Longer-Term Morbidity/Mortality of Severe Left Ventricular Primary Graft Dysfunction after Heart Transplantation

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Abstract

Background: Severe primary graft dysfunction (PGD) is seen in approximately 5% of all heart transplant recipients per the International Society for Heart and Lung Transplantation (ISHLT) PGD grading scale. These patients suffer endothelial cell damage and are known to have increased risk of early mortality. It is not known whether the survivors of severe PGD develop more donor specific antibody (DSA), have more treated rejections, have increased risk for the development of cardiac allograft vasculopathy (CAV), and have increased mortality at 3 years post transplantation. We sought to assess this potential association.

Methods: Between 2010-16 we assessed 24 heart transplant patients who developed severe PGD per the ISHLT PGD grading scale. These patients who developed severe PGD were compared to those without severe PGD in a contemporaneous era. Patients were then followed for 3 years and assessed for the following endpoints: 3-year survival, 3-year freedom from CAV, 3-year freedom from non-fatal major adverse cardiac events (NF-MACE, defined as myocardial infarction, percutaneous coronary intervention/angioplasty, new congestive heart failure, pacemaker/implantable cardioverter-defibrillator placement, and stroke), and 1-year freedom from rejection, including any treated rejection (ATR), acute cellular rejection (ACR), and antibody mediated rejection (AMR).

Results: Patients with severe PGD had decreased 3-year survival, 1-year freedom from any treated rejection, and 3-year freedom from NF-MACE compared to those patients who did not have severe PGD. There were no significant differences between the two groups in terms of 3-year freedom from CAV and freedom from DSA.

Conclusion: Severe PGD appears to have increased mortality and morbidity with more rejection and more NF-MACE. More intense therapies to offset the inflammatory response from severe PGD should be pursued.

Background

- Severe primary graft dysfunction (PGD) is seen in approximately 5% of all heart transplant recipients per the International Society for Heart and Lung Transplantation (ISHLT) PGD grading scale.
- These patients suffer endothelial cell damage and are known to have increased risk of early mortality.
- It is not known whether the survivors of severe PGD develop more donor specific antibody (DSA), have more treated rejections, have increased risk of the development of cardiac allograft vasculopathy (CAV), and have increased mortality at 3 years post transplantation.

Purpose

To assess the outcome of heart transplant patients who develop severe left ventricular primary graft dysfunction (LV-PGD).

Methods

- Between 2010-16 we assessed 24 heart transplant patients who developed severe PGD per the ISHLT PGD grading scale.
- These patients who developed severe PGD were compared to those without severe PGD in a contemporaneous era.
- Patients were then followed for 3 years and assessed for the following endpoints:
  - 3-year survival
  - 3-year freedom from CAV
  - 3-year freedom from non-fatal major adverse cardiac events (NF-MACE, defined as myocardial infarction, percutaneous coronary intervention/angioplasty, new congestive heart failure, pacemaker/implantable cardioverter-defibrillator placement, and stroke)
  - 1-year freedom from rejection, including any treated rejection (ATR), acute cellular rejection (ACR), and antibody mediated rejection (AMR).

Demographics

Demographics	HTx Patients with Severe PGD-LV (n=24)	HTx Patients without Severe PGD-LV (n=572)	P-value
Mean Recipient Age, Years ± SD	56.3 ± 14.4	55.2 ± 12.9	0.689
Mean Donor Age, Years ± SD	38.4 ± 11.8	35.5 ± 15.4	0.374
BMI, Mean ± SD	26.1 ± 5.5	25.2 ± 4.6	0.342
Female (%)	25.0%	28.7%	0.820
Ischemic Time, Mean Mins ± SD	209.6 ± 63.7	172.1 ± 55.5	0.002
Primary Reason For Transplant, Underlying Diagnosis of CAD (%)	54.2%	36.5%	0.088
Status 1 at Transplant (%)	66.7%	80.7%	0.113
Cytomegalovirus Mismatch (%)	25.0%	22.3%	0.803
Diabetes Mellitus (%)	29.2%	30.4%	1.000
Treated Hypertension (%)	52.2%	54.5%	0.834
Insertion of Mechanical Circulatory Support Device (%)	20.8%	27.1%	0.641
Prior Blood Transfusion (%)	54.2%	39.7%	0.202
Pre-Transplant PRA ≥ 10% (%)	33.3%	30.9%	0.823
Pre-Transplant Creatinine, Mean ± SD	1.2 ± 0.7	1.5 ± 1.2	0.289

Outcomes

Endpoints	HTx Patients with Severe PGD-LV (n=24)	HTx Patients without Severe PGD-LV (n=572)	P-value
3-Year Survival	41.7%	88.3%	<0.001
3-Year Freedom from CAV	87.5%	87.6%	0.317
3-Year Freedom from NF-MACE	37.5%	83.2%	<0.001
3-Year Freedom from DSA	87.5%	85.7%	0.365
1-Year Freedom from ATR	79.2%	85.3%	0.038
1-Year Freedom from ACR	100.0%	93.0%	0.301
1-Year Freedom from AMR	91.7%	94.9%	0.221

Results Summary

- Patients with severe PGD had significantly decreased 3-year survival, 1-year freedom from any treated rejection, and 3-year freedom from NF-MACE compared to those patients who did not have severe PGD.
- There were no significant differences between the two groups in terms of 3-year freedom from CAV and freedom from DSA.

Conclusion

- Severe PGD has increased 3-year mortality and morbidity with more rejection and more NF-MACE.
- More intense therapies to offset the inflammatory response from severe PGD should be pursued.

Author Disclosures

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. 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. A Trento has received research grants from Edwards Lifesciences Corporation. 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. M Kittleson, K Nishihara, A Shen, A Patel, A Velleca, B Azarbal, and D Emerson have no financial relationships to disclose.