



# Hedeflenmiş Sıcaklık Yönetimi (Targeted Temperature Management-TTM) Teröpatik Hipotermi

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# Resuscitation

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## Clinical paper

# Impact of hypothermia on cardiac performance during targeted temperature management after cardiac arrest



Kevin G. ...  
Abh...

## Abstract

**Introduction:** Targeted temperature management (TTM) is a well-accepted neuro-protective intervention in the management of comatose survivors of cardiac arrest (CA). However, the impact of TTM on cardiac performance has not been adequately evaluated.

**Methods:** We reviewed data on consecutive CA survivors undergoing TTM at a quaternary cardiac intensive care unit between January 2015 and June 2017. Enrollment was restricted to cases with invasive hemodynamics (iHDs) at TTM initiation, every 8 h at target temperature (32–34 °C) and at completion of rewarming (>36 °C), unless precluded by mortality. Cardiac index and cardiac index-derived variables were adjusted for a decreased oxygen consumption during hypothermia. We assessed the serial impact of cooling on iHDs and cardiac performance utilizing longitudinal data analysis accounting for the effects of time as surrogate for the expected change from the post arrest syndrome and instituted treatments. A Frank-Starling construct was used to evaluate changes in cardiac contractility.

**Results:** We evaluated the effects of cooling on iHDs and cardiac performance in 46 CA survivors. Heart rate decreased with cooling ( $p < 0.001$ ), to return to baseline after rewarming ( $p = 0.6$ ). Mean arterial pressure and pulmonary wedge pressure decreased by cooling ( $p < 0.001$  for both), with sustained improvement after rewarming ( $p < 0.001$  for both). Systemic vascular resistance was unaffected by hypothermia ( $p > 0.05$ ). Left stroke work index increased with cooling ( $p < 0.001$ ), with return to baseline after rewarming ( $p = 0.6$ ). Cooling was associated with a left-upward shift in the Frank-Starling curve indicative of increased contractility.

**Conclusion:** Mild hypothermia in CA survivors appears associated to positive changes in iHDs and cardiac performance, including a potential increase in cardiac contractility. Larger studies are needed to conclusively confirm these findings.

**Keywords:** Targeted temperature management, Cardiac performance, Cardiac contractility, Cardiac arrest

# Invasive Hemodynamics and Outcomes in Cardiac Arrest Survivors Undergoing Targeted Temperature Management



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Most important prognostic factors in the postcardiac arrest patients who underwent targeted temperature management (TTM) derive from the periarrest period. Whether early invasive hemodynamics predict survival or neurologic outcomes remains unknown. We retrospectively reviewed all comatose survivors of cardiac arrest who underwent TTM at the Coronary Intensive Care Unit of a Quaternary Center between January 2015 and June 2017. Patients were required to have a set of invasive hemodynamics available at initiation of TTM to be included. Those with cooling initiated before admission and temperature of  $<36^{\circ}\text{C}$  before obtaining hemodynamics were excluded. Univariate logistic and multivariate regression were conducted to test whether cardiac index (Fick-cardiac index  $\geq 2.2$  vs  $<2.2$  L/min/m<sup>2</sup>), pulmonary capillary wedge pressure (PCWP  $\geq 18$  vs  $<18$  mm Hg), systemic vascular resistance (SVR  $>1200$  vs  $800$  to  $1200$  vs  $<800$  dynes/cm<sup>5</sup>) or Forrester hemodynamic profiles were predictive of survival and favorable neurologic outcomes at hospital discharge. Total of 52 consecutive arrest survivors who underwent TTM were studied demonstrating a wide variability in invasive hemodynamic parameters. There was no association between cardiac index ( $p = 0.45$  and  $p = 0.10$ ), PCWP ( $p = 0.90$  and  $p = 0.60$ ), SVR ( $0.95$  and  $p = 0.17$ ) or Forrester hemodynamic profiles ( $p = 0.40$  and  $p = 0.42$ ) and survival or favorable neurologic outcome at discharge. In conclusion, comatose arrest survivors who underwent TTM presents with a wide spectrum of invasive hemodynamics highlighting the heterogeneity of the postcardiac arrest syndrome. Early invasive hemodynamics did not predict survival or favorable neurologic outcomes at hospital discharge. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1255–1261)

# Targeted Temperature Management and Postcardiac arrest Care



Amy C. Walker, MD<sup>a,\*</sup>, Nicholas J. .

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## KEYWORDS

- Targeted temperature management • Cardiac arrest • Therapeutic hypothermia
- Shockable rhythm • Out-of-hospital cardiac arrest

## KEY POINTS

- Targeted temperature management (TTM) has been shown to reduce neurologic injury after cardiac arrest and is a cornerstone of postarrest care.
- The optimal dose (defined as temperature achieved multiplied by duration) of TTM is controversial, but current evidence suggests targeting 32°C to 36°C for at least 24 hours in adults with initial shockable cardiac rhythms, and consideration in patients with non-shockable rhythms.
- There is currently no role for prehospital induction of TTM using cold intravenous fluid, and targeted normothermia is the preferred approach in pediatric cardiac arrest.
- Key aspects of postarrest care, in addition to TTM, include ventilator management, hemodynamic optimization, identifying and addressing precipitating pathologic condition, and prognostication.

# Kardiyak Arrest

- Hastane dışı kardiyak arrestte en sık

## Kardiyak Arrest

- Terapötik hipotermi standart postkardiyak arrest bakım ile kombine edildiğinde nörolojik sonuçları düzeltmektedir.

- Nörolojik
- Hipertermi arrest sonrası beklenen bir durumdur ve nörolojik sonuçları kötüleştirmektedir .



# TTM

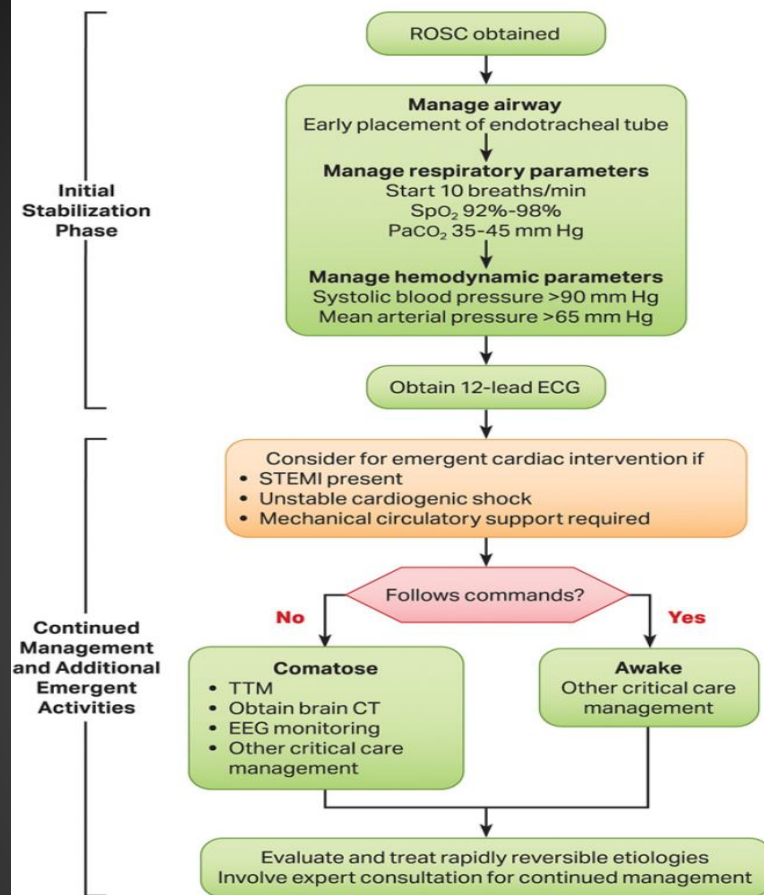


## Adult IHCA Chain of Survival



## Adult OHCA Chain of Survival

# Adult Post-Cardiac Arrest Care Algorithm



## Initial Stabilization Phase

Resuscitation is ongoing during the post-ROSC phase, and many of these activities can occur concurrently. However, if prioritization is necessary, follow these steps:

- **Airway management:**  
Waveform capnography or capnometry to confirm and monitor endotracheal tube placement
- **Manage respiratory parameters:**  
Titrate FiO<sub>2</sub> for SpO<sub>2</sub> 92%-98%; start at 10 breaths/min; titrate to PaCO<sub>2</sub> of 35-45 mm Hg
- **Manage hemodynamic parameters:**  
Administer crystalloid and/or vasopressor or inotrope for goal systolic blood pressure >90 mm Hg or mean arterial pressure >65 mm Hg

## Continued Management and Additional Emergent Activities

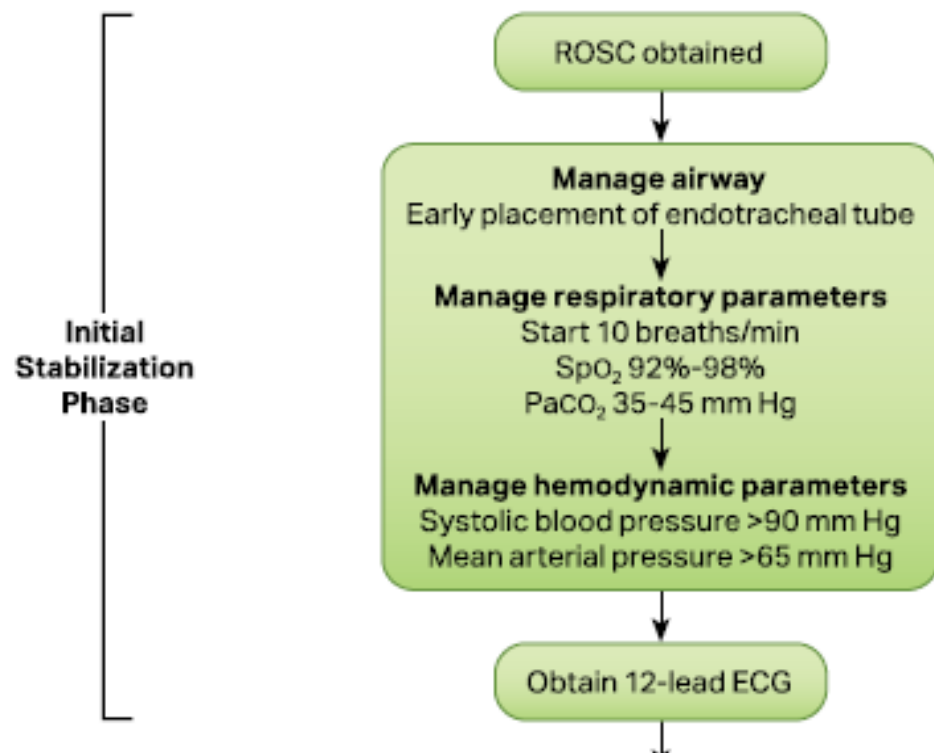
These evaluations should be done concurrently so that decisions on targeted temperature management (TTM) receive high priority as cardiac interventions.

- **Emergent cardiac intervention:**  
Early evaluation of 12-lead electrocardiogram (ECG); consider hemodynamics for decision on cardiac intervention
- **TTM:** If patient is not following commands, start TTM as soon as possible; begin at 32-36°C for 24 hours by using a cooling device with feedback loop
- **Other critical care management**
  - Continuously monitor core temperature (esophageal, rectal, bladder)
  - Maintain normoxia, normocapnia, euglycemia
  - Provide continuous or intermittent electroencephalogram (EEG) monitoring
  - Provide lung-protective ventilation

## H's and T's

**Hypovolemia**  
**Hypoxia**  
**Hydrogen ion (acidosis)**  
**Hypokalemia/hyperkalemia**  
**Hypothermia**  
**Tension pneumothorax**  
**Tamponade, cardiac**  
**Toxins**  
**Thrombosis, pulmonary**  
**Thrombosis, coronary**

## Adult Post-Cardiac Arrest Care Algorithm

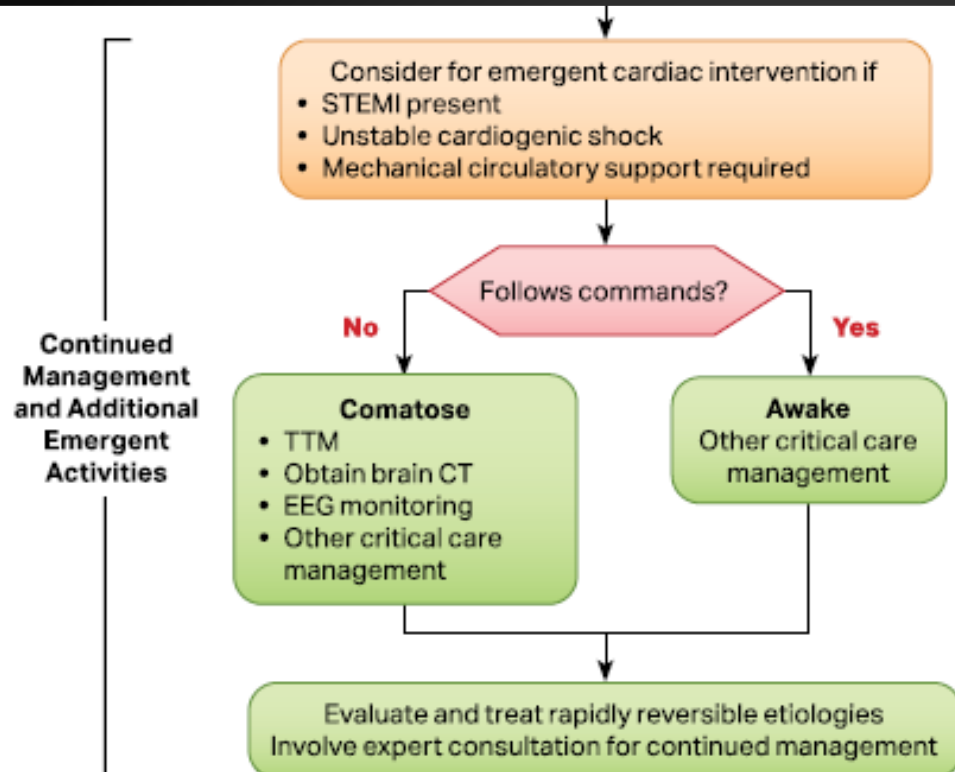


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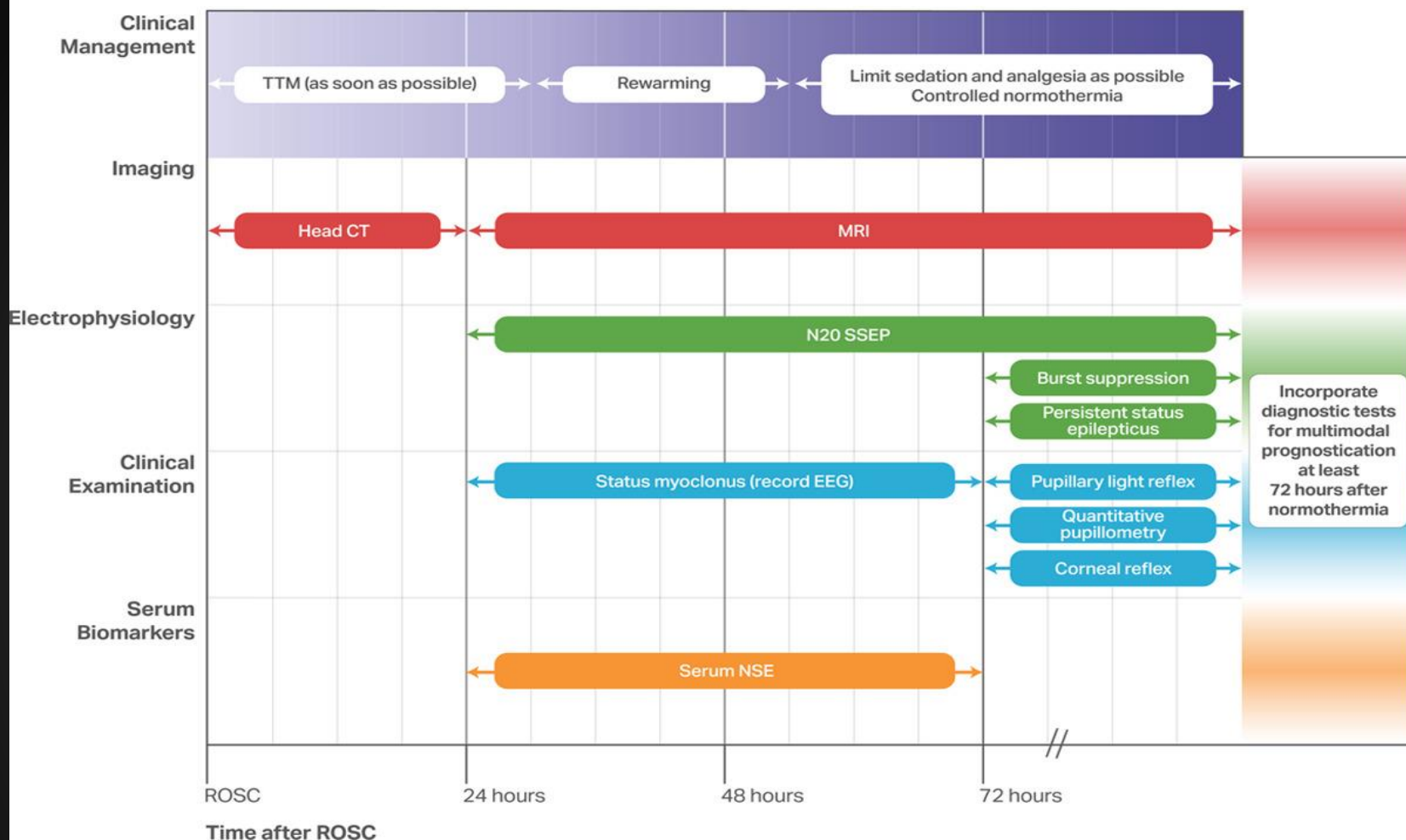
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Thrombosis, coronary

# Neuroprognostication Diagram



**Figure 10. Recommended approach to multimodal neuroprognostication.**

Neurologic prognostication incorporates multiple diagnostic tests that are synthesized into a comprehensive multimodal assessment at least 72 hours after return to normothermia and with sedation and analgesia limited as possible. Awareness and incorporation of the potential sources of error in the individual diagnostic tests is important. The suggested timing of the multimodal diagnostics is shown here. CT indicates computed tomography; EEG, electroencephalogram; MRI, magnetic resonance imaging; NSE, neuron-specific enolase; ROSC, return of spontaneous circulation; SSEP, somatosensory evoked potential; and TTM, targeted temperature management.

# TTM

## Recommendations for Indications for TTM

COR	LOE	Recommendations
1	B-R	1. We recommend TTM for adults who do not follow commands after ROSC from OHCA with any initial rhythm.
1	B-R	2. We recommend TTM for adults who do not follow commands after ROSC from IHCA with initial nonshockable rhythm.
1	B-NR	3. We recommend TTM for adults who do not follow commands after ROSC from IHCA with initial shockable rhythm.

# TTM

## Recommendations for Performance of TTM

COR	LOE	Recommendations
1	B-R	1. We recommend selecting and maintaining a constant temperature between 32°C and 36°C during TTM.
2a	B-NR	2. It is reasonable that TTM be maintained for at least 24 h after achieving target temperature.
2b	C-LD	3. It may be reasonable to actively prevent fever in comatose patients after TTM.
3: No Benefit	A	4. We do not recommend the routine use of rapid infusion of cold IV fluids for prehospital cooling of patients after ROSC.



# TTM Etkileri

- Nörotransmitter salımını engeller
- Serbest radikal oluşumunu engeller
- Serebral metabolizma oranı azalır (Her 1 °C'de %5-8)
- Oksijen tüketimini azaltır
- Kan beyin bariyeri sağlamlığı korunur ve serebral ödem azalır
- KİB (kafaiçi basınç) ve serebral ödem azalır
- Kan basıncını azaltır

# TTM Etkileri

- Bozulmuş pıhtılaşma kaskadı
- Bozulmuş platelet fonksiyonu (kanama riski ↑)
- Düşük beyaz küre sayısı, immün sistem baskılanır
- Barsak hareketleri yavaşlar – ***Dikkat ileus !!***
- İnsülin salgısı azalır
- Laktik asidoz
- Elektrolit bozuklukları

# TTM Etkileri

## EKG Değişiklikleri

- Uzunlaşmış PR aralığı
- Genişleyen QRS kompleksi
- Yükselmiş QT aralığı
- J ya da Osborn dalgası
- Bradikardi yapabilir

# TTM Etkileri

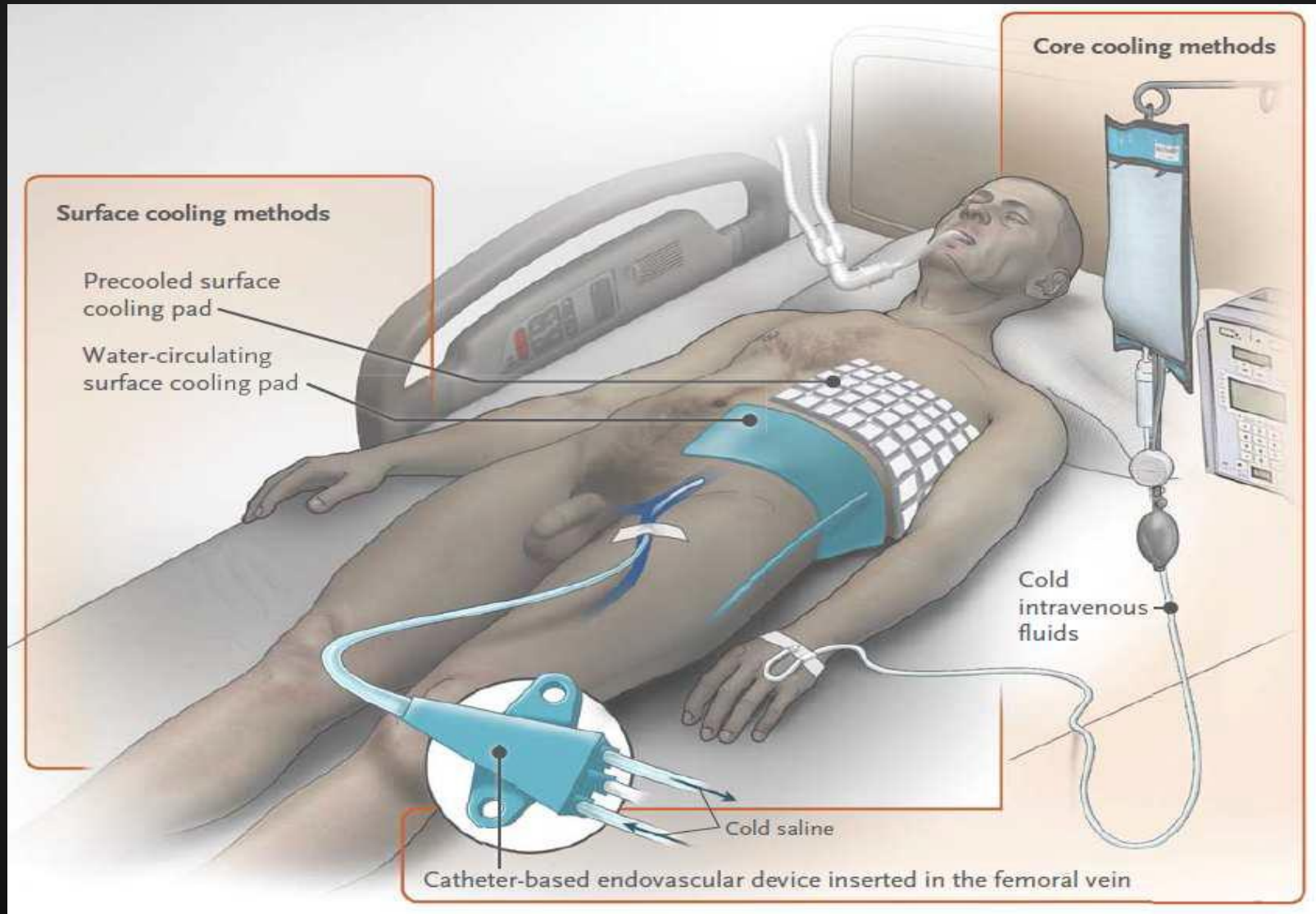
- Titreme ve kasılmalar
- Vücut ısını arttırır
- Uygun sedasyon ve nöromuskuler blokaj
  - *Dikkat – yavaş metabolize edilebilir*
- Metabolizma yavaş olduğu için ilaçlar birikebilir
- Konvülziyon maskelenebilir. Bu nedenle EEG monitörizasyonu



# TTM Yöntemleri

- Basit buz paketleri ve / veya ıslak havlular , soğutma battaniyeleri veya yastıkları
- Yüzeyel soğutma sistemleri - Su ile dolaşan jel kaplı pedler
  - *Cilt yanıkları*
- İntravasküler ısı kontrolü , genellikle femoral veya subklavyan damarlara yerleştirilir.
  - *Damar içi pıhtılaşma - Trombüs*
- Ekstrakorporal dolaşım (e.g., cardiopulmonary bypass,ECMO)

# TTM Uygulama



**a**



**b**



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# Resuscitation

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## Review

### Efficacy of the cooling method for targeted temperature management in post-cardiac arrest patients: A systematic review and meta-analysis



Jae Guk Kim<sup>a,b,†</sup>, Chiwon Ahn<sup>c,d,†</sup>, Hyungoo Shin<sup>e,\*</sup>, Wonhee Kim<sup>a,d</sup>, Tae Ho Lim<sup>f</sup>,  
Bo-Hyoung Jang<sup>g</sup>, Youngsuk Cho<sup>a,d</sup>, Kyu-Sun Choi<sup>h</sup>, Juncheol Lee<sup>i</sup>, Min Kyun Na<sup>j</sup>

#### Abstract

**Objective:** This review aimed to compare the efficacy of endovascular cooling devices (ECD), such as Thermogard<sup>®</sup>, with surface cooling devices (SCD), such as Arctic Sun<sup>®</sup>, in reducing mortality and improving neurological status for patients with post-cardiac arrest undergoing targeted temperature management.

**Data sources:** A systematic literature search was conducted using MEDLINE, EMBASE, and the Cochrane Library to identify randomized controlled trials (RCT) and observational studies (OS) comparing mortality and neurological status for patients treated with ECD or SCD.

**Results:** The meta-analysis comprised 4,401 patients from 2 RCT and 7 OS. For mortality, the overall pooled analysis showed no statistically significant difference between ECD and SCD recipients (RR, 0.93; 95% CI 0.86–1.00;  $I^2 = 0\%$ ). Further, no statistically significant difference was observed between RCT (RR, 0.80; 95% CI 0.56–1.14;  $I^2 = 0\%$ ) and OS (RR, 0.94; 95% CI 0.85–1.04;  $I^2 = 18\%$ ) for in-hospital mortality.

For good neurological status of survivors after TTM, the overall pooled analysis showed no statistically significant difference between ECD and SCD (RR, 1.08; 95% CI 0.99–1.18;  $I^2 = 71\%$ ). No statistically significant difference was found between ECD and SCD at hospital discharge in RCT (RR, 0.88; 95% CI 0.61–1.28;  $I^2 = 0\%$ ) and at 6 months in OS (RR, 1.03; 95% CI 0.99–1.09;  $I^2 = 32\%$ ).

**Conclusions:** The study findings could not show that either ECD or SCD was more effective in terms of survival and improved neurological status for post-cardiac arrest patients.

**Systematic review registration number:** CRD42019129770.

**Keywords:** Hypothermia, induced, Heart arrest, Patient outcome assessment, Meta-analysis



RESEARCH

Open Access



# Effect of different methods of cooling for targeted temperature management on outcome after cardiac arrest: a systematic review and meta-analysis

Lorenzo Calabró<sup>1†</sup>, Wulfran Bougouin<sup>2,3,4†</sup>, Alain Cariou<sup>3,4,5</sup>, Chiara De Fazio<sup>1</sup>, Markus Skrifvars<sup>6</sup>, Eldar Soreide<sup>7</sup>, Jacques Creteur<sup>1</sup>, Hans Kirkegaard<sup>8</sup>, Stéphane Legriel<sup>9</sup>, Jean-Baptiste Lascarrou<sup>10</sup>, Bruno Megarbane<sup>11</sup>, Nicolas Deye<sup>11†</sup> and Fabio Silvio Taccone<sup>1\*†</sup>

## Abstract

**Background:** Although targeted temperature management (TTM) is recommended in comatose survivors after cardiac arrest (CA), the optimal method to deliver TTM remains unknown. We performed a meta-analysis to evaluate the effects of different TTM methods on survival and neurological outcome after adult CA.

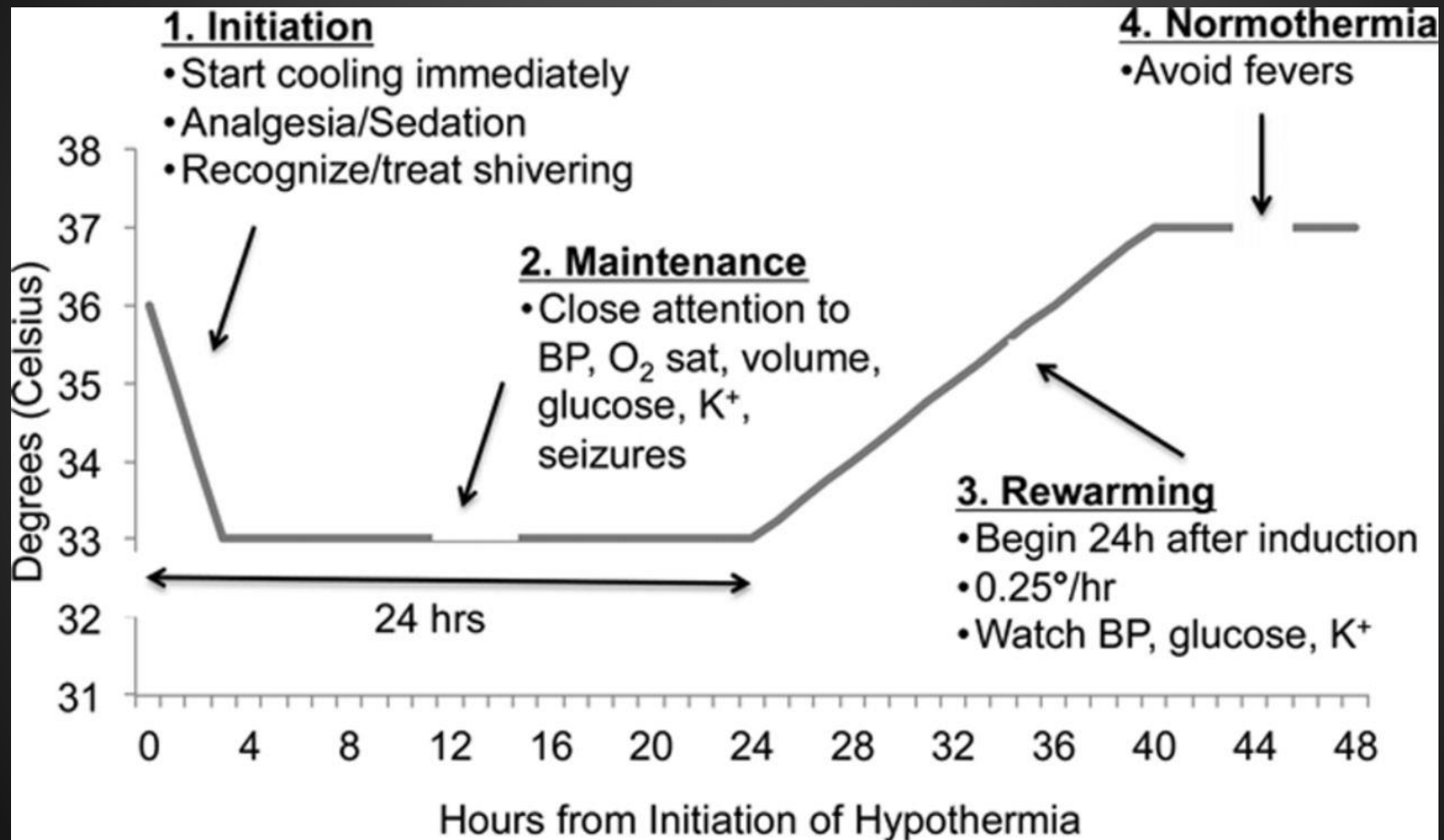
**Methods:** We searched on the MEDLINE/PubMed database until 22 February 2019 for comparative studies that evaluated at least two different TTM methods in CA patients. Data were extracted independently by two authors. We used the Newcastle-Ottawa Scale and a modified Cochrane ROB tools for assessing the risk of bias of each study. The primary outcome was the occurrence of unfavorable neurological outcome (UO); secondary outcomes included overall mortality.

**Results:** Our search identified 6886 studies; 22 studies ( $n = 8027$  patients) were included in the final analysis. When compared to surface cooling, core methods showed a lower probability of UO (OR 0.85 [95% CIs 0.75–0.96];  $p = 0.008$ ) but not mortality (OR 0.88 [95% CIs 0.62–1.25];  $p = 0.21$ ). No significant heterogeneity was observed among studies. However, these effects were observed in the analyses of non-RCTs. A significant lower probability of both UO and mortality were observed when invasive TTM methods were compared to non-invasive TTM methods and when temperature feedback devices (TFD) were compared to non-TFD methods. These results were significant particularly in non-RCTs.

**Conclusions:** Although existing literature is mostly based on retrospective or prospective studies, specific TTM methods (i.e., core, invasive, and with TFD) were associated with a lower probability of poor neurological outcome when compared to other methods in adult CA survivors (CRD42019111021).

**Keywords:** Targeted temperature management, Methods, Endovascular, Surface cooling, Survival, Neurological outcome, Meta-analysis

# TTM Uygulama



# TTM Uygulama

## Isı Monitörizasyonu

- Vücut çekirdek ısısı sürekli monitörize edilmeli.
- Altın standart yöntem santral venöz ısı ölçümüdür.
- Özefagial ısı ölçümü alternatif en iyi metotdur.
- Mesaneden ısı ölçümü idrar çıkışı  $<0.5$  ml/kg/saat ise yanlış sonuç verebilir.
- Rektal ısı ölçümü vücut iç ısısında oluşan akut değişikliklerde 1.5 derece kadar daha geride kalabilir.
- Timpanik, aksiller ölçümler yetersizdir ve yanlış sonuçlar verir.

## ABSTRACT

*Background:* It has been insufficiently investigated whether neurological function after out-of-hospital cardiac arrest (OHCA) would differ by 1 °C change in ordered target temperature of 33–36 °C among patients undergoing targeted temperature management (TTM) in the real-world setting.

*Methods:* This nationwide hospital-based observational study (The Japanese Association for Acute Medicine-OHCA Registry) conducted between June 2014 and December 2015 in Japan included OHCA patients aged  $\geq 18$  years who were treated with TTM. The primary outcome was one-month survival with neurologically favorable outcomes defined by cerebral performance category 1 or 2. To investigate the effect of TTM by 1 °C change in ordered target temperature of 33–36 °C on each outcome, random effects logistic regression analyses were performed.

*Results:* The final analysis included 738 patients. The proportion of patients with neurologically favorable outcome was 30.4% (7/23), 31.7% (175/552), 28.9% (11/38), and 30.4% (38/125) in the 33 °C, 34 °C, 35 °C,

*Resuscitation 133 (2018) 82–87*

0.90; 95% confidence interval [CI] 0.25–3.12, vs. 35 °C group, AOR 1.17; 95% CI 0.44–3.13, vs. 36 °C group, AOR 1.26; 95% CI 0.78–2.02).

*Conclusions:* In this population, we evaluated the difference in outcomes after adult OHCA patients received TTM by 1 °C change in ordered target temperature of 33–36 °C and demonstrated that there was no statistically significant difference in neurologically favorable outcomes after OHCA irrespective of target temperature.



VIEWPOINT

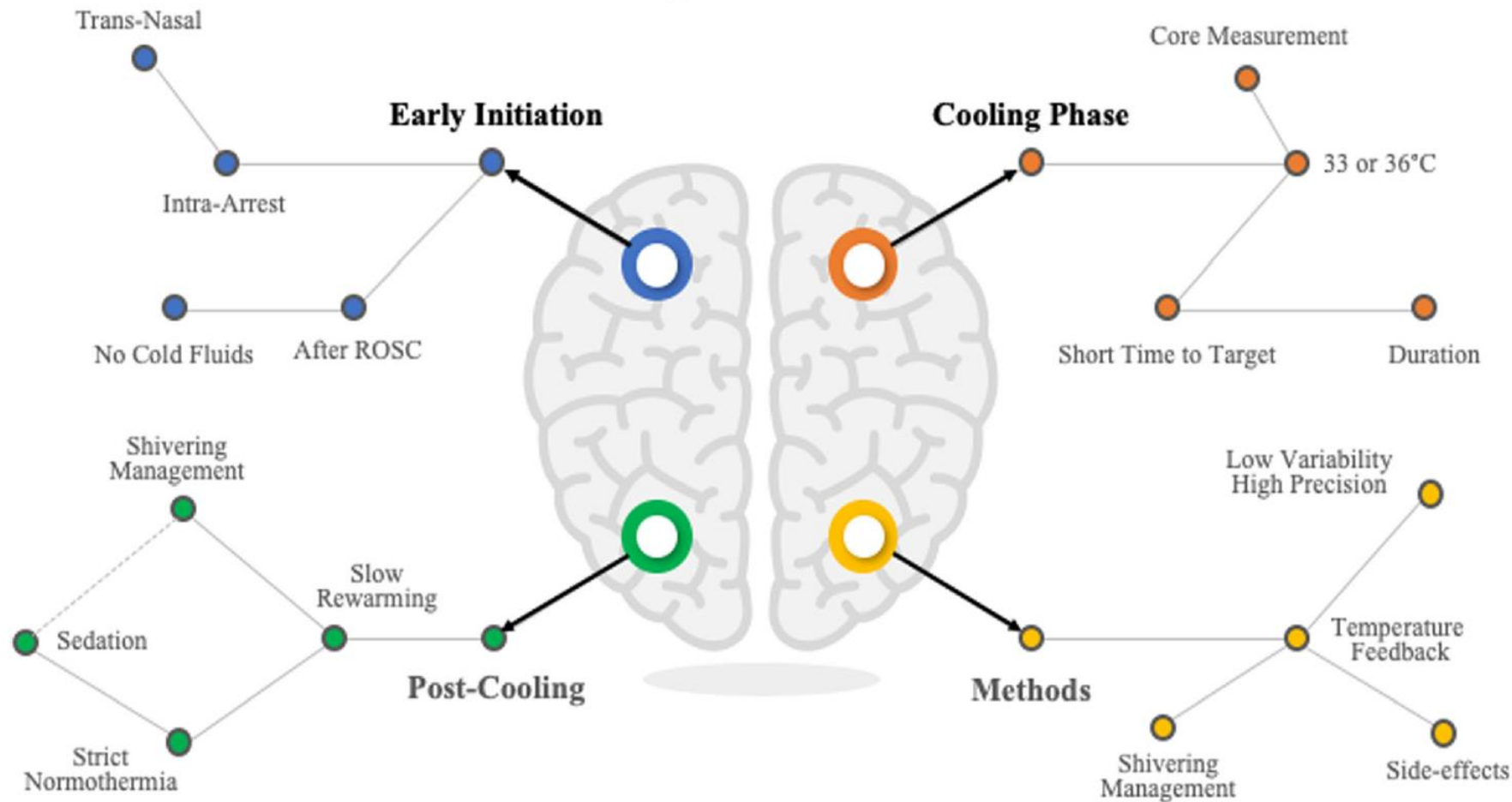
Open Access

# High Quality Targeted Temperature Management (TTM) After Cardiac Arrest

Fabio Silvio Taccone<sup>1\*</sup>, Edoardo Picetti<sup>2</sup> and Jean-Louis Vincent<sup>1</sup>



## HIGH QUALITY TTM



**Fig. 2** Some of the various factors related to targeted temperature management (TTM) which are relevant to providing “high-quality” TTM

# SON SÖZ

- Özellikle;
- Kardiyak Etiyolojiye Sahip Arrest Olgularında
- Kısa Süreli CPR
- Ve İlk Arrest Ritmi Şoklanabilir Bir Ritim İse

**TTM Faydalı Olabilir.**