

Title: Insulin Sensitivity in Out of Hospital Cardiac Arrest Patients Treated with Hypothermia

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Abstract

Introduction: Therapeutic hypothermia (TH) is widely recommended to treat out-of-hospital cardiac arrest (OHCA) patients; however, cooling may significantly contribute to worsen stress-induced hyperglycemia, which has been associated with poor outcome in this setting.

Objective: This study analyzes insulin sensitivity (SI) profiles of OHCA patients undergoing TH to assess its impact on glucose metabolism.

Methods: Clinically validated model-based SI was identified using data from 20 OHCA patients (total of 710 hours of observation) admitted to the Christchurch Hospital ICU of Christchurch (New Zealand), immediately treated with TH after admission. Blood glucose (BG) control was provided using Specialised Relative Insulin-Nutrition Titration (SPRINT, targeting 4.0-6.1mmol/L. Data was divided into TH period ($\leq 35^{\circ}\text{C}$) and normothermia after ($>35^{\circ}\text{C}$) periods. The impact on SI was assessed by: **1**) median SI for each period; **2**) per-patient median [IQR] SI area under the cumulative distribution function (CDF) curve (AUC_iSI), as a measure of the range of SI in each period; **3**) area under the CDF of normalized hourly percentage changes in SI ($\text{AUC}_i\%\Delta\text{SI}$) for each period, as a measure of hour-to-hour variability.

Results:

Patients had between 15 and 24 hours in each temperature period and the two periods were contiguous. When in TH, patients had higher BG levels (6.1 [5.1-7.3] mmol/L) than in the normothermia phase (5.40 [4.7-6.2] mmol/L ($p < 0.05$)). Median SI were 1.93×10^{-4} [1.12 - 3.38×10^{-4}] and 3.60×10^{-4} [2.12 - 6.48×10^{-4}] L/mU.min, respectively ($p < 0.001$). Per-patient analysis showed a lower SI for TH than normothermia period (1.57×10^{-4} [0.92 - 2.55×10^{-4}] vs. 3.11×10^{-4} [2.17 - 4.90×10^{-4}] L/mU.min) ($p < 0.001$). Per-patient AUC_iSI was 4.82×10^{-4} [3.20 - 7.22×10^{-4}] in TH and 10.1×10^{-4} [4.03 - 19.7×10^{-4}] - $p < 0.05$) in the normothermia, whereas per-patient $\text{AUC}_i\%\Delta\text{SI}$ were 7.72 [3.92 -12.64] and 3.34 [2.57 - 5.85] ($p < 0.001$), respectively.

Conclusions: OHCA patients treated with TH showed a higher resistance to insulin and had a higher hour-hour SI variability when compared to the normothermia phase. This would imply a greater need for insulin administration and more frequent changes in insulin dosing to maintain safe glycemic control and avoid hypoglycemia during cooling.