Presence of de Novo Donor-Specific Antibodies to HLA-DQ in Lung Transplant Recipients Predicts Poor Survival

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Background

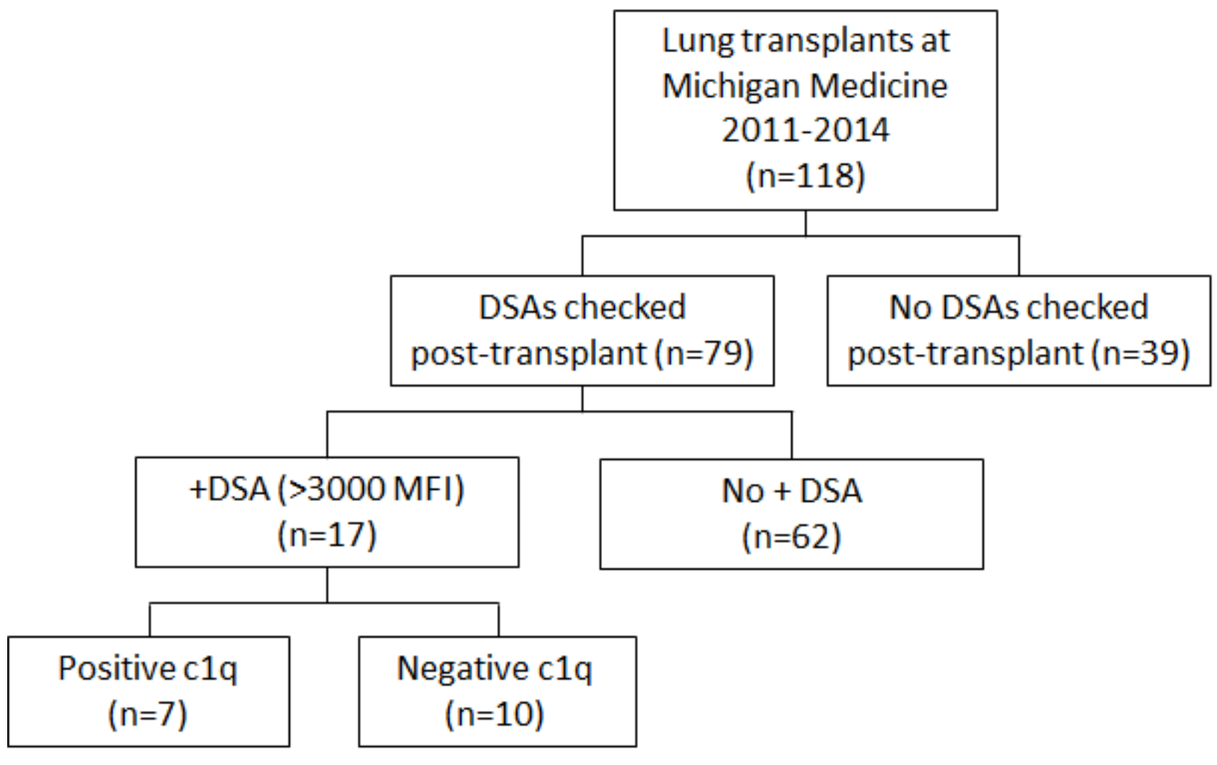
- Donor-specific anti-human leukocyte antigen antibodies (DSAs) contribute to antibody-mediated rejection (AMR) in solid organ transplants.
- To definitively diagnose AMR, a combination of graft dysfunction, histologic changes, and DSA detection are required.
- AMR is a recognized cause of lung allograft dysfunction. Data regarding frequency and impact of this entity are needed to improve clinical monitoring and care of patients with this complication.

We aimed to describe the incidence and outcomes of de novo DSA formation in lung transplant recipients at our center.

Methods

- Patients who received a lung transplant at our institution between 2011 and 2014 were reviewed.
- DSA presence was assessed either for surveillance purposes or in the setting of a patient's clinical decline.
- Solid phase Luminex bead-based immunoassay was used to detect the presence of DSAs in lung transplant recipient serum.
- A positive DSA was defined as a mean fluorescence intensity (MFI) of > 3000.
- T-tests and chi-square statistics were used to compare baseline characteristics.
- Kaplan Meier and Log Rank methods were used to compare survival between groups.

Results



- 17/79 patients (22%) had at least one + DSA.
- The median time to first + DSA was 91 days (range 7-1556 days).

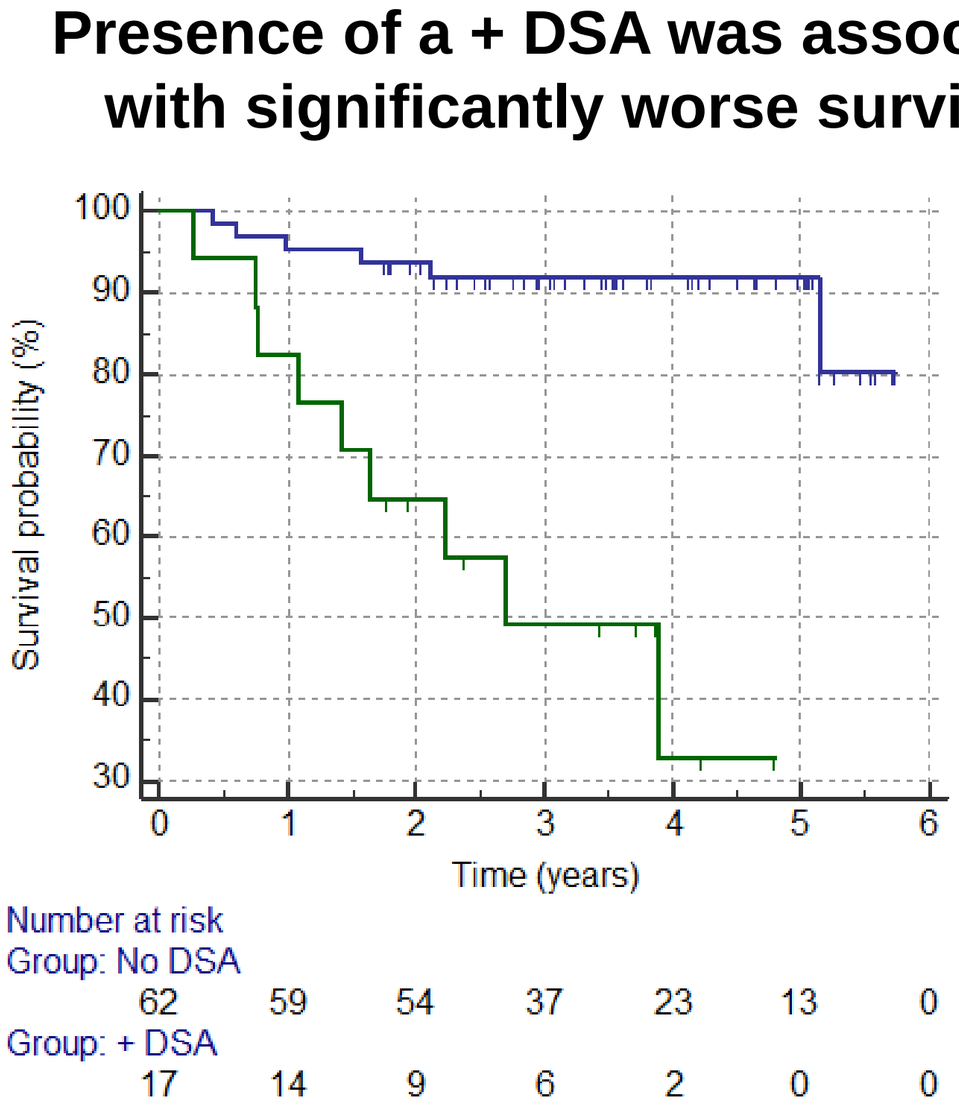
Baseline characteristics of patients with + DSA and no + DSA were similar.

	+ DSA (n=17)	No + DSA (n=62)	p
Age at transplant, yr	49 ± 18	50 ± 14	0.75
Male	13 (76%)	38 (61%)	0.25
Baseline FEV_1 (% predicted)	86 ± 15	85 ± 25	0.89
Class 1 PRA pre-transplant	4 (24%)	13 (21%)	0.82
Class 2 PRA pre-transplant	2 (12%)	5 (8%)	0.66

Class II donor specific antibodies predominated.

- All patients with a + DSA had at least 1 class II DSA.
- DQ antibodies accounted for the majority of class II DSAs (15/17; 88%).
- Of those with a + DSA, 7/17 (41%) had a positive c1q assay.

Presence of a + DSA was associated with significantly worse survival.



p<0.0001

Peak DSA MFI correlated with C1q positivity.

- Patients with a + DSA who were C1q+ had an average peak MFI of 16,245 versus peak MFI of 8,094 in those who were not C1q+ (p=0.016).

Conclusions

- Our findings are similar to other studies in the literature:
  - DQ DSAs are the most common type of DSA following lung transplant.
  - The development of de novo DSAs post-lung transplant is associated with decreased survival.
- Monitoring for development of DSAs following lung transplant may impact patient outcomes and should be routinely performed.
- Randomized trials for treatment strategies of antibody mediated rejection are needed to better understand optimal therapeutic strategies and improve outcomes of patients who develop DSAs.

References

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