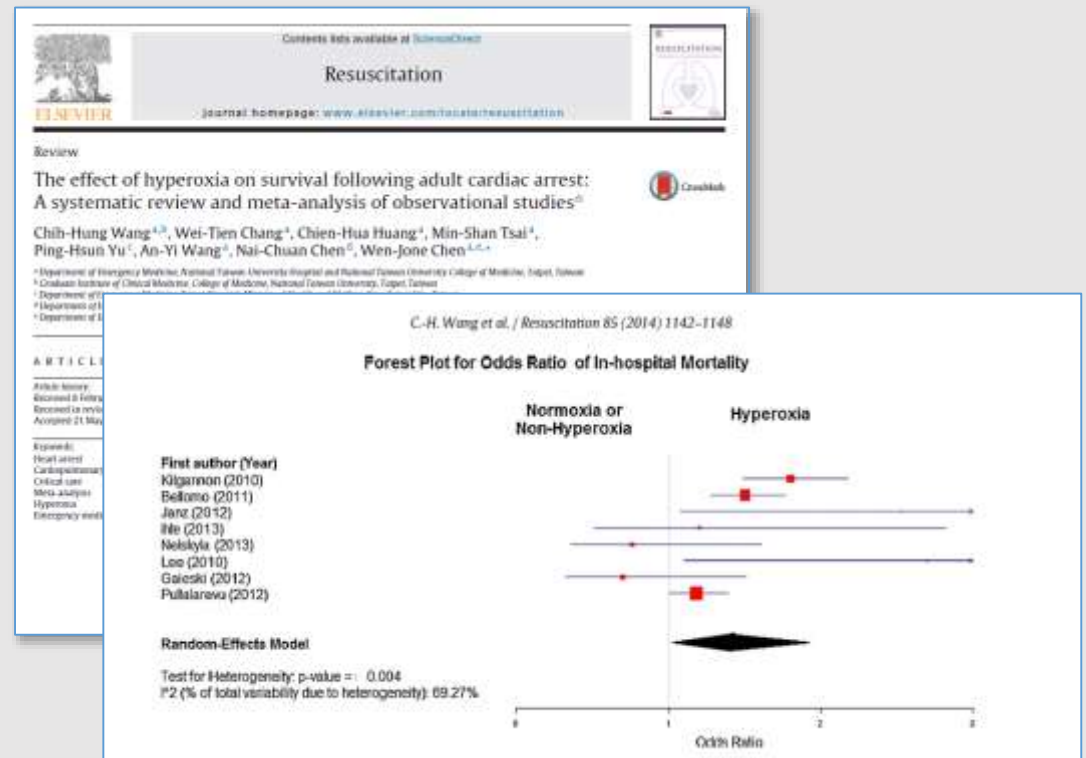
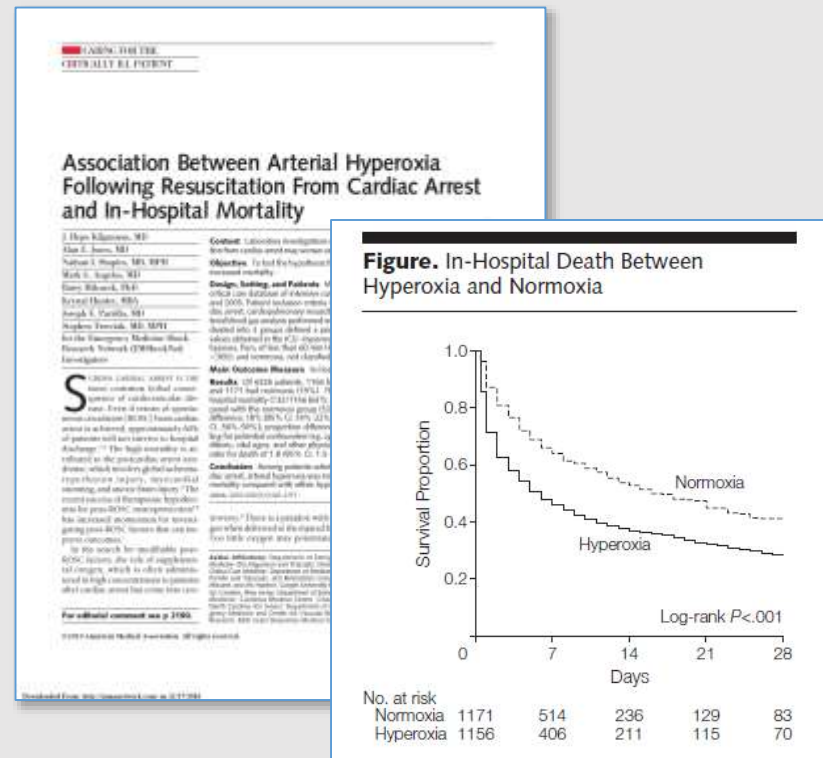
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JAMA, October 2, 2013; 309(14):1681-1690

# Vztah PaO<sub>2</sub> a klinických výsledků

Hyperoxemie (PaO<sub>2</sub>>300 mmHg) a hypoxemie hod (PaO<sub>2</sub>< 60 mmHg) v prvních 24 hod zvyšuje mortalitu oproti normoxemii. Každé zvýšení PaO<sub>2</sub> o 100 mmHg zvyšuje mortalitu o 24% !

Hyperoxemie (PaO<sub>2</sub>>300 mmHg) koreluje se zvýšenou nemocniční mortalitou, ale pravděpodobně nezhoršuje neurologické výsledky. Autoři upozorňují na heterogenitu studií a jejich malý počet!



# Vztah PaCO<sub>2</sub> a klinických výsledků

## Poznámky:

- PaCO<sub>2</sub> je určující faktor regulace mozkové perfúze (CBF)
- Hypokapnie (PaCO<sub>2</sub> < 35mmHg) vede k cerebrální vazokonstrikci a redukci CBF o 40-50% a ke zhoršení mozková ischemie
- Hyperkapnie (PaCO<sub>2</sub> > 45 mmHg) zvyšuje CBF

## Závěry studií:

Hypokapnie (PaCO<sub>2</sub> < 35) je spojena s vyšší mortalitou a horšími neurologickými výsledky v porovnání s normokapnií (PaCO<sub>2</sub> 35-45) a mírnou hyperkapnií (PaCO<sub>2</sub> 45-50).

Contents lists available at ScienceDirect  
Resuscitation  
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Clinical paper  
Arterial carbon dioxide tension and outcome in patients admitted to the intensive care unit after cardiac arrest<sup>a</sup>

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ABSTRACT  
Background: Arterial carbon dioxide tension (PaCO<sub>2</sub>) affects neuronal function and cerebral blood flow. However, its association with outcome in patients admitted to intensive care units (ICU) after cardiac arrest (CA) has not been evaluated.  
Methods and results: Observational cohort study using data from the Australian New Zealand (ANZ) Intensive Care Society Adult-Patients-Database (ANZICS-APD). Outcomes analyses were adjusted for illness severity, co-morbidities, hypothermia, treatment limitations, age, year of admission, glucose, source of admission, PaO<sub>2</sub>, and propensity score.  
We studied 9,542 consecutive patients admitted to 125 ANZ ICUs after CA between 2006 and 2011. Using the APD PaCO<sub>2</sub> (obtained within 24h of ICU admission), 3601 (38.2%) were classified into the hyperventilation (PaCO<sub>2</sub> < 35 mmHg), 4265 (44.8%) into the normocapnia (35–45 mmHg) and 4827 (51.3%) into the hypercapnia (> 45 mmHg) group. The hyperventilation group, compared with the normocapnia group, had a trend toward higher in-hospital mortality (OR 1.12 [95% CI 1.05–1.24, p=0.04]), lower rate of discharge home (OR 0.81 [0.75–0.84, p<0.001]) and higher likelihood of suffering composite adverse outcome of death and no discharge home (OR 1.22 [1.10–1.37, p<0.001]). In contrast, the hypercapnia group had similar in-hospital mortality (OR 1.06 [0.97–1.15, p=0.38]) but higher rate of discharge home among survivors (OR 1.16 [1.02–1.32, p=0.01]) and similar likelihood of fulfilling the composite outcome (OR 0.97 [0.89–1.06, p=0.52]). Cox-proportional hazards modelling supported these findings.  
Conclusions: Hypo- and hypercapnia are common after ICU admission post-CA. Compared with normocapnia, hyperventilation was independently associated with worse clinical outcomes and hypercapnia a greater likelihood of discharge home among survivors.  
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1. Introduction  
Cardiac arrest (CA) is common<sup>1–3</sup> with an incidence up to 2.0 per 1000 person years.<sup>4,5</sup> CA is associated with a high morbidity and mortality.<sup>6,7</sup> Even among patients admitted to the hospital after return of a spontaneous circulation only 40% are discharged alive.<sup>8–10</sup> Even fewer have sufficient neurological recovery to be able to return home.<sup>11</sup> To date, therapeutic hypothermia is the only intervention shown to improve neurological outcome among such patients.<sup>12</sup> However, other modifiable components of patient care may also deliver better neurological outcomes. Arterial oxygen and carbon dioxide tensions (PaCO<sub>2</sub>) could be one such

# Doporučení I.

1. Během KPR používáme 100% O<sub>2</sub>
2. Post ROSC spontánně ventilující: O<sub>2</sub> maska při SpO<sub>2</sub> < 94%
3. Po dosažení ROSC - *protektivní ventilaci*: Vt 6-8 ml/kg, PEEP 4-8 cmH<sub>2</sub>O, Pplat < 30 cmH<sub>2</sub>O
4. Udržujeme PaO<sub>2</sub> 60 - 300 mmHg nebo SpO<sub>2</sub> 94-98%
5. Udržujeme PaCO<sub>2</sub> 35 – 50 mmHg
6. Zavedení nosogastrické sondy (dekomprese žaludku, uvolnění bránice, zlepšení ventilace)
7. Doporučujeme protokol sedace a event. myorelaxace
8. ATB prevence pneumonie při TTM – spíše ano (*ANTHARTIC trial ? ...*)

# Krevní oběh po ROSC

## Poznámky:

- Post cardiac arrest syndrom – myokardiální dysfunkce + vazodilatace (SIRS) (hypotenze, ↓CO, arytmie)
- Zotavení ↓CO cca 24 hod (i déle), zotavení vazodilatace až 3 dny (i déle)
- myokardiální dysfunkce – často inotropní podpora
- SIRS – vazoplegie – noradrenalin, tekutiny
- Kardiovaskulární selhání – nejčastější příčina úmrtí během prvních cca 3 dnů

# Optimální hodnota TK

- Optimální TK post-CA sy není znám
- Hodnoty často odvozeny z prací u sepse
- Post CA-syndrom je jistě více komplexnější než sepse
- Mozková autoregulace je porušena u více jak 1/3 pacientů po CA na rozdíl od sepse
- MAP > 65-70 mmHg - lepší neurologický outcome a nižší mortalita (TTM trial)

## Arterial Blood Pressure and Neurologic Outcome After Resuscitation From Cardiac Arrest\*

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at low-weighted average mean arterial pressure value of 65 mmHg. This threshold (mean arterial pressure > 70 mmHg) had the strongest association with good neurologic outcome (odds ratio, 4.11; 95% CI, 1.54–12.66,  $p = 0.014$ ). A sustained low hypotension surge was relatively uncommon and was associated with neurologic outcome.

**Conclusion:** We found that low-weighted average mean arterial pressure was associated with good neurologic outcome at a level of mean arterial pressure greater than 70 mmHg. (Crit Care Med 2014; 42:2049–2059)

**Words:** brain injury; cardiopulmonary resuscitation; ischemic stroke; status of spontaneous circulation

## Hemodynamics and Vasopressor Support During Targeted Temperature Management at 33°C Versus 36°C After Out-of-Hospital Cardiac Arrest: A Post Hoc Study of the Target Temperature Management Trial\*

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\*See 490 p. 882.

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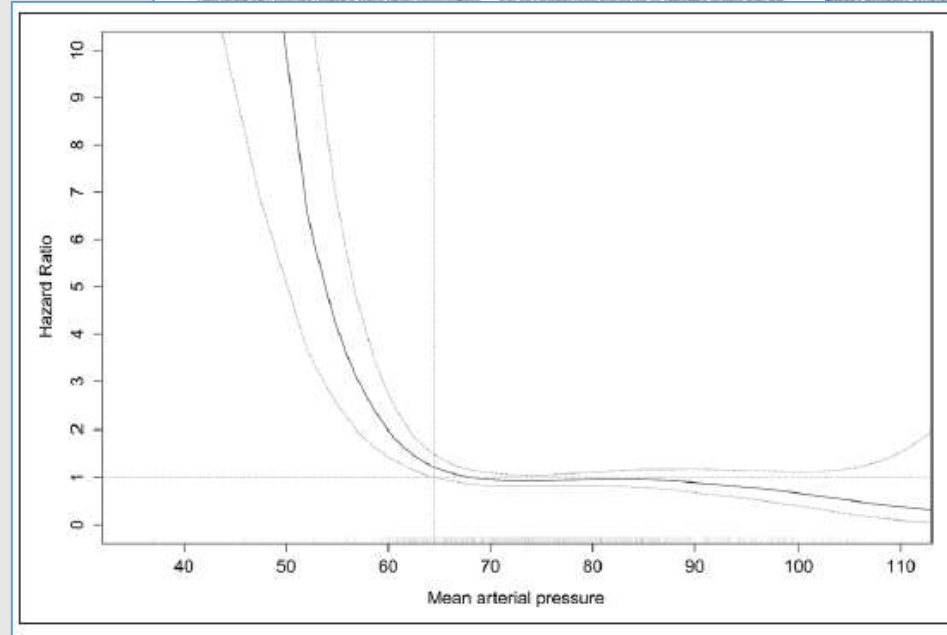
<sup>2</sup>Department of Anesthesia and Intensive Care, Lund University, Skane University Hospital, Lund, Sweden

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<sup>4</sup>graduate for research. Dr. Nielsen received speaker's honorarium from Bard International. His institution received grant support from the Swedish Heart and Lung Association, Almqvistströms Forskningsstiftelse, Insurance Foundation, Swedish Research Council, and from Regional and Governmental funds within the Swedish Health Care system. Dr. Friberg received a Bard Medical Future. His institution received grant support from the Perseus Foundation, American MA, Dr. Kjergaard received grant support for research. Dr. Nielsen received speaker's honorarium from Bard International. His institution received grant support from the Swedish Heart and Lung Association, Almqvistströms Forskningsstiftelse, Insurance Foundation, Swedish Research Council, and from Regional and Governmental funds within the Swedish Health Care system. Dr. Friberg received a Bard Medical Future. His institution received grant support from the Perseus Foundation, American MA, Dr. Kjergaard received grant support for research.

The post-cardiac arrest syndrome is a state of severe, global ischemia-reperfusion injury with potentially devastating consequences (1, 2). The mortality associated with this condition is extremely high, and among those survivors, many are left with persistent disabling neurologic injury. The discovery that controlling body temperature (normo- or hypothermia) after spontaneous circulation (ROSC) may improve neurologic function (3–5) provides hope that additional resuscitation interventions may be found to reduce the extent of brain injury and further improve clinical outcomes. Patients with post-cardiac arrest syndrome experience organ-system damage (6, 7), profound systemic acidemia (8), myocardial stunning (11, 12), and adrenal axis suppression (13, 14), which collectively result in major hemodynamic instability (15–18). Given that the injured brain extremely has additional autoregulation of the cerebral blood flow, including cerebral perfusion pressure (CPP) (19, 20), it is possible that CPP may be a factor in neurologic outcome. With the autoregulation, cerebral blood flow (CBF) is maintained at a constant level despite changes in arterial pressure (MAP). Clinical studies suggest that CPP associated with lower neurologic outcomes suggest that hypotensive surge may confer neurologic injury.

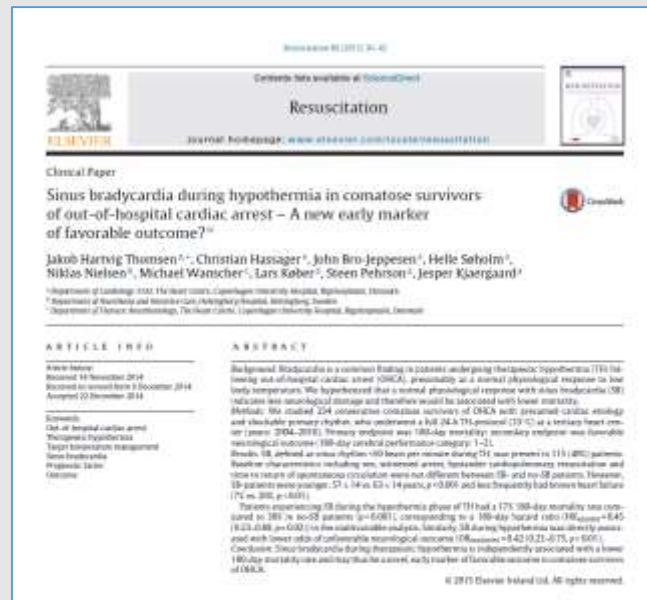
2013





# Optimální hodnota TF

- Bradykardie – fyziologická reakce při hypotermii
- Bradykardie během TTM může představovat prognostický marker
- Bradykardie  $\geq 40$ /min lze tolerovat , pokud je TK, laktát, diureza..., nutno zvážit EF ...)



### 1. Introduction

Therapeutic hypothermia (TH) is widely used and has been supported by guidelines as a neuro-protective treatment strategy in comatose survivors of out-of-hospital cardiac arrest (OHCA) for more than a decade.<sup>1,2</sup>

It is recognized that the main cause of short-term mortality in comatose OHCA patients is secondary brain neurological injury.<sup>3</sup> Early cerebral reperfusion is challenging, especially in the era of TH, where prognostic tools are useful only 72 h after normothermia is obtained.<sup>4,5</sup> Initial shockable rhythm, witnessed arrest, bystander cardiopulmonary resuscitation (CPR) and shorter time to

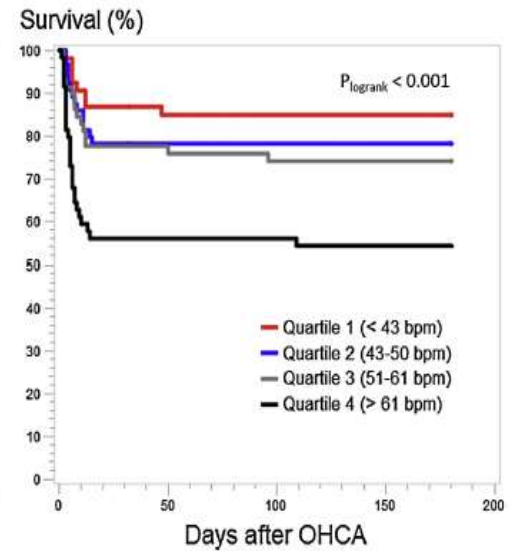
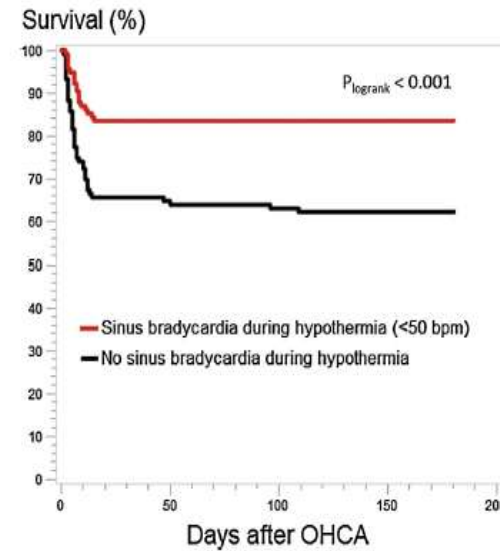
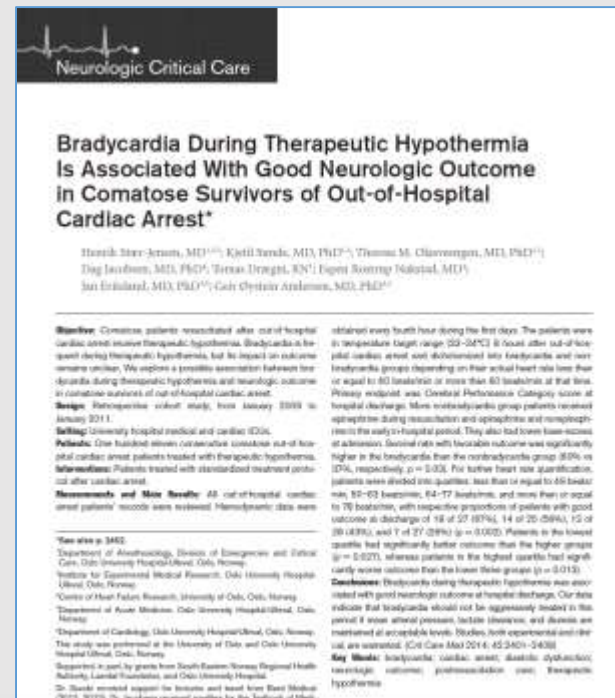



Fig. 3. Kaplan Meier 180-day survival. Left panel: patients with incident sinus bradycardia (<50 bpm) during the hypothermia phase of therapeutic hypothermia compared to no sinus bradycardia patients. Right panel: patients stratified by quartiles of minimum heart rate during the hypothermia phase of therapeutic hypothermia.

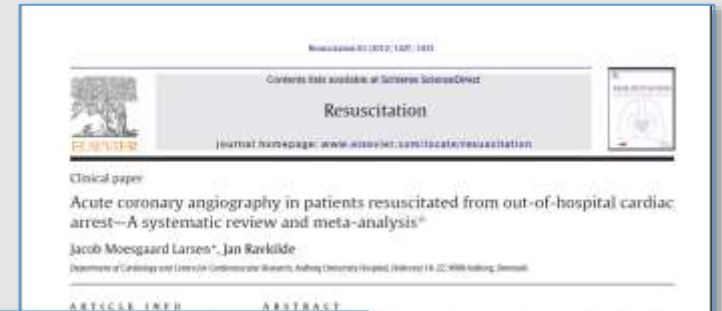


# Doporučení II.

1. Tekutiny k optimalizaci plicích tlaků (F1/1)
2. MAP  $\geq$  65 mmHg a TF  $\geq$  40/min – použij NA  $\pm$  DOBU
3. Cíl:  diuréza 1 ml/kg/hod  
normální/klesající laktát  
smíšená žilní saturace > 70%  
(cave: hypotermie  $\uparrow$  diurézu a  $\downarrow$  clearance laktátu)
4. vždy zvážit pacientův normální TK, myokardiální dysfunkci, komorbidity...
5. Vhodná invazivní monitorace TK a event. CŽK, dle potřeby PAC
6. Použij info z ECHO, RTG S+P
7. SKG – viz dále

# Koronární reperfuze

- Prevalence akutních koronárních lézí (AKL) u OHCA 59-71%
- STE nebo BBB 80% má AKL
- nonSTE 25-58% má AKL



**Resuscitation**  
journal homepage: www.elsevier.com/locate/resuscitation

**Clinical paper**  
**Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—A systematic review and meta-analysis\***  
Jacob Moesgaard Larsen<sup>a</sup>, Jan Ravkilde<sup>b</sup>  
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ARTICLE INFO ABSTRACT



**Clinical paper**  
**Post-resuscitation electrocardiograms, acute coronary findings and in-hospital prognosis of survivors of out-of-hospital cardiac arrest\***  
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**ABSTRACT**  
Background: Identification of acute coronary lesions amenable to urgent intervention in survivors of out-of-hospital cardiac arrest is crucial. We aimed to compare the clinical and electrocardiographic characteristics to organic coronary findings, and to analyze in-hospital prognosis of these patients.  
Methods: From January 2005 to December 2012 we retrospectively identified consecutive patients resuscitated from out-of-hospital cardiac arrest, and analyzed the clinical characteristics, post-resuscitation electrocardiogram and coronary angiogram of those who underwent emergent angiography. Mortality and neurologic status at discharge were also assessed.  
Results: Patients with ST-elevation more frequently had obstructive coronary artery disease (88% vs. 51%,  $p < 0.001$ ) or acute coronary occlusion (82% vs. 85%,  $p = 0.0001$ ) than patients without ST-elevation. Independent predictors of an acute coronary occlusion were time past before arrest (OR 0.18, 95% CI 0.04–0.72,  $p = 0.01$ ), a shockable initial rhythm (OR 0.16, 95% CI 0.03–0.85,  $p = 0.03$ ), and ST-elevation on the post-resuscitation electrocardiogram (OR 0.03, 95% CI 0.004–0.13,  $p = 0.001$ ). Survival with favorable neurologic recovery at discharge was 50%. Independent predictors of mortality or unfavorable neurological outcome at discharge were absence of base: tip segment (OR 0.1, 95% CI 0.003–0.8,  $p = 0.04$ ), prolonged resuscitation time (OR 0.8, 95% CI 0.6–0.9,  $p < 0.001$ ), and necessity of vasopressor (OR 1.63, 95% CI 1.1–2.4,  $p = 0.001$ ).  
Conclusions: Most patients with ST-elevation on the post-resuscitation electrocardiogram had an acute coronary occlusion, as opposed to patients without ST-elevation. Absence of base: tip segment, prolonged resuscitation time and use of vasopressor were independent predictors of worse in-hospital outcome.  
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**1. Introduction**  
Sudden out-of-hospital cardiac arrest (OHCA) is a common clinical problem with a very high mortality.<sup>1,2</sup> Coronary artery disease and acute coronary syndromes are leading causes of OHCA.<sup>3–5</sup> Therefore, identification of acute cardiac lesions amenable to urgent percutaneous coronary intervention (PCI) in the setting of OHCA is crucial. Decision to perform emergent coronary angiography (CA) is classically taken on the basis of ECG findings after recovery of spontaneous circulation.<sup>6</sup> However, clinical and electrocardiographic data before angiography have inconsistent value for selecting patients for CA.<sup>7,8</sup> Besides, the utility of performing ECA and PCI in all survivors of OHCA is controversial, especially in the subgroup of patients without ST-segment elevation on the post-resuscitation electrocardiogram.<sup>9</sup> The need for triage is justified not only by the fact that not all OHCA patients benefit from CA<sup>10</sup> but also by the limited availability, the cost and the potential complications of the technique.<sup>11–13</sup> In the present study, we analyzed the clinical characteristics, the post-resuscitation electrocardiogram and the acute angiographic findings of a series of consecutive OHCA patients who underwent CA. Such information would be important for better selection of OHCA patients for ECA after successful resuscitation. We also analyzed hospital management, PCI results and in-hospital prognosis in this series.

of cardiac arrest has a poor prognosis. The main setting in which to focus on resuscitation is the hospital. To patients with return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest, acute coronary angiography with coronary intervention is recommended.<sup>14</sup> However, the utility of performing ECA and PCI in all survivors of OHCA is controversial, especially in the subgroup of patients without ST-segment elevation on the post-resuscitation electrocardiogram.<sup>9</sup> The need for triage is justified not only by the fact that not all OHCA patients benefit from CA<sup>10</sup> but also by the limited availability, the cost and the potential complications of the technique.<sup>11–13</sup> In the present study, we analyzed the clinical characteristics, the post-resuscitation electrocardiogram and the acute angiographic findings of a series of consecutive OHCA patients who underwent CA. Such information would be important for better selection of OHCA patients for ECA after successful resuscitation. We also analyzed hospital management, PCI results and in-hospital prognosis in this series.

return of spontaneous circulation (ROSC) after OHCA is less clear, especially in comatose survivors. The topic was resolved in the 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (2010 Consensus).<sup>14</sup> The recommendation was: acute CA should be considered in STEMI or clinical suspicion of coronary ischemia as a likely cause of the arrest, and that it may be reasonable to be included in a systematic standardized post cardiac arrest protocol. Several new studies have emerged. The aim of this study was to make an updated systematic review of the evidence on performing acute CA following ROSC after OHCA.

**2. Methods**  
The study was conducted in accordance with the principles stated by the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) group.<sup>15,16</sup> In short, we defined a structured question describing the Population,

\* A Spanish translated version of the abstract of this article appears in *Revista Española de Cardiología* 67 (10):1111–1118, 2016.  
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# Koronární reperfuze

## Indikace urgentní koronarografie

### Periprocedurální antitrombotická léčba

- 1) ASA 250 mg (Kardegic ½ amp) i.v.
- 2) heparin 70-100 IU/kg i.v.
- 3) P2Y12 blokátory rozdrtit do NGS
  - prasugrel 60mg
  - ticagrelor 180 mg
  - clopidogrel neúčinný

*J. Czechoslov. J. Intern. Med.* 2011; 250(1): 1-10

**Antiplatelet efficacy of P2Y<sub>12</sub> inhibitors (prasugrel, ticagrelor, clopidogrel) in patients treated with mild therapeutic hypothermia after cardiac arrest due to acute myocardial infarction**

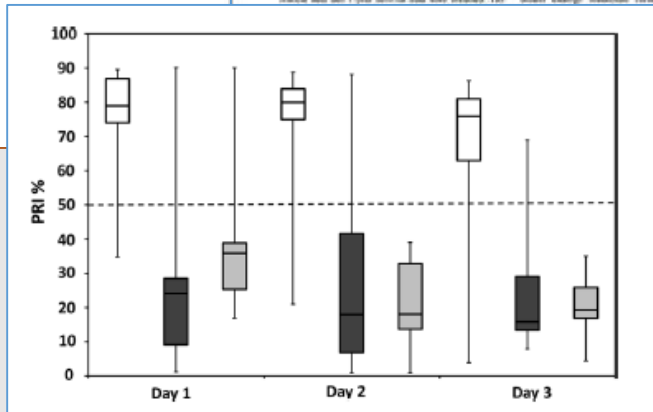
Frantisek Bolek<sup>1</sup>, Josef Kravaj<sup>2</sup>, Martina Holubova<sup>1</sup>, Feroz Chasani<sup>1</sup>, Milan Simek<sup>3</sup>, Zdenek Mrazek<sup>4</sup>

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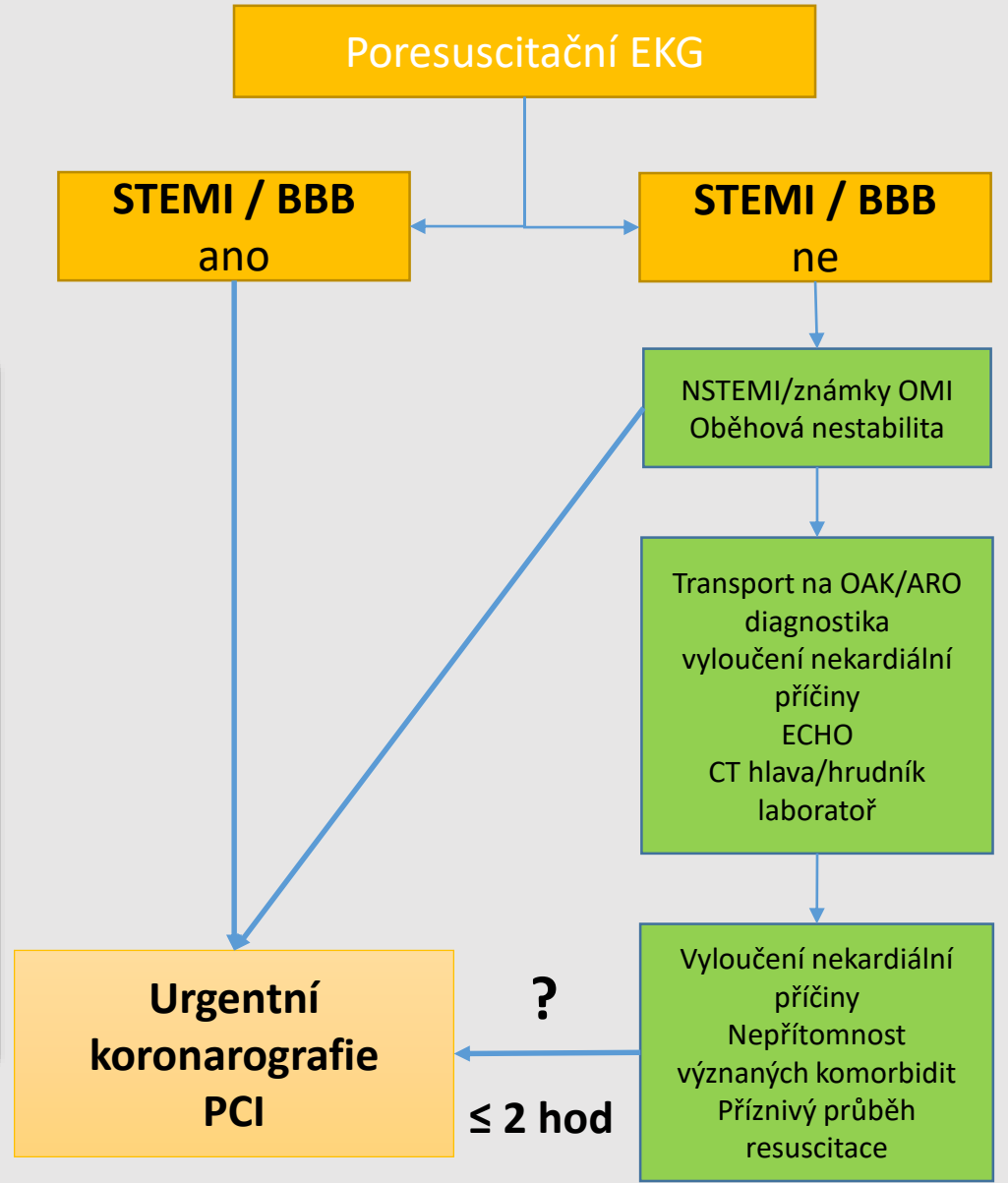
**Abstract:** Reperfusion after cardiac arrest (CA) due to acute myocardial infarction (AMI) and then severe dual antiplatelet therapy (DAPT) treatment (prasugrel, ticagrelor, clopidogrel) is recommended for secondary prevention after CA to improve anatomical outcomes. MTH may attenuate the effect of P2Y<sub>12</sub> inhibitors by reducing platelet activation. The combined effect of these conditions on the efficacy of P2Y<sub>12</sub> inhibitors is unknown. We compared the antiplatelet efficacy of two P2Y<sub>12</sub> inhibitors in AMI patients after CA treated with MTH. Forty patients after CA for AMI treated with MTH and received one P2Y<sub>12</sub> inhibitor (prasugrel or ticagrelor) were enrolled in a prospective observational single-center study. Platelet inhibition was measured by VASP-IRIS on days 1, 2, and 3 after drug administration. In-hospital clinical data and 1-year survival data were obtained. The

**Introduction:** Patients with recent of spontaneous circulation after out-of-hospital cardiac arrest (OHCA) who have thrombotic-prone arteries for acute myocardial infarction (AMI) should undergo immediate coronary angiography with

**Keywords:** Myocardial infarction · Cardiac arrest · Hypothermia · Prasugrel · Ticagrelor · Clopidogrel



Neúčinnost (PRI > 50%) clopidogrelu (bílé obdélníky) podávaného NGS během prvních tří dnů po OHCA pro AIM.



# Vnitřní prostředí

## acido-bazická rovnováha

### Poznámky:

- CA – ischemie – tkáňová hypoxie - produkce laktátu - ↓pH
- ↓pH – hyperventilace - ↓pCO<sub>2</sub> – vazokonstrikce- zhoršení mozkové ischemie
- Těžká acidóza (pH < 7.20) - ↓CO, ↓TK, arytmie, ↓účinnosti KA
- ABR při hypotermii:
  - a) hodnoty krevních plynů závislé na teplotě
  - b) ↓ T zvyšuje rozpustnost O<sub>2</sub> a CO<sub>2</sub> a tím snižuje pO<sub>2</sub> a pCO<sub>2</sub> (O<sub>2</sub> / pCO<sub>2</sub> snižuje o 5/2 mmHg/1°C)
  - c) ↓ T snižuje spotřebu O<sub>2</sub> a produkci CO<sub>2</sub>
  - d) Měření krevních plynů:  
alpha-stat (teplota nekorigována, 37°C) nebo pH –stat (korigováno na aktuální teplotu pacienta)  
v klinické praxi nemá větší význam

# Vnitřní prostředí hladina draslíku

- Hypokalemie ( $\leq 3.5$  mmol/l) nacházíme u 30-50% pacientů po OHCA
- **Příčiny:**
  - uvolnění katecholaminů
  - korekce metabolické a respirační acidózy
  - hypotermie
- Hypokalemie zvyšuje riziko arytmií ( $\leq 2.5$   $\uparrow$ QT a VT)
- Udržovat v rozmezí 4-4.5mmol/l



# Kontrola glykemie

- Přísná kontrola glykemie (4-6 mmol/l) zvyšuje riziko hypoglykemie a mortalitu oproti méně striktní kontrole ( $\leq 10$  mmol/l) u ICU pacientů
- závislost mezi hodnotami glykemie a mortalitou má tvar U-křivky
- Závislost platí především pro nediabetiky, pro pacienty s DM je méně vyjádřena
- Hypotermie:  $\uparrow$  glykemie ( $\downarrow$  inzulínová sekrece a senzitivita),  $\uparrow$  potřeba inzulínu





## Doporučení III.

1. Těžká acidóza ( $\text{pH} < 7.20$ )- korekce oběhu, oxygenace a ventilace a až následně bikarbonát (2mmol/kg)
2. Udržovat glykemii 6-10 mmol/l
3. Udržovat kalemii v rozmezí 4.0-4.5mmol/l

# Kontrola tělesné teploty po OHCA

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### MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP\*

#### ABSTRACT

**Background** Cardiac arrest with widespread cerebral ischemia frequently leads to severe impairment. We studied whether mild hypothermia increases the rate of neurologic recovery after resuscitation from cardiac arrest due to ventricular fibrillation.

**Methods** In this multicenter trial with assessment of the outcome, patients who were resuscitated after cardiac arrest due to ventricular fibrillation were randomly assigned to undergo hypothermia (target temperature, 32°C to 34°C) or normothermia (target temperature, 36°C to 37°C) over a period of 24 hours. The primary end point was a favorable neurologic outcome within six months after cardiac arrest. Secondary end points were mortality within six months and the rate of complications within seven days.

**Results** Seventy-five of the 136 patients in the hypothermia group for whom data were available had a favorable neurologic outcome (performance category, 1 [good recovery] or 2 [mild disability]), as compared with 54 of 136 patients in the normothermia group (risk ratio, 1.08 to 1.81; 95 percent confidence interval, 0.74 to 1.51). Six months after cardiac arrest, 41 percent of patients in the hypothermia group (56 of 137 patients) died, as compared with 46 percent in the normothermia group (76 of 165 patients) (risk ratio, 0.74; 95 percent confidence interval, 0.56 to 0.96). The complication rate did not differ between the two groups.

**Conclusions** In patients who have been fully resuscitated after cardiac arrest due to ventricular fibrillation, therapeutic mild hypothermia increases the rate of a favorable neurologic outcome and reduces mortality. (N Engl J Med 2002;346:1013-22.)

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INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

### TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

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BRUCE M. JONES, M.B., B.S., WILLIAM SELVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.Sc.

#### ABSTRACT

**Background** Cardiac arrest outside the hospital is common and has a poor outcome. Studies in laboratory animals suggest that hypothermia induced shortly after the restoration of spontaneous circulation may improve neurologic outcome, but there have been no conclusive studies in humans. In a randomized, controlled trial, we compared the effects of moderate hypothermia with normothermia on neurologic outcome in comatose survivors of out-of-hospital cardiac arrest.

Currently, the treatment of patients with coma after resuscitation from out-of-hospital cardiac arrest is largely supportive. Because cerebral ischemia may persist for some hours after resuscitation,<sup>1</sup> the use of induced hypothermia to decrease cerebral oxygen demand has been proposed as a treatment option.<sup>2</sup> Although this suggestion has been supported by studies

in laboratory animals that have controlled or reduced the feasibility of treatment,<sup>3,4</sup> several studies comparing normothermia and moderate hypothermia after cardiac arrest,

including a large study from Australia, between normothermia and moderate hypothermia in the study when cardiac arrest was due to a cardiac rhythm, such as ventricular fibrillation, were conducted after the criteria were set at least 50 years for cardiac arrest (depression cardiac arrest accident). Patients were not available as a

had been normothermic moderate hypothermia to the day of the study in the field (including and Australia) to patients assigned normothermia or moderate hypothermia, the physicians, including

Sanderson (S.A.), Victoria South, Melbourne Services, Melbourne, Australia; Medical Director, Austin Health, Austin Health (A.H.); and the Melbourne Medical Centre, Melbourne, Australia, or at

## ILCOR Advisory Statement

### Therapeutic Hypothermia After Cardiac Arrest An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

#### ILCOR Recommendations

On the basis of the published evidence to date, the Advanced Life Support (ALS) Task Force of the International Liaison Committee on Resuscitation (ILCOR) made the following recommendations in October 2002:

- Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was ventricular fibrillation (VF).
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.

## ORIGINAL ARTICLE

## Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

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## ABSTRACT

## BACKGROUND

Unconscious survivors of out-of-hospital cardiac arrest have a high risk of death or poor neurologic function. Therapeutic hypothermia is recommended by international guidelines, but the supporting evidence is limited, and the target temperature associated with the best outcome is unknown. Our objective was to compare two target temperatures, both intended to prevent fever.

## METHODS

In an international trial, we randomly assigned 950 unconscious adults after out-of-hospital cardiac arrest of presumed cardiac cause to targeted temperature management at either 33°C or 36°C. The primary outcome was all-cause mortality through the end of the trial. Secondary outcomes included a composite of poor neurologic function or death at 180 days, as evaluated with the Cerebral Performance Category (CPC) scale and the modified Rankin scale.

## RESULTS

In total, 939 patients were included in the primary analysis. At the end of the trial, 50% of the patients in the 33°C group (235 of 473 patients) had died, as compared with 48% of the patients in the 36°C group (225 of 466 patients) (hazard ratio with a temperature of 33°C, 1.06; 95% confidence interval [CI], 0.89 to 1.28;  $P=0.51$ ). At the 180-day follow-up, 54% of the patients in the 33°C group had died or had poor neurologic function according to the CPC, as compared with 52% of patients in the 36°C group (risk ratio, 1.02; 95% CI, 0.88 to 1.16;  $P=0.78$ ). In the analysis using the modified Rankin scale, the comparable rate was 52% in both groups (risk ratio, 1.01; 95% CI, 0.89 to 1.14;  $P=0.87$ ). The results of analyses adjusted for known prognostic factors were similar.

## CONCLUSIONS

In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C. (Funded by the Swedish Heart-Lung Foundation and others; TTM ClinicalTrials.gov number, NCT01020916.)

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\*A complete list of investigators participating in the Targeted Temperature Management 33°C versus 36°C after Out-of-Hospital Cardiac Arrest (TTM) trial is provided listed in the Supplementary Appendix, available at NEJM.org.

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## Targeted temperature management (TTM)

Table 2. Outcomes.

Outcome	33°C Group	36°C Group	Hazard Ratio or Risk Ratio (95% CI)*	P Value
	<i>no./total no. (%)</i>			
Primary outcome: deaths at end of trial	235/473 (50)	225/466 (48)	1.06 (0.89–1.28)	0.51
Secondary outcomes				
Neurologic function at follow-up†				
CPC of 3–5	251/469 (54)	242/464 (52)	1.02 (0.88–1.16)	0.78
Modified Rankin scale score of 4–6	245/469 (52)	239/464 (52)	1.01 (0.89–1.14)	0.87
Deaths at 180 days	226/473 (48)	220/466 (47)	1.01 (0.87–1.15)	0.92

## CONCLUSIONS

In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C. (Funded by the Swedish Heart-Lung Foundation and others; TTM ClinicalTrials.gov number, NCT01020916.)

Mild therapeutic hypothermia

Targeted temperature management  
(TTM)

Zahájení chlazení

•Optimální doba zahájení není známa

•Přednemocniční zahájení  
•nezlepšuje prognózu

Cílová TT, doba chlazení

Cílová teplota: 32-36°C

Doba trvání: min 24 hod

Ohřívání

0.25-0.5°C / hod

Normothermie ( $\leq 37.5^{\circ}\text{C}$ )  
po dobu 48-72 hod

## Doporučení IV.

1. Udržovat teplotu na 32°C - 36°C
2. Doba TTM 24 hod
3. Zabránit hypertermii ( $\geq 37.5^{\circ}\text{C}$ ) po dobu 48-72 hod po CA

### Probíhající studie o TH:

- *TTH48* 33°C 24h vs. 48 hod
- *CAPITAL CHILL* 31°C vs. 34°C

# Doporučení pro poresuscitační péči

