Prehospital Cooling Does Not Improve Outcomes in Cardiac Arrest

Written by Nicola Parry

Francis Kim, MD, University of Washington, Seattle, Washington, USA, presented the final results from a randomized trial evaluating prehospital cooling for patients resuscitated from cardiac arrest and showed that prehospital cooling did not improve survival or outcomes compared with standard cooling procedures [Kim F et al. *JAMA* 2013].

Although therapeutic hypothermia has been shown to significantly reduce mortality and improve neurologic outcomes in cardiac arrest survivors, its optimal timing is unknown. This randomized clinical trial was designed to evaluate whether prehospital cooling in cardiac arrest patients, with and without ventricular fibrillation (VF), would reduce adverse clinical outcomes after resuscitation, compared with cooling that was initiated upon arrival in the emergency room.

To be included in the trial, patients had to have return of spontaneous circulation (ROSC), tracheal intubation, intravenous access, unconsciousness, and successful esophageal temperature probe placement. Patients with traumatic cardiac arrest, aged <18 years, temperature <34°C, mental status that was awake and following commands were excluded. The primary endpoints of the study were survival and neurological status at hospital discharge.

A total of 1359 patients were enrolled in the study and randomized to standard care with or without prehospital cooling with an infusion of up to 2 L of 4°C normal saline as soon as possible after ROSC. Of these, there were 583 patients with VF (292 assigned to prehospital cooling and 291 to control) and 776 patients without VF (396 assigned to prehospital cooling and 380 to control).

Mean temperature at randomization was ~36°C and prehospital cooling significantly lowered temperature at hospital arrival (–1.2°C vs –0.1°C for VF patients; –1.3°C vs –0.1°C for non-VF patients; p<0.0001 for both) compared with standard care. Patients randomized to prehospital cooling achieved a goal temperature by 4.2 hours, compared with 5.5 hours in those patients treated with hospital cooling alone (p<0.001).

The primary endpoint of survival to hospital discharge was similar between the prehospital cooling and hospital-only cooling groups (62.7% vs 64.3%; p=0.69 for VF; 19.2% vs 16.3%; p=0.30 for non-VF).

Additionally, prehospital cooling did not improve neurologic outcomes for either patients with VF (57.5% experienced full recovery or mild impairment vs 61.9% of controls; p=0.69) or for those with non-VF (14.4% vs 13.4%; p=0.30; Figure 2) compared with cooling at hospital arrival.

Re-arrest following randomization was also higher in the prehospital cooling arm (26% vs 21%; p=0.008). And upon hospital arrival, patients who received prehospital cooling had an increased incidence of pulmonary edema on chest x-ray (41% vs 30%; p<0.001) and requirement for diuretics in the first 12 hours of arrival (18% vs 13%; p=0.009).

Dr. Kim concluded that while prehospital cooling in cardiac arrest patients did reduce core temperature by hospital arrival, it did not improve outcomes in patients with and without VF when compared with hospital-only cooling. He also noted that since prehospital cooling increased the incidence of re-arrest, pulmonary edema on first chest x-ray, and need for diuretics, its routine use is not advocated in cardiac arrest patients.

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Lower-Temperature Target in Therapeutic Cooling Does Not Improve Outcomes

Written by Nicola Parry

Niklas Nielsen, MD, PhD, EDIC, DEAA, Helsingborg Hospital, Lund University, Helsingborg, Sweden, presented the final results from the Target Temperature Management After Cardiac Arrest trial [TTM; Nielsen N et al. *N Engl J Med* 2013], which demonstrated that therapeutic

cooling to a lower-temperature target does not improve outcomes of unconscious survivors of out-of-hospital cardiac arrest (OHCA) compared with cooling to standard temperature targets.

OHCA carries a high risk of death and poor neurological outcomes. Since induced hypothermia is associated with improved outcomes in these patients, its use is recommended in clinical guidelines. However, the optimal target temperature is unknown [Nielsen N et al. *Int J Cardiol* 2011].

The TTM trial [Nielsen N et al. *N Engl J Med* 2013] is the largest trial to study hypothermia in cardiac arrest patients. This international, multicenter, randomized trial was designed to evaluate whether cooling to a target temperature of 33°C compared with 36°C improved outcome in patients with OHCA.

Inclusion criteria were OHCA, age ≥18 years, unconscious, presumed cardiac cause, and stable return of spontaneous circulation (ROSC).

Exclusion criteria included unwitnessed cardiac arrest with initial rhythm of asystole, ROSC to screening interval >240 minutes, known or suspected acute intracranial hemorrhage or stroke, and body temperature <30°C.

The primary endpoint of the study was all-cause mortality through the end of the trial, and the main secondary outcome was a composite of death or poor neurologic function at 180 days, as evaluated by the Cerebral Performance Category scale and modified Rankin scale.

A total of 939 OHCA patients were enrolled in the study and randomized 1:1 to either target temperature managements of 33°C (n=473) or 36°C (n=466) for 24 hours.

At the end of the trial, there was no significant difference in the primary endpoint of patient mortality between the 33°C and 36°C groups (50% vs 48%; p=0.51).

And similarly, at 180-day follow-up, there was no significant difference in the percentage of patients who had died or had poor neurologic function, as evaluated with either the Cerebral Performance Category scale (54% vs 52%; p=0.78), or the modified Rankin scale (both 52%; p=0.87).

Serious adverse events, including bleeding, pneumonia, and electrolyte disturbances, were frequent in both the 33°C group and the 36°C group (93% vs 90%; p=0.09), with a significant increase in the incidence of hypokalemia (19% vs 13%; p=0.02)

Prof. Nielsen concluded that these results do not suggest any benefit for a target body temperature of 33°C in unconscious OHCA patients compared with 36°C. The optimal temperature for therapeutic hypothermia in this patient population therefore remains unclear, and further study is needed to determine the optimal temperature goal for patients with OHCA being treated with therapeutic hypothermia.

Results From the ROSE AHF Study

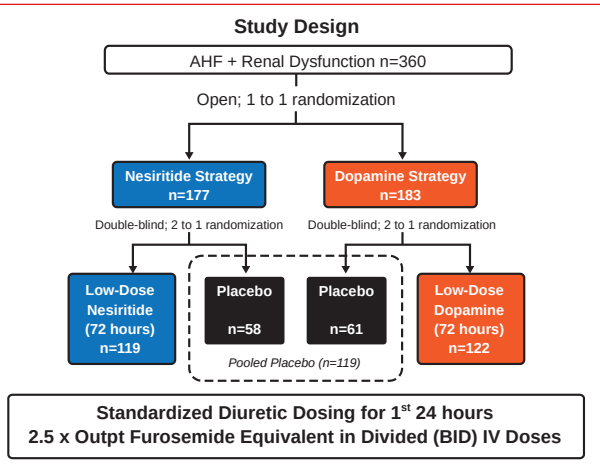
Written by **Mary Mosley**

In the Renal Optimization Strategies Evaluation in Acute Heart Failure Study [ROSE AHF; NCT01132846] treatment with low-dose dopamine or low-dose nesiritide did not improve renal dysfunction compared with placebo. The results of the National Heart, Lung, and Blood Institute -funded study were presented by Horng H. Chen, MD, Mayo Clinic, Rochester, Minnesota, USA.

ROSE-AHF examined whether the addition of low-dose dopamine (2 µg/kg/min) or low-dose nesiritide (0.005 µg/kg/min without bolus) to diuretic therapy would enhance decongestion and preserve renal function when compared with placebo in patients with acute heart failure (AHF) and ≥1 symptom (dyspnea, orthopnea, edema) or ≥1 sign (rales, edema, ascites, chest x-ray), and an estimated glomerular filtration rate (eGFR) 15 to 60 mL/min/1.73 m^2. For the first 24 hours, all patients received standardized diuretic dosing (2.5-times the outpatient dose) and patients were enrolled within 24 hours of hospitalization.

The randomization schema and number of patients in each group are shown in Figure 1. The two coprimary endpoints were cumulative urinary volume from randomization through 72 hours (decongestion endpoint), and change in serum cystatin-C concentration from randomization to 72 hours (renal function endpoint).

Figure 1. ROSE AHF Study Design



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Patients randomized had a median age of 70 years, 73% were male, and 26% had an ejection fraction (EF) >50%. Over half of patients (67%) had been hospitalized for AHF in the prior year. Their median eGFR was 44.5 mL/min/1.73 m^2, NT-proBNP was 4972 pg/mL, and the median outpatient dose of furosemide was 80 mg/day.