Role of targeted temperature management (TTM) in hanging-induced cardiac arrest

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Proposals Plenary Session
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Background: Hanging

- 2nd most common suicide method in the U.S. behind firearms, resulting in over 10,000 annual deaths
- Most common suicide method globally
- Leads to 77% - 88% mortality in younger population

No treatment currently exists for hanging-induced cardiac arrest

Background: TTM

- Recent case reports and small retrospective studies have suggested that TTM may lead to good neurologic outcome for survivors who sustained asphyxial cardiac arrest
- Studies in animals and newborns have demonstrated beneficial effects of TTM in reducing hypoxic encephalopathy caused by asphyxia
- A retrospective study of 138 patients from our institution suggests that cardiac arrest is associated with higher severity of injury and mortality in suicidal hanging survivors, and that TTM may improve the survival and functional outcome of hanging-induced cardiac arrest patients at hospital discharge
Hypothesis

We hypothesize that TTM may improve the survival and neurologic outcome of hanging-induced cardiac arrest adult survivors

Aims

- **Primary Aim:** To determine whether TTM improves the overall survival of hanging-induced cardiac arrest at hospital discharge
- **Secondary Aims:**
  - To determine whether TTM improves the neurologic outcome of hanging-induced cardiac arrest survivors at hospital discharge
  - To determine whether TTM improves the one-year survival of hanging-induced cardiac arrest survivors

Methods

- **Study type:** Multicenter retrospective
- **Data source:** Institutional trauma registry & cardiac arrest databases
- **Inclusion criteria:**
  - Patients age ≥ 18 years with hanging as primary injury type
  - Any above patients who received TTM during post-arrest care
- **Exclusion criteria:** Patients with age < 18 years, with asphyxia from other causes, or with cardiac arrests from other causes
Variables

- **Demographics:** Age, sex, race, co-morbidities, ISS, AIS head
- **Prehospital Variables:** GCS, location of arrest, total scene and transport time, initial rhythm, bystander CPR, time to ROSC, total hanging time
- **Admission Variables:** GCS, vital signs, labs (pH, lactate, BE)
- **Diagnostic Studies:** Cerebral anoxia, C spine injury, BCVI, airway injury
- **TTM Variables:** Timing and methods, goal temperature, duration, rate of rewarming
- **TTM-related Complications:** Seizure, arrhythmia, bleeding, hemodynamic instability, electrolyte derangements, pneumonia, sepsis
- **Operative Procedures:** Tracheostomy, feeding access
- **Discharge Outcomes:** GCS, Hospital and ICU LOS, mortality, cause of death, Cerebral Performance Category score at hospital discharge, length of survival after discharge

Cerebral Performance Category (CPC)

- CPC 1: Good neurological outcome; conscious, alert, able to work, might have mild neurologic or psychologic deficit
- CPC 2: Moderate neurological deficit; conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment
- CPC 3: Severe cerebral disability; conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory to severe dementia or paralysis
- CPC 4: Coma or vegetative state; any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep-wake cycles. Central temperature
- CPC 5: Brain death; apnea, arrest, EEG silence, etc.

Methods Analysis Plan

- Continuous variables will be compared with Student’s t-test or Wilcoxon rank-sum test. Categorical variables will be compared with Chi-squared test or Fisher’s exact tests
- All variables with a p value <0.2 on univariate analysis will be entered into a multivariable logistic regression analysis to identify independent risk factors for in-hospital mortality and poor neurologic outcome. Multiple-logistic regression model analyses will be performed to estimate the odds ratios (ORs) of the neurologic outcomes with 95% confidence intervals (CIs)
- Data analysis will include comparisons between the patient characteristics, survival, and functional outcome of suicidal hanging patients who suffered out-of-hospital cardiac arrest to those who did not, and between cardiac arrest patients who received TTM to those who did not receive TTM
Methods Analysis Plan

- For long-term outcome analysis, the 1-month, 6-month, and 12-month survival after hospital discharge of cardiac arrest patients will be determined.
- Survival time will be calculated as the difference between date of death and discharge date.
- Nonparametric Kaplan-Meier survival analysis will be used to compare survival between the groups. The association of unadjusted and adjusted long-term survival with TTM will be calculated.
- For the adjusted model, we will adjust for age, sex, race, shockable rhythm, hanging time, time to TTM initiation, time to ROSC, and withdrawal of life-sustaining measures.
- Data will be reported as adjusted odds ratios with 95% confidence intervals. Statistical significance will be set at a p<0.05.

Progress / Needs

- Progress
  - Single center retrospective data from the Shock Trauma Center already collected and analyzed (IRB approved)
  - IRB revision pending for multicenter retrospective trial
  - Development of EAST/AAST online data portal

- Needs for participating centers
  - Trauma registry data
  - Cardiac arrest data
  - Data entry into online data portal

Single Center Data

<table>
<thead>
<tr>
<th></th>
<th>TTM (n=9)</th>
<th>No TTM (n=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean ± SD)</td>
<td>32.2 ± 11.3</td>
<td>27.5 ± 7.8</td>
<td>0.26</td>
</tr>
<tr>
<td>Male (%)</td>
<td>88.9</td>
<td>76.9</td>
<td>0.62</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>88.9</td>
<td>69.2</td>
<td>0.36</td>
</tr>
<tr>
<td>ISS 90</td>
<td>12 ± 7</td>
<td>16 ± 14</td>
<td>0.38</td>
</tr>
<tr>
<td>Admission SBP (mmHg, mean ± SD)</td>
<td>167 ± 56</td>
<td>105 ± 50</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lowest SBP in initial 5 hours (mmHg, mean ± SD)</td>
<td>107 ± 30</td>
<td>78 ± 36</td>
<td>0.07</td>
</tr>
<tr>
<td>Prehospital GCS (%)</td>
<td>3 to 8</td>
<td>3 to 8</td>
<td>1.0</td>
</tr>
<tr>
<td>Admission GCS (%)</td>
<td>3 to 8</td>
<td>9 to 12</td>
<td>0.53</td>
</tr>
<tr>
<td>Admission Labs (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.29 ± 0.1</td>
<td>7.27 ± 0.2</td>
<td>0.86</td>
</tr>
<tr>
<td>Base Excess</td>
<td>-5.5 ± 3.5</td>
<td>-7.1 ± 7.6</td>
<td>0.56</td>
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<tr>
<td>Lactate</td>
<td>5.4 ± 3.4</td>
<td>6.6 ± 4.8</td>
<td>0.56</td>
</tr>
<tr>
<td>Cerebral anoxia (%)</td>
<td>66.7</td>
<td>61.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Overall survival (%)</td>
<td>44.4</td>
<td>23.1</td>
<td>0.38</td>
</tr>
<tr>
<td>Discharged with good neurologic outcome (%)</td>
<td>33.3</td>
<td>7.7</td>
<td>0.25</td>
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</tbody>
</table>
Goals / Timeline

- Statistical and protocol revisions by February 1st, 2016
- Participating centers identified by March 1st, 2016
- IRB approval by March 31st, 2016
- Data collection from April 1st to October 1st, 2016
- Analysis completion by November 1st, 2016

Goal: AAST or EAST submission 2017