The Clinical Impact of Early vs. Late HLA Donor-Specific Antibody After Heart Transplantation

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Abstract

Background: Formation of donor-specific antibodies (DSA) after heart transplant (HTx) impacts short and long-term outcome including rejection, cardiac allograft vasculopathy(CAV), and survival. DSA class may be important with Class II associated with CAV. Timing of Ab development (i.e. early or late) may also impact outcome. We assessed early vs late DSA development and DSA class on short and long-term outcome after HTx. DSA are drawn routinely in our program at 1,3,6 months and annually after HTx.

Methods: Between 2010-2014, we identified 460 HTx patients(pts) at our center. 89 pts developed DSA early (≤1 yr) and 42 pts developed DSA late (>1 yr). Endpoints included subsequent 3-yr survival, 1-yr freedom from rejection and infection, 3-yr freedom from CAV (≥ 30% angiographic stenosis), and 3-yr freedom from non-fatal major adverse cardiac events (NF-MACE) [Table].

Results: Subsequent 3-yr survival was significantly different for pts with early vs late DSA (p=0.011). Late vs early DSA development led to significantly lower freedom from any-treated rejection (p=0.03), NF-MACE (p=<0.001) and CAV (p=0.012) (see table). Trend towards lower freedom from acute cellular rejection with late DSA was noted (p=0.083) . Antibody-mediated rejection rates were comparable. Late Class II DSA vs early Class II DSA had significantly lower freedom from 3-yr CAV (75% vs 90%, p=0.004).

Conclusion: Late DSA development after HTx correlates with worse outcomes, with Class II associated with risk for CAV. Switch to proliferation signal inhibitor immunosuppression may be of value for these pts.

Background

- Formation of donor-specific antibodies (DSA) after heart transplant (HTx) impacts short and long-term outcome including rejection, cardiac allograft vasculopathy(CAV), and survival
- DSA class may be important with Class II associated with CAV
- Timing of antibody development (i.e. early or late) may also impact outcome

Purpose

- To assess early vs late DSA development and DSA class on short and long-term outcome after heart transplantation

Methods

- Between 2010-2014, we identified 460 HTx patients (pts) at our center
- 89 pts developed DSA early (≤1 yr) and 42 pts developed DSA late (>1 yr)
- DSA are drawn routinely in our program at 1,3,6 months and annually after HTx
- Subsequent endpoints included:
  - 3-yr survival
  - 1-yr freedom from any-treated rejection, acute cellular rejection and antibody-mediated rejection
  - 1-yr freedom from infection
  - 3-yr freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new onset heart failure, coronary intervention, defibrillator/pacemaker implant, stroke)
  - 3-yr freedom from CAV (≥ 30% angiographic stenosis)

Demographics

Demographics	Early DSA Development (n=89)	Late DSA Development (n=42)	P-Value
Mean Recipient Age, Years ± SD	53.0 ± 12.4	53.1 ± 14.0	0.949
Mean Donor Age, Years ± SD	33.7 ± 13.0	32.8 ± 11.1	0.688
Body Mass Index, Mean ± SD	24.6 ± 4.6	25.3 ± 4.7	0.388
Female (%)	46.1%	28.6%	0.085
Previous Pregnancy in Females (%)	92.7%	83.3%	0.329
Ischemic Time, Mean Mins ± SD	162.3 ± 68.1	165.1 ± 60.1	0.819
Primary Reason for Transplant, Underlying Diagnosis of Coronary Artery Disease (%)	34.1%	20.5%	0.329
Status 1 at Transplant (%)	79.8%	76.2%	0.640
Cytomegalovirus Mismatch (%)	17.0%	22.0%	0.505
Diabetes Mellitus (%)	29.2%	35.7%	0.453
Treated Hypertension (%)	50.6%	62.5%	0.219
Insertion of Mechanical Circulatory Support Device (%)	28.1%	33.3%	0.540
Prior Blood Transfusion (%)	48.7%	47.2%	0.885
Pre-Transplant PRA ≥ 10% (%)	28.6%	40.5%	0.009
Pre-Transplant Creatinine, Mean ± SD	1.3 ± 0.8	1.4 ± 0.7	0.847
ATG Induction Therapy (%)	60.7%	52.4%	0.369

Outcomes

Endpoints	Early DSA Development (n=89)	Late DSA Development (n=42)	Log Rank P-Value
Subsequent 3-Year Survival	87.6%	76.2%	0.011
Subsequent 3-Year Freedom from NF-MACE	87.6%	66.7%	<0.001
Subsequent 3-Year Freedom from CAV	86.5%	76.2%	0.012
Subsequent 1-Year Freedom from Any-Treated Rejection	70.8%	54.8%	0.030
Subsequent 1-Year Freedom from Acute Cellular Rejection	86.5%	76.2%	0.083
Subsequent 1-Year Freedom from Antibody-Mediated Rejection	86.5%	85.7%	0.816
Subsequent 1-Year Freedom from Infection	36.8%	21.4%	0.028

Endpoints*	Early Class I Antibody Development (n=24)	Late Class I Antibody Development (n=3)	Log Rank P-Value
Subsequent 3-Year Freedom from CAV	79.2%	100.0%	0.622

Endpoints*	Early Class II Antibody Development (n=55)	Late Class II Antibody Development (n=36)	Log Rank P-Value
Subsequent 3-Year Freedom from CAV	90.0%	75.0%	0.004

**Mixed Class I/Class II antibodies excluded*

Results Summary

- Subsequent 3-yr survival was significantly different for pts with early vs late DSA (p=0.011).
- Late vs early DSA development led to significantly lower freedom from any-treated rejn (p=0.03), NF-MACE (p=<0.001) and CAV (p=0.012) (see table)
- Trend towards lower freedom from acute cellular rejn with late DSA was noted (p=0.083)
- Antibody-mediated rejn rates were comparable
- Late Class II DSA vs early Class II DSA had significantly lower freedom from 3-yr CAV (75% vs 90%, p=0.004)

Conclusion

- Late DSA development after HTx correlates with worse outcomes, with Class II associated with risk for CAV
- Switch to proliferation signal inhibitor immunosuppression may be of value for these pts

Author Disclosures

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