Heart Transplantation Outcomes in Donation After Circulatory Death – Large Animal Model

Marian Urban, Department of Surgery, Division of Cardiothoracic Surgery, University of Nebraska Medical Center, Omaha, NE 68198

University of Nebraska Medical Center

Background/Introduction

- Donation after brain death versus donation after circulatory death
- Thoracoabdominal Normothermic Regional Perfusion

Objective

Increase the quantity and quality of cardiac allografts from donation after circulatory death

Aims

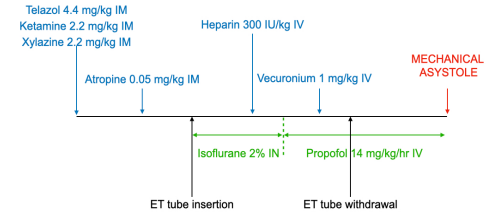
Aim 1: Develop a large animal heart transplantation model utilizing DCD grafts reanimated with in-situ normothermic regional perfusion (NRP)

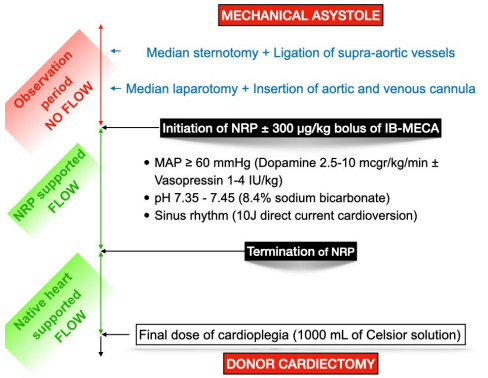
Aim 2: Assess the impact of warm ischemia on ventricular function, cardiomyocyte energy metabolism, structural changes and level of oxidative stress during reanimation process and subsequent transplantation od DCD hearts

Experimental design

- Single arm non-randomized study
- 10 domestic pigs subjected to asphyxiation circulatory arrest
- Donor hearts were reanimated after 15 minutes of warm ischemia with TA-NRP for 60 minutes
- Animals were weaned from TA-NRP and cardiac allografts were evaluated with transesophageal echocardiography and systolic and diastolic function was measured with conductance catheters and analyzed with pressure-volume loops
- Tissue and blood samples were collected at baseline, at the end of warm ischemia, and after reperfusion
- Samples were processed and stored

Methods





Cell death

- Cell cytoarchitecture in H&E stained slides
- Immunohistochemistry (Caspase-3, TUNEL)
- Transcriptomics with RNA seek

Oxidative stress

- Superoxide levels measured using electron paramagnetic resonance (EPR) spectroscopy and a superoxide-sensitive cyclic hydroxylamine spin probe

Results

Out of 10 experiments, we were able to successfully reanimate 6 cardiac allografts that were subjected to functional and molecular analyses

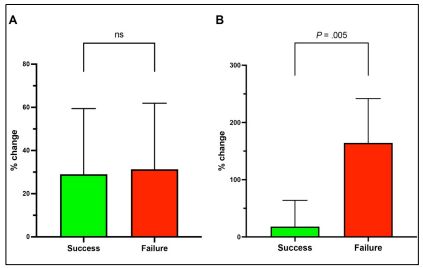
All reanimated allografts demonstrated satisfactory post ischemia contractile function and were deemed transplantable

Aim 1:

We have optimized the circuit configuration and developed a reproducible animal model of hypoxic cardiac arrest. This model will serve for all future studies evaluating different strategies/compounds aimed at functional optimization of DCD cardiac allografts.

Aim 2:

Our experiments demonstrated that during the reperfusion phase of in-situ DCD heart resuscitation superoxide levels are increased. Organs that failed to regain satisfactory contractile function displayed a greater elevation of superoxide levels in comparison to successfully resuscitated organs.



Contact

E-mail: marian.urban@unmc.edu

Phone: (402) 559-4481

University of Nebraska Medical Center