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Canadian Clinical Study Presented in The Journal of American Heart Association May 7th

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The clinical study published in the JAHA on May 7th shows that earlier cooling was associated with improved survival and improved neurological outcome.

The objective of this observational study was to observe the impact of early cooling initiation (door-to-TTM; DTT) on clinical outcomes of OHCA patients (out of the hospital cardiac arrest). The hypothesis was that shorter DTT initiation intervals would be associated with improved survival with favorable neurological outcome. The primary outcome was favorable neurological status (modified Rankin score of 0-3) at hospital discharge.

The study population consisted of 570 (68% shockable initial rhythm; 32% non-shockable) of the 3805 British Columbia patients who were enrolled in the CCC trial (Continuous Chest Compressions) and who survived to hospital admission. The median DTT duration was 122 minutes (Range: 35-218) in the entire cohort, including 35 minutes (Range 20-81) in the early group, and 218 minutes (Range 167-319) in the delayed group. The results of the study have several important clinical implications.

> **Firstly,** the researchers found that shorter DTT was associated with increased survival and with better neurological outcome, particularly in shockable rhythms, which is the patient group with the strongest indication for TTM. This association was strongest among those with initial shockable rhythms; early TTM initiation was associated with statistically significant improvement in survival and neurological outcome.
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> **Secondly,** because shorter DTT was demonstrative of a positive clinical outcome, these data should serve as a catalyst to enact more rigid and comprehensive protocols to ensure that prompt TTM initiation is of key priority in the OHCA patient population.

BrainCool's CEO, Martin Waleij comments;

- There are numerous reasons apart from neuroprotection why implementing TTM early may improve prognosis in patients resuscitated from OHCA, which this study clearly indicates. Although BrainCool has not been part of this trial published in The Journal of American Heart Association (impact factor 5.1) on May 7th, the same day as the PRINCESS clinical trial was published in JAMA (impact factor 47.6), it is worth highlighting a few comparison/reflections.
- First, PRINCESS study aimed to evaluate whether intra-arrest hypothermia, initiated as early as possible already in the patient's home or at the latest in the ambulance with trans nasal evaporative cooling (RhinoChill™), would provide outcome benefits when compared to standard of care in patients being resuscitated from OHCA.

The Canadian study had a similar hypothesis. The earlier cooling is started, the better outcome. To measure DDT, door to TTM initiation – meaning, how soon temperature management could be started after hospital arrival is shown to be very important. The median time was 122 minutes. In the PRINCESS trial, the corresponding time of initiation, the cooling would not only be directly upon arrival at the hospital but even before hospital arrival. Although the median time to start cooling by EMS personnel was 19 min after onset, one should note in a randomized trial, the randomization takes a few minutes and RhinoChill™ was applied in the

second vehicle. Thus, in clinical practice, the product could be applied in a very early phase (even earlier than 19 minutes or in the ideal case during CPR). As such, it might be worth emphasizing that BrainCell concept (RhinoChill™ System + BrainCool™ System for both out of the hospital as well as in-hospital) could potentially save 154 minutes on the average in a very early phase, as compared to this Canadian study. In PRINCESS, the difference in survival with CPC 1-2 between the studied groups was 3.1% in favor of early cooling. In the group with shockable rhythm, this difference was ~9%.

This sheds light on the statistical challenge in showing improved survival in the PRINCESS trial, as also the control group-initiated cooling in hospital diligently. As noted in the editorial of JAMA where it was pointed out that an overall increase of 1 – 2 % in survival would be considered as an enormous achievement in a cardiac arrest trial, although difficult to show given the need for very large trials. The increased survival was even more powerful in the group of patients presented with ventricular fibrillation. Similar findings were found in the Canadian trial.

The Canadian trial published in JAHA, where the American Heart Association (AHA) is the body that develops the US guidelines, is yet another piece of evidence supporting that the earlier one initiates cooling, the better the results become in both survival and neurological outcome. BrainCool is the only company in the temperature management space that not only could offer a DDT of zero (0) minutes with the BrainCell concept – combing the RhinoChill™ and BrainCool™ System to ensure early adaption of cooling and continuum of care – BrainCool also strives to initiate cooling even earlier in the chain, on the scene of the cardiac arrest followed by the EMS transport.

BrainCool's CEO, Martin Waleij concludes;

- The earlier the treatment is started, in particular in patients presented in ventricular fibrillation the more effective it will be in preventing brain damage and thus it is imperative to start as soon as possible, i.e., in the field, before arriving in hospital, or in the ED. There is a 20% increase in the mortality rate for every hour of delay in the initiation of cooling, as indicated in the previous clinical study.[1] Accordingly, we at BrainCool firmly believe and will strive to implement early safe cooling.

Reference:

1. Mooney MR, Unger BT, Boland LL, Burke MN, Kebed KY, Graham KJ, Henry TD, Katsiyiannis WT, Satterlee PA, Sendelbach S, Hodges JS, Parham WM. Therapeutic hypothermia after out-of-hospital cardiac arrest: Evaluation of a regional system to increase access to cooling. *Circulation*. 2011;124:206-214

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About BrainCool AB (publ)

BrainCool AB (publ) is an innovative medical device company that develops, markets, and sells leading medical cooling systems for indications and areas with significant medical benefits within the healthcare sector. The company focuses on two business segments, Brain Cooling and Pain Management. BrainCool AB (publ) is based in Lund, Sweden, and its share is listed on Spotlight Stock Market.