Active intrathoracic pressure regulation during post cardiac arrest care significantly reduces vasopressor requirements, improves cerebral blood flow, and promotes neurologically intact survival

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I have the following financial interests or relationships to disclose:

none

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Intrathoracic Pressure Regulation Physiology

• Active intrathoracic pressure regulation (a-IPR) lowers intrathoracic pressures during the expiratory phase of positive pressure ventilation
• a-IPR enhances venous return and lowers central venous pressure.
• a-IPR improves venous drainage from the brain, lowers ICP, and reduces the resistance to forward blood flow to the brain.
• The increase in venous blood flow back to the heart, increases cardiac preload and consequently stroke volume and cardiac index.
• Combined, these effects result in an increase in mean systemic arterial pressure, cardiac output, and cerebral perfusion
Manipulating Intrathoracic Pressures

Background

Hemodynamics are often extremely unstable after ROSC in cardiac arrest patients.

During this period of time, vasopressors are often required.

However, vasopressors can increase myocardial dysfunction, cause ischemia and life-threatening arrhythmias, and elevate ICP.

Study Hypothesis

- Active IPR after ROSC may enhance cerebral perfusion and simultaneously reduce the need for vasopressor support.
Study Overview

- Protocol approved by the animal care committee
- Number of animals: 12
- Animal weights 39 ± 1 kg
- Anesthesia: 1.5% Isoflurane
- FiO₂ adjusted to maintain SpO₂ > 95%
- RR adjusted to maintain ETCO₂ = 40 mmHg
- Groups: aIPR or no aIPR
- Epinephrine infusion adjusted to maintain a MAP of 75 mmHg
- Primary Endpoints: vasopressor requirements and cerebral blood flow (CBF) were recorded continuously for five hours
- Statistical Methods: Study powered only for primary endpoints. Results expressed as mean ± SD, Student’s t-test.

Methods - Study Timeline

Study Intervention

Results: MAP

MAP throughout the study (5 hours) was matched between groups through careful control of IV epinephrine.
Total epinephrine during the post-ROSC period was significantly reduced with a-IPR (0.08 ± 0.09 vs 0.29 ± 0.12 mg, p<0.01).

CBF, measured with a Bowman Perfusion Monitor® Hemedex invasive thermospectral analysis
Mean CBF was significantly higher in the a-IPR group for the first five hours of post-ROSC care (30.4 ± 6.6 vs 18.7 ± 4.4 ml/100gm/min, p<0.05).

Additional Observations: 24-Hour Survival and Cerebral Performance
Conclusions

- IPR has the potential to treat cardiovascular instability and brain injury during the post-resuscitation phase of cardiac arrest.
- IPR therapy after ROSC reduced the amount of epinephrine needed to maintain a MAP of 75 mmHg and it improved cerebral hemodynamics.
- These are important new findings given the potential negative effects of epinephrine administration after resuscitation.

Thank you!

Questions: nosegal@umn.edu

Manipulating Intrathoracic Pressures

- Founding Concept: Lower intrathoracic pressure in the chest during the decompression phase of CPR enhances venous return to the thorax.
- Each time the chest wall recoils following a compression, a one-way pressure regulating valve can be used to transiently block air/oxygen from entering the lungs, creating a small regulated vacuum in the chest, resulting in improved preload and venous return.
- Studies show that survival after cardiac arrest with favorable neurologic outcomes can improve by 25% or more when using a device to lower negative intrathoracic pressure.}

References:
5. Dudley et al., Circulation 2010;122:A51.
The fundamental relationship between intrathoracic pressure and changes in blood flow back to the heart were first described in 1967 by Moreno et al. The pressure relationships between the thorax, CSF spaces, and the brain and the detrimental effects of positive end expiratory pressure (PEEP) and increases in mean airway pressure were first described in the late 70s by Huseby, Frost, Aidinis and others.

Manipulating Intrathoracic Pressures

![Diagram showing intrathoracic pressures and effects on blood flow](source)

**Pre-Clinical Studies**

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<td>Cardiac Arrest (Adult Porcine)</td>
<td>IPR-CPR significantly improved vital organ perfusion pressures, S3/S5, and 1 hr survival compared to S-CPR.</td>
<td>Yannopoulos et al., Circulation 2005;112(6):803-11</td>
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<tr>
<td>Hemorrhagic Shock (Adult Porcine)</td>
<td>IPR significantly improved MAP and CERP in 35% and 50% hemorhaged animals.</td>
<td>Yannopoulos et al., Resuscitation 2001;70(3):445-51</td>
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<td>Sepsis (Adult Porcine)</td>
<td>IPR significantly increased CO, SV and MAP when applied in a pulsed fashion. PA pressure was significantly decreased.</td>
<td>Can et al., Crit Care Med 2010;38(10):2555-64</td>
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<tr>
<td>Peet SCA Elevated ICP (Adult Porcine)</td>
<td>IPR increased significantly improved CERP and MAP, and MAP when applied in a pulsed fashion. PA pressure was significantly decreased.</td>
<td>Yannopoulos et al., Crit Care Med 2001;30(5):1041-57</td>
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<tr>
<td>Traumatic Brain Injury (Adult Porcine)</td>
<td>IPR significantly decreased ICP and increased CERP and carotid blood flow in a TBI model.</td>
<td>Metzger et al., Circulation 2008;118(18):S664-72 Neurocrit Care 2010; 13:S183</td>
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**Clinical Studies**

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<td>Huffmeyer et al., The Intrathoracic Pressure Regulator Lowers ICP in Patients with Altered Intracranial Elastance. ASA, Abstract 2010</td>
<td>In 8 of 9 patients, ICP was reduced by 25% during IPR in patients with elevated ICP from multiple causes including TBI.</td>
</tr>
<tr>
<td>Birch et al., Hemodynamic Effects of the Intrathoracic Pressure Regulator for Treatment of Intraoperative Hypotension. ASA, Abstract 2010</td>
<td>During IOH in 14 patients, IPR improved hemodynamics as manifested by a significant increase in SBP of 10 mmHg and a significant increase in MAP of 8 mmHg.</td>
</tr>
<tr>
<td>Segal et al., Intrathoracic pressure regulation during cardiopulmonary resuscitation: a feasibility case-series. Resuscitation, 2013;84(4):450-56.</td>
<td>ETCO2 levels and ROSC rates were significantly higher in the 11 IPR patient compared to the 74 control patient.</td>
</tr>
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Results: Potential Clinical Concerns

The mean PaO2/FiO2 ratio for the a-IPR group was 230 ± 30 vs 386 ± 22 mmHg in the non a-IPR treated group suggestive of pulmonary shunting in the a-IPR group.

However, no evidence of respiratory distress was witnessed once the animals had been weaned from the ventilator and no pulmonary compromise was evident upon autopsy. Previous histological evaluation of porcine lungs exposed to 24 hours of a-IPR therapy did not show significant pulmonary compromise compared to control animals.