INTRODUCTION

- 4,545 deceased donor cardiac transplants were performed in the United States in 2023.
- The donor hearts are inevitably subjected to ischemia-reperfusion injury (IRI) that triggers a sequence of adverse effects.
- IRI is first encountered by microvascular endothelial cells (ECs), causing endothelial injury and predisposing the donor heart to higher immunogenicity.
- Endothelial autophagy, or "self-eating," the process of disposing of and recycling cellular machinery, has been implicated as a response to cardiac IRI.
- IRI results in a summative microvascular EC injury. EC injury then triggers a cascade of innate and adaptive immunological signaling, predisposing the donor hearts to higher immunogenicity.

RESEARCH OBJECTIVES

1) Describe changes in microvascular EC autophagy during IRI.
2) Understand whether the impact of EC autophagy is protective or detrimental as related to IRI and cellular immunogenicity.

METHODS

- To mimic conditions of the donor heart during cold preservation and warm reperfusion, we subjected a 2,3 (ECs), causing endothelial injury and predisposing ECs to higher immunogenicity.
- Delivery of autophagy-inducing rapamycin via nanoparticles to cardiac ECs has the potential to increase the longevity of cardiac allografts and reduce the burden of systemic immunosuppression.

CONCLUSIONS

- MCEC autophagy increases during early post-reperfusion time points, likely as a natural adaptation to stress.
- EC autophagy may be protective during IRI by mitigating EC immunogenicity, as deletion was deleterious to cell health.
- Bolstering microvascular EC autophagy in donor hearts during CS prior to transplantation may mitigate insults incurred during IRI.
- Delivery of autophagy-inducing rapamycin via nanoparticles to cardiac ECs has the potential to increase the longevity of cardiac allografts and reduce the burden of systemic immunosuppression.

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REFERENCES