

**Control/Tracking Number:** 09-LBCT-20045-AHA

**Activity:** Late Breaking Clinical Trial Application

**Date/Time:** 11/15/2009 6:15PM

**Intra-arrest Transnasal Cooling: A Randomized Prehospital Study: PRINCE (Pre-ROSC Intra Nasal Cooling Effectiveness)**

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*Abstract:*

**Introduction:** Animal studies suggest a life-saving benefit for intra-arrest cooling. No human studies to date have demonstrated an effective, practical method. Trans-nasal evaporative cooling has sufficient heat transfer capacity for effective intra-arrest cooling and improves survival in swine.

**Aim:** To study the safety and feasibility of trans-nasal cooling in the pre-hospital setting and determine effects on neurologically intact survival to hospital discharge from the addition of intra-arrest trans-nasal cooling compared to hospital-based cooling alone.

**Method:** Patients in witnessed cardiac arrest with CPR  $\leq$ 20 min were randomized to intra-arrest trans-nasal cooling (treatment) vs standard ACLS care (control) in 15 European EMS systems. Trans-nasal cooling (RhinoChill, BeneChill Inc. San Diego, CA) was initiated using a mixture of volatile coolant plus oxygen for rapid evaporative heat transfer. In treatment patients, cooling was initiated as soon as feasible without interfering with ACLS protocols, during ongoing CPR. Patients in both groups were cooled upon hospital arrival.

**Results:** Of 200 patients, 18 were excluded from analysis. Patients randomized to prehospital cooling (n=83) or standard care (n=99) had similar demographics, initial rhythms, bystander CPR, intervals to CPR, ALS arrival, and ROSC. Eighteen device-related adverse events (one periorbital emphysema, 3 epistaxes, 1 peri-oral bleed, 13 nasal discolorations) were reported. In the treatment group, cooling was initiated at ~23 minutes following arrest and lowered admission tympanic and core temperatures significantly (34.2°C vs 35.5°C, p=0.000 and 35.1°C vs 35.8°C, p=0.012 respectively). Neurologically intact survival to discharge (CPC 1-2) was significantly better in intra-arrest cooled patients where CPR was started  $\leq$ 10 min irrespective of rhythm (45.5% vs 17.7%, 0.013, OR 7.52). No significant difference was seen if CPR was delayed >10 minutes.

**Conclusion:** Intra-arrest trans-nasal cooling is safe and feasible in the pre-hospital setting and significantly lowers tympanic and core temperature upon arrival at hospital. Neurologically intact survival to discharge is significantly improved in witnessed arrests where CPR is initiated  $\leq$ 10 minutes of collapse.