

Summary:

Currently, the outcomes from traumatic exsanguination cardiac arrest (CA) show that over 50% of deaths due to trauma occur at the scene, where medical care is limited. Less than 10% of patients who become pulseless from trauma survive. However, in an appropriate setting, some of those traumatic injuries could be surgically repairable.

Emergency preservation and resuscitation (EPR) is a novel approach for resuscitation of exsanguination CA victims. EPR uses deep hypothermic preservation for prolonged CA to buy time for transport, damage control surgery, and delayed resuscitation with cardiopulmonary bypass (CPB). Initially, we used a dog model to maximize clinical relevance. We showed that the efficacy of EPR is related to the depth of hypothermia and duration of CA. Pharmacologic adjuncts tested to augment hypothermia generally failed. Extended hemorrhagic shock did not prevent the success of EPR vs. conventional resuscitation if extended post-resuscitative hypothermia was provided. Oxygenation of the flush allowed extending of survivable duration of deep hypothermic CA.

Because of the lack of molecular tools available for use in dogs, we developed a rat EPR model to study the cellular and molecular mechanisms underlying deep hypothermic neuroprotection to allow us to define specific targets for future interventions, assess markers of reversibility, and screen novel therapies. We showed that (1) rat EPR model with miniaturized CPB was feasible; (2) shorter durations of CA and deeper hypothermia yielded better outcome; (3) extended durations of normothermic CA prior to induction of hypothermia resulted in worse outcome, extensive neuronal death and neuroinflammation; (4) blood-brain barrier was not permeable even in insults with poor outcome; (5) three neuroprotective pharmacological strategies failed to confer additional benefits to hypothermia; (6) neuronal degeneration and neuroinflammation after EPR exhibited a characteristic temporo-regional pattern that may require selective therapeutical approaches.