Post-Heart Transplant Outcomes of Sensitized Patients who have Undergone Desensitization Therapy

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Abstract

Background: Sensitized patients awaiting heart transplantation are at increased risk for mortality as their waitlist time is lengthened due to incompatible donors and a subsequently narrowed donor pool. Therefore, these patients undergo desensitization therapies to lower circulating antibodies and to restore the donor pool for these patients. These patients subsequently undergo heart transplantation; however it has not been well established as to their longer-term outcome following heart transplantation.

Methods: Between 2010 and 2014 we assessed 42 patients awaiting heart transplantation who were sensitized (average cPRA 84%) and subsequently underwent desensitization therapy prior to heart transplantation. These patients then underwent heart transplant and were followed for 5-year outcome. Endpoints post-transplant included 5-year survival, 5-year freedom from cardiac allograft vasculopathy (CAV), 5-year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, percutaneous coronary intervention/angioplasty, new congestive heart failure, pacemaker/implantable cardioverter-defibrillator placement, stroke), and 1-year freedom from rejection (any treated rejection (ATR), acute cellular rejection (ACR), antibody mediated rejection (AMR)). Patients were compared to a contemporaneous group of heart transplant patients that did not receive desensitization therapy prior to transplant conditional to 1-year survival (n=329) for the same endpoints.

Results: Sensitized patients that received desensitization therapy prior to transplantation had significantly lower freedom from AMR. These is a trend for increased freedom from NF-MACE in this desensitized group. There were no differences between the two groups in terms of survival, freedom from CAV, and freedom from ACR.

Conclusion: Sensitized patients awaiting heart transplantation who undergo desensitization therapy appear to have decreased freedom from first-year AMR. However, these patients appear to have comparable outcome (ie survival and CAV) at 5-years post-transplantation to heart transplant patients that do not undergo desensitization therapy.

Background

- Sensitized patients awaiting heart transplantation are at increased risk for mortality as their waitlist time is lengthened due to incompatible donors and a subsequently narrowed donor pool.
- Therefore, these patients undergo desensitization therapies to lower circulating antibodies and to restore the donor pool for these patients.
- These patients subsequently undergo heart transplantation; however it has not been well established as to their longer-term outcome.

Purpose

To examine the long-term outcomes of desensitized patients following heart transplantation.

Methods

- Between 2010 and 2014 we assessed 42 patients awaiting heart transplantation who were sensitized (average cPRA 84%) and subsequently underwent desensitization therapy prior to heart transplantation.
- These patients then underwent heart transplant and were followed for 5-year outcome.
- Endpoints post-transplant included:
  - 5-year survival
  - 5-year freedom from cardiac allograft vasculopathy (CAV)
  - 5-year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, percutaneous coronary intervention/angioplasty, new congestive heart failure, pacemaker/implantable cardioverter-defibrillator placement, stroke)
  - 1-year freedom from rejection including any treated rejection (ATR), acute cellular rejection (ACR), and antibody mediated rejection (AMR).
- Patients were compared to a contemporaneous group of heart transplant patients that did not receive desensitization therapy prior to transplant conditional to 1-year survival (n=329) for the same endpoints.

Demographics

Demographics	Sensitized HTx Patients with desensitization (n=42)	HTx Patients without desensitization (n=329)	P-value
Mean Recipient Age, Years ± SD	49.0 ± 13.2	56.1 ± 12.9	<0.001
Mean Donor Age, Years ± SD	32.9 ± 12.1	35.4 ± 17.0	0.350
Body Mass Index, Mean ± SD	25.4 ± 4.9	25.0 ± 4.2	0.577
Female (%)	71.4%	25.5%	<0.001
Previous Pregnancy in Females (%)	83.3%	77.1%	0.606
Ischemic Time, Mean Mins ± SD	192.6 ± 60.1	171.1 ± 58.7	0.027
Primary Reason For Transplant, Underlying Diagnosis of CAD (%)	31.0%	38.9%	0.399
Status 1 at Transplant (%)	88.1%	76.3%	0.114
Cytomegalovirus Mismatch (%)	14.3%	22.2%	0.316
Diabetes Mellitus (%)	28.6%	28.9%	1.000
Treated Hypertension (%)	51.2%	51.9%	1.000
Insertion of Mechanical Circulatory Support Device (%)	38.1%	22.5%	0.035
Prior Blood Transfusion (%)	58.5%	38.2%	0.017
Pre-Transplant PRA ≥ 10% (%)	95.1%	26.7%	<0.001
Pre-Transplant Creatinine, Mean ± SD	1.47 ± 1.1	1.50 ± 1.2	0.877
ATG Induction Therapy (%)	85.7%	38.4%	<0.001

Outcomes

Endpoints	Sensitized HTx Patients with desensitization (n=42)	HTx Patients without desensitization (n=329)	P-value
5-Year Survival	92.9%	91.2%	0.704
5-Year Freedom from CAV	83.3%	79.9 %	0.534
5-Year Freedom from NF-MACE	90.5%	77.5%	0.053
1-Year Freedom from ATR	76.2%	86.6%	0.081
1-Year Freedom from ACR	90.5%	93.3%	0.603
1-Year Freedom from AMR	85.7%	97.0%	0.001

Results Summary

- Sensitized patients that received desensitization therapy prior to transplantation had significantly lower freedom from AMR.
- These is a trend for lower freedom from NF-MACE in this desensitized group.
- There were no differences between the two groups in terms of survival, freedom from CAV, and freedom from ACR.

Conclusion

- Sensitized patients awaiting heart transplantation who undergo desensitization therapy appear to have decreased freedom from first-year AMR.
- However, these patients appear to have comparable outcome (ie survival and CAV) at 5-years post-transplantation to heart transplant patients that do not undergo desensitization therapy.

Author Disclosures

J Kobashigawa has received research grants and/or honoraria from CareDx, Inc., Sanofi-Genzyme, CSL-Behringer and One Lambda Inc. and is part of the advisory board for TransMedics. D Chang has received research grants from Mesoblast, Amgen, and Biocardia and is a stock shareholder of Abbott Laboratories, AbbVie Inc, Repligen, Portola Pharmaceuticals, and Amarin Corp. L Czer has received research grants from St. Jude Medical and Abbott Laboratories. D Ramzy has received honoraria from Abiomed, Cardiac Assist Inc, Medtronic Vascular Inc, and Zoll Services LLC and is a consultant/speaker for Abbott Laboratories, Baxter Healthcare, and Intuitive Surgical Inc. F Esmailian has received research grants from TransMedics Inc and is a consultant for Biom Up SA. J Patel has received research grants from Alexion Pharmaceuticals, Pfizer, Alnylam Pharmaceuticals and Astra Zeneca and is part of the advisory board/speaker bureau for Mallinckrodt Pharmaceuticals, Therakos and Akcea. M Kittleson, K Nishihara, A Shen, G Jamero, and B Coleman have no financial relationships to disclose.