Morbidity and Mortality of Heterotopic Partial Heart Transplantation in Rodent Models

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INTRODUCTION

Congenital heart disease (CHD) is a serious problem, as it remains the most prevalent congenital disorder. Valvular dysfunction represents a significant portion of these babies born with CHD. The status quo for heart valve replacements in babies is homograft valve replacements, bioprosthetic valve replacements, Ross pulmonary auto-transplant procedures or orthotopic heart transplantation. Infants who have to undergo any of these procedures are consistently going to outgrow their replacement valve, or the valve will degenerate and cause complications. In regard to orthotopic heart transplantation, there are limited donors and recipient pools due to extensive eligibility criteria. Approximately 20–25% of infants on the waiting list die prior to this life-saving procedure.

Partial heart transplantation presents a new type of transplant procedure that has the potential to improve patient outcomes and decrease the need for repeated surgeries across the patient's lifespan. Partial heart transplantation involves transplanting only the valves of a donor heart into the recipient. The partial heart transplant differs from conventional homografts in that the cells remain viable. Conventional homografts are harvested from cadavers, and this process incurs a long ischemic time that kills the cells in the tissue. In the proposed partial heart transplant procedure, the ischemic time is reduced to ensure a living graft. A living graft has the ability to grow and repair, processes that are essential for the long-term success of the procedure.

In this study, we sought to evaluate rodent models for heterotopic aortic valve transplantation.

METHODS

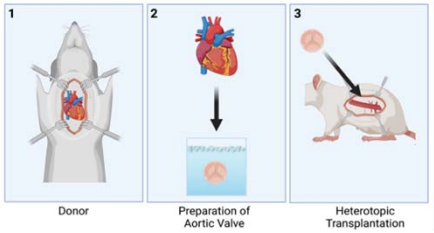
The heterotopic heart valve transplant was tested in young rat pups, with the goal to assess for valve growth over time. Thirty-three partial heart transplants using the abdominal aortic model were completed, and thirty-three partial heart transplants using the renal subcapsular model were completed. There were 47 total donor animals. Thirty-three donor animals were used for the abdominal aortic model, donating their entire valve. Fourteen donors were used for the renal subcapsular model, and they each donated 3 leaflets that were separated and used in multiple recipients.

METHODS

Donors- A laparotomy was performed, exposing the inferior vena cava and the abdominal aorta. Next, the animal was heparinized via the vena cava. At this point, the animal was euthanized by exsanguination via aortic transection. The aortic valve and root were then dissected and extracted from the heart.

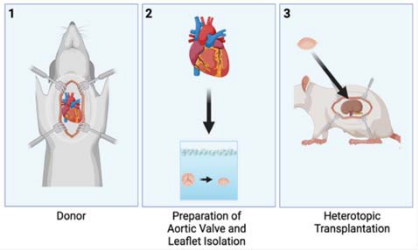
Abdominal Aortic Model:

Recipient - A laparotomy was performed, and the animal was subsequently heparinized the same as the donor procedure. The abdominal aorta was circumferentially mobilized from below the renal arteries to the bifurcation of the iliac arteries. This segment was isolated by applying vascular clamps. At this point, the aorta was incised, and the donor heart valve was anastomosed to the arteriotomies.



Renal Subcapsular Model:

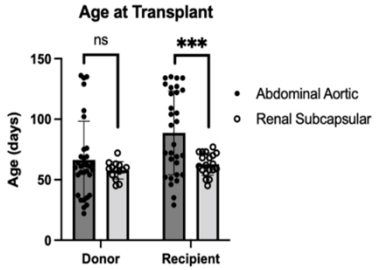
Recipient - For this model, only one leaflet of the aortic valve was required. The donor aortic valve was dissected into the three leaflets, and only one was implanted per recipient animal. The kidney of the recipient animal was exposed using a flank incision. Next, a small incision was made in the capsule of the kidney using Vannas spring scissors. Then, a shallow subcapsular pocket was made using a blunt probe, and the valve leaflet was implanted.

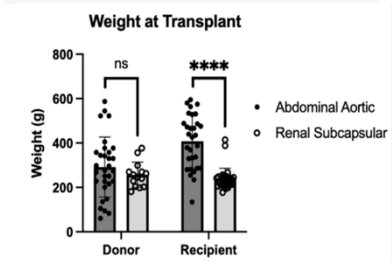


RESULTS

The abdominal aortic model and the renal subcapsular model were compared using the age of the animal at transplant (for both the donor and recipient), weight of the animal at transplant (for both the donor and recipient). Continuous variables are presented with standard deviations (SD). *T*-tests were used to assess if there was a statistically significant difference between the two models. The significance level was set at a *p*-value of 0.05.

Demographics:





Mortality:

A total of 33 animals underwent heterotopic partial heart transplantation in the abdominal aortic position. The results of this model found a **60.61% (*n* = 20/33)** intraoperative mortality rate and a **39.39% (*n* = 13/33)** perioperative mortality rate. Intraoperative mortality was due to vascular complications from the procedure, and perioperative mortality was due to graft thrombosis. A total of 33 animals underwent heterotopic partial heart transplantation in the renal subcapsular position. The results of this model found a **3.03% (*n* = 1/33)** intraoperative mortality rate, and the remaining **96.97%** survived **(*n* = 32/33).**

CONCLUSIONS

While the heterotopic transplantation of valves into the abdominal aortic position had significant morbidity and mortality in the rodent model, the renal subcapsular model provided evidence for successful heterotopic transplantation. We still believe that larger animal models will be pivotal for studying the immunobiology and growth potential of this new type of transplant procedure. More research needs to be conducted to adjust the methodology and the model to achieve optimal postoperative survival and assessment. The goal moving forward will be to demonstrate the success of the procedure in a larger, more comparable model to humans. In future studies, the growth of the valves over time should be measured, all with the goal of improving outcomes and quality of life for patients with congenital valve dysfunction.

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DISCLOSURE

The presenting author has no financial relationships to disclose.