## **Abstract**

In comatose out-of-hospital cardiac arrest victims, there is insufficient evidence for the timing of coronary angiography (CAG) in the absence of ST elevations on the baseline electrocardiogram, for the optimal body temperature during the temperature control procedure, or for S100 protein levels and regional brain saturation values measured by near-infrared spectroscopy regarding neurological prognostication.

The aim of this study was to compare the six-month survival and neurological outcome, evaluated by the Cerebral Performance Category (CPC) scale, in patients without ST-segment elevations indicated to immediate CAG and those initially treated conservatively, six-month CPC and acute complications according to the temperature target range of  $34-36\,^{\circ}\text{C}$  versus  $32-34\,^{\circ}\text{C}$  during therapeutic hypothermia, and S100 protein levels and regional brain saturation values with regard to the six-month CPC score.

We analysed a prospective registry of 283 unconscious patients after an out-of-hospital cardiac arrest undergoing therapeutic hypothermia. We evaluated the neurological outcome as the numerically lowest CPC score from 72 hours to six months after hospital admission: we defined a favourable outcome as CPC 1-2, while unfavourable as CPC 3-4. We included all registry patients in the target temperature range analysis, and we evaluated 158 of them without ST-segment elevations for the CAG timing. For prognostication, the S100 levels were determined in 48 and the regional brain saturation measured in 23 patients. We identified variables associated with six-month survival or CPC scores in a multivariate regression analysis. For the S100 protein, we plotted a receiver operating characteristic curve to detect a cut-off value for CPC 3-4.

In patients without ST-segment elevations, an immediate CAG as compared to the initially conservative approach was not associated with six-month survival (62% vs. 53%, p = 0.32) or CPC 1-2 (65% vs. 58%, p = 0.46), even in the myocardial infarction subgroup. However, immediate CAG was safe and did not prolong the time until hypothermia was achieved. In the whole cohort, the incidence of CPC 1-2 did not differ between the group aimed at the temperature target of 34 - 36 °C as compared to 32 - 34 °C (59% vs. 66%, p = 0.21). Nevertheless, we demonstrated a higher incidence of complications in patients with the lower temperature range. Serum S100 levels 48 hours after admission to the hospital, but not the baseline S100 levels or regional brain saturation values, were independently associated with a CPC score with an area under the receiver operating characteristic curve of 0.85. Serum S100 levels at 48 hours  $\geq 0.37 \mu g/L$  had 100% specificity and 39% sensitivity in predicting CPC 3-4.

In unconscious patients after an out-of-hospital cardiac arrest, immediate timing of CAG affects neither mid-term mortality nor neurological outcome as compared to the initially conservative approach in patients without ST-segment elevations. The neurological outcome is not associated with a target temperature range of 34 – 36 °C or 32 – 34 °C during hypothermia but can be independently predicted by the S100 protein levels determined 48 hours after hospital admission.