The Impact of Candida Colonization After Lung Transplant

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BACKGROUND:

- Candida colonization is common in lung transplant recipients, however, the impact on outcomes after transplantation has not been systematically studied.
- Subjects with Candida colonization are at greater risk for invasive disease.
- Use of antifungal prophylaxis targeting Candida colonization varies significantly among transplant centers with very little data for a standardized approach.

RESULTS:

Table 1: Demographics

Coveriete	Overall	D+ or R+	D- / R -
Covariate	(N=358)	(N=140)	(N=218)
Male	187 (52.2%)	77 (55.0%)	110 (50.5%)
Age at Transplant	53 (12.6%)	52 (14%)	54 (11.4%)
Pediatric Transplant	3 (0.8%)	1 (0.7%)	2 (0.9%)
Primary Disease			
- COPD/Alpha1	132 (36.9%)	47 (33.6%)	85 (39.0%)
- Cystic Fibrosis	63 (17.6%)	33 (23.6%)	30 (13.8%)
- IPF/ILD	119 (33.2%)	43 (30.7%)	76 (34.9%)
- Other	44 (12.3%)	17 (12.1%)	27 (12.4%)
Single Lung Tx	167 (46.6%)	55 (39.3%)	112 (51.4%)
Second Tx	5 (1.4%)	1 (0.7%)	4 (1.8%)
PGD 3	83 (23.2%)	41 (29.3%)	42 (19.3%)
Airway Complication	93 (26.0%)	35 (25.0%)	58 (26.6%)
Pseudomonas			
- Don+ Rec+	3 (0.8%)	0 (0.0%)	3 (1.4%)
- Don+ Rec-	8 (2.2%)	5 (3.6%)	3 (1.4%)
- Don- Rec+	58 (16.2%)	31 (22.1%)	27 (12.4%)
- Don- Rec-	289 (80.7%)	104 (74.3%)	185 (84.9%)
Aspergillus			
- Don+ Rec+	1 (0.3%)	1 (0.7%)	0 (0.0%)
- Don+ Rec-	4 (1.1%)	3 (2.1%)	1 (0.5%)
- Don- Rec+	15 (4.2%)	5 (3.6%)	10 (4.6%)

OBJECTIVE:

To assess Candida colonization at the time of transplant on outcomes

METHODS:

- Subjects receiving a lung transplant from 2006-2016 at our center.
- Chart review data collected included microbiology, primary graft dysfunction and airway complications.
- **Definitions**:
 - Invasive Candidiasis: Candida isolated from a normally sterile site. •
 - PGD: ISHLT definition 2004.
 - Airway Complications: Dehiscence, stricture, stenosis & bronchomalacia for 6 months after transplant.

Table 2: Candida Colonization Isolates		Table 3: Invasive Candida Disease					
	R+	D+	Invasive Candida	D+/R-	D+/R+	D-/R+	D-/R-
Candida Type	(N=37)	(N=119)	Fungemia alone	5	2	2	1
C. albicans	27 (73%)	107(90%)	Empyema alone	7	2	1	
C. alabrata	6 (16%)	9 (7.6%)	Fungemia & Empyema	2	1	1	
C. tropicalis	1 (2.7%)	6 (5.0%)	Sternal Osteomyelitis / Surgical site infection	1	1	1	1
C. parapsilosis	3 (8.0%)	3 (2.5%)	Hilar abscess		1		
C. krusei	1 (2.7%)	2 (1.6%)	Candida Retinitis			1	
C. kefvr	2 (5.4%)	0 (0.0%)	Endocarditis / Vascular		1	1	
C. auillermondii	、 2 (5.4%)	0 (0.0%)	Mediastinitis	2			
*D+/R- n= 103, D-R+ n= 21, D+/R+ n= 16 *29			*29 episodes of IC in 23 subjects at 34 sites of infection				

Table 4:Adjusted* Logistic Regression Analysis

Outcome	Coefficient	Odds Ratio (95% CI)	P-value
	Candida: D+ or R+ vs. D- and R- (Single)	0.92 (0.42, 2.00)	0.839
Airway Complication	Candida: D+ or R+ vs. D- and R- (Bilateral)	0.85 (0.44, 1.64)	0.634
	Single vs. Bilateral (<i>Candida</i> D+ or R+)	1.35 (0.57, 3.21)	0.501
	Single vs. Bilateral (Candida D- and R-)	1.25 (0.62, 2.49)	0.534



Figure 1: Cox proportional hazards ratio





PGD

<i>Candida</i> : D+ or R+ vs. D- and R- (Single)	3.11 (1.36, 7.13)	0.007
Candida: D+ or R+ vs. D- and R- (Bilateral)	1.26 (0.65, 2.43)	0.489
Single vs. Bilateral (Candida D+ or R+)	0.86 (0.38, 1.96)	0.722
Single vs. Bilateral (Candida D- and R-)	0.35 (0.16, 0.76)	0.008

*model also included covariates for underlying disease, pseudomonas colonization, age, sex, **Donor smoking history**

Table 5: Microbe Associations Until 6 Months After Transplant: Cumulative Incidence Analysis

Outcome	Predictor at Tx	Predictor +	Predictor –	SHR [+/-]	P_valuo	
		(95% CI)	(95% CI)	(95% CI)	F -value	
Candida (N=218)	Pseudomonas	76.7	53.2	1.71	0.010	
		(60.9, 92.5)	(46.0, 60.3)	(1.14, 2.56)		
Candida (N=218)	Aspergillus	50.0	56.7	0.96	0.040	
		(16.7, 83.3)	(50.0, 63.5)	(0.96, 2.59)	0.340	
Pseudomonas (N=289)	Candida	17.4	14.7	1.25	0.680	
		(1.5, 33.3)	(10.4, 18.9)	(0.43, 3.58)		
Aspergillus (N=338)	Candida	15.6	35.0	0.39	0 0/1	
		(2.8, 28.4)	(29.6, 40.3)	(0.16, 0.96)	0.041	

CONCLUSIONS:

- Among SLTs, the odds of PGD-3 were 3-fold higher in those colonized with Candida at transplant compared to those not colonized.
- Among those without Candida colonization at transplant, the odds of PGD-3 were 3fold lower in SLTs compared to BLTs.
- There was no association between *Candida* colonization and airway complications or overall, rejection free, or BOS free survival.
- Donor *Candida* colonization was more frequent than recipient, indicating that reassessment of donor antimicrobial management might be warranted.
- Subjects colonized with *Pseudomonas* at the time of transplant were 71% more likely to have Candida isolated 6 months after transplant. Subjects colonized with Candida at the time of transplant were 61% less likely to have Aspergillus isolated 6 months after transplant.

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