Pre-Transplant Collagen Vascular Disease as a Risk Factor for Increase in Cardiac Allograft Vasculopathy after Heart Transplantation

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Abstract

Background: Collagen vascular disease, including disease states such as systemic lupus erythematosus, rheumatoid arthritis, and scleroderma, have auto-antibodies in common as their etiology. These patients develop an inflammatory disease state and are known to be triggered by IgG and IgM autoantibodies. It is not clear whether patients with underlying collagen vascular disease face an increased risk of developing donor specific antibodies (DSA), rejection, and cardiac allograft vasculopathy (CAV).

Methods: Between 2010-18, we assessed 22 heart transplant patients who had pre-transplant diagnoses of collagen vascular disease specified as lupus (n=7), rheumatoid arthritis (n=9), scleroderma (n=3), and mixed connective tissue disease (n=3). All patients had no signs of currently active collagen vascular disease. Pre-transplant immunotherapy, first-year post-transplant survival, and freedom from CAV (as defined by stenosis ≥30% by angiography), non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke), acute cellular rejection (ACR), antibody-mediated rejection (AMR), DSA, and left ventricular dysfunction (as defined by left ventricular ejection fraction <40%) were recorded. Collagen vascular disease patients who were treated with pre-transplant disease-modifying agents were then compared as a subgroup to those patients who did not have a disease-modifying agent.

Results: Patients with pre-transplant underlying collagen vascular disease compared to those without have significantly lower freedom from CAV (77.3% vs 95.4%, p<0.001). First year freedom from NF-MACE, rejection, and DSA appear to be similar between study and control groups. Patients treated with pre-transplant disease-modifying agents compared to those without had similar post-transplant outcome.

Conclusion: Patients with pre-transplant collagen vascular disease appear to have increased risk of CAV. Heightened immunosuppression may be warranted in this group of patients undergoing heart transplantation.

Background

- Collagen vascular disease, including disease states such as systemic lupus erythematosus, rheumatoid arthritis, and scleroderma, have auto-antibodies in common as their etiology.
- These patients develop an inflammatory disease state and are known to be triggered by IgG and IgM autoantibodies
- It is not clear whether patients with underlying collagen vascular disease face an increased risk of developing donor specific antibodies (DSA), rejection, and cardiac allograft vasculopathy (CAV).

Purpose

To assess whether patients with underlying collagen vascular disease face an increased risk of developing rejection and cardiac allograft vasculopathy.

Methods

- Between 2010-18, we assessed 22 heart transplant patients who had pre-transplant diagnoses of collagen vascular disease specified as lupus (n=7), rheumatoid arthritis (n=9), scleroderma (n=3), and mixed connective tissue disease (n=3).
- All patients had no signs of currently active collagen vascular disease.
- Endpoints assessed:
  - 1-year clinical outcomes:
    - Survival
    - Freedom from CAV (as defined by stenosis ≥30% by angiography)
    - Freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke)
  - 1-year rejection outcomes:
    - Freedom from acute cellular rejection (ACR) and antibody-mediated rejection (AMR)
    - Freedom from DSA
    - Freedom from left ventricular dysfunction defined as left ventricular ejection fraction <40%
- Collagen vascular disease patients who were treated with pre-transplant disease-modifying agents were then compared as a subgroup to those patients who did not have a disease-modifying agent.

Demographics

Demographics	Collagen Vascular Disease (n=22)	No Collagen Vascular Disease (n=772)	P-value
Mean Recipient Age, Years ± SD	57.1 ± 11.4	55.3 ± 12.9	0.532
Mean Donor Age, Years ± SD	32.8 ± 13.9	35.7 ± 14.5	0.361
Body Mass Index, Mean ± SD	23.5 ± 4.3	25.2 ± 4.6	0.079
Female (%)	31.8%	28.2%	0.811
Previous Pregnancy in Females (%)	85.7%	71.8%	0.677
Ischemic Time, Mean Mins ± SD	181.0 ± 47.0	172.6 ± 53.8	0.493
Primary Reason For Transplant, Underlying Diagnosis of CAD (%)	36.4%	33.7%	0.821
Status 1 at Transplant (%)	77.3%	83.2%	0.402
Cytomegalovirus Mismatch (%)	20.0%	23.2%	1.00
Diabetes Mellitus (%)	22.7%	32.3%	0.488
Treated Hypertension (%)	47.6%	54.6%	0.658
Insertion of Mechanical Circulatory Support Device (%)	27.3%	28.8%	1.00
Prior Blood Transfusion (%)	27.3%	41.0%	0.271
Pre-Transplant PRA ≥ 10% (%)	27.3%	31.0%	0.818
Pre-Transplant Creatinine, Mean ± SD	1.4 ± 1.0	1.5 ± 1.1	0.752
ATG Induction Therapy (%)	54.5%	53.5%	1.00

Outcomes

Endpoints	Collagen Vascular Disease (n=22)	No Collagen Vascular Disease (n=772)	P-value
1-Year Survival	95.5%	90.8%	0.450
1-Year Freedom from CAV	77.3%	95.4%	<0.001
1-Year Freedom from NF-MACE	77.3%	87.5%	0.190
1-Year Freedom from AMR	100.0%	94.6%	0.268
1-Year Freedom from ACR	95.2%	93.3%	0.641
1-Year Freedom from DSA	95.5%	81.9%	0.450
1-Year Freedom from LV Dysfunction	90.9%	89.7%	0.736

Endpoints	Patients Treated with Disease-Modifying Agents (n=9)	Patients Not Treated (n=13)	P-value
1-Year Survival	88.9%	100.0%	0.229
1-Year Freedom from CAV	88.9%	69.2%	0.315
1-Year Freedom from NF-MACE	77.8%	76.9%	0.968
1-Year Freedom from AMR	100.0%	100.0%	1
1-Year Freedom from ACR	100.0%	91.7%	0.386
1-Year Freedom from DSA	88.9%	100.0%	0.229
1-Year Freedom from LV Dysfunction	77.8%	100.0%	0.125

Results Summary

- Patients with pre-transplant underlying collagen vascular disease compared to those without have significantly lower freedom from CAV).
- First year freedom from NF-MACE, rejection, and DSA appear to be similar between study and control groups.
- Patients treated with pre-transplant disease-modifying agents compared to those without had similar post-transplant outcome.

Conclusion

- Patients with pre-transplant collagen vascular disease appear to have increased risk of CAV.
- Heightened immunosuppression may be warranted in this group of patients undergoing heart transplantation.

Author Disclosures

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