Bronchiolitis Obliterans Syndrome in Lung Transplantation: A Predictive Model

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Background

- Chronic allograft rejection and bronchiolitis obliterans syndrome (BOS) are the leading causes of late mortality among lung transplant recipients.
- Identification of patients at risk for BOS may allow for prophylactic measures to be tailored appropriately.
- We sought to develop a predictive model for BOS-free survival following lung transplantation.

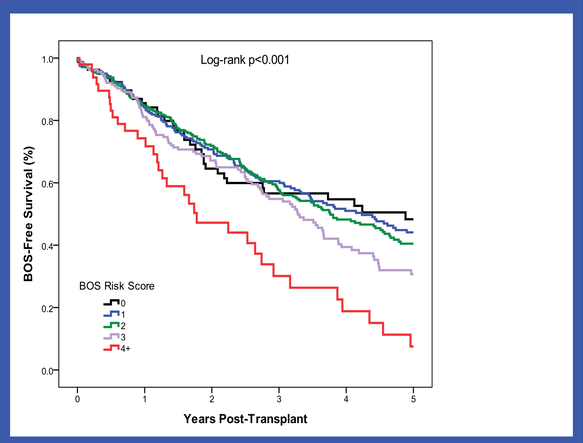
Methods

- Retrospective analysis of UCLA's lung transplant database was performed.
- Analysis was limited to primary adult lung transplant recipients (age ≥ 18) transplanted between 1999-2016.
- Follow-up pulmonary function tests were queried via chart review and BOS-free survival at 5 years was utilized as the primary end point.
- Multivariable Cox hazard regression modeling was utilized to identify preoperative, operative, and donor factors predictive of BOS development.
- A predictive score was then calculated based on hazard ratio weights, and receiver operating characteristic analysis was utilized to assess model performance.

Results

Variables	Hazard Ratio (95% CI) (N=888)	p-value
Recipient Age (years)	1.01 (1.00-1.02)	0.007
Body Mass Index (kg/m^2)	1.03 (1.01-1.05)	0.014
Diagnosis Category		
A – Obstructive	0.96 (0.77-1.19)	0.676
B – Primary Pulmonary Hypertension	1.69 (0.97-2.94)	0.065
C – Cystic Fibrosis	0.54 (0.31-0.93)	0.028
D – Restrictive	Ref	
Lung Allocation Score	1.00 (0.99-1.01)	0.601
Single Lung Transplantation	1.33 (1.07-1.66)	0.011
Wait Time (days)	1.00 (1.00-1.00)	0.412
Diabetes Mellitus	1.15 (0.91-1.46)	0.254
Gastroesophageal Reflux Disease	1.09 (0.99-1.19)	0.099
Preoperative Labs		
Hemoglobin (g/dL)	1.04 (0.99-1.10)	0.095
Albumin (g/dL)	0.78 (0.63-0.95)	0.016
Alanine Aminotransferase (U/L)	1.00 (1.00-1.01)	0.092
Preoperative Pulmonary Status		
Mechanical Ventilation	0.63 (0.34-1.18)	0.148
Extracorporeal Membrane Oxygenation	0.45 (0.14-1.39)	0.163
Forced Expiratory Volume in one second (%)	1.00 (1.00-1.01)	0.138
Forced Vital Capacity (%)	1.00 (1.00-1.01)	0.194
Donor Characteristics		
Age (years)	1.00 (1.00-1.01)	0.202
Female Donor	0.86 (0.71-1.03)	0.100
Smoking History	1.35 (1.10-1.66)	0.004
Donor Cytomegalovirus Positive	1.17 (0.95-1.45)	0.150
Donor Cause of Death		
Stroke	Ref	
Head Trauma	1.08 (0.78-1.49)	0.648
Anoxia	1.03 (0.69-1.52)	0.902
Central Nervous System Tumor	0.87 (0.27-2.79)	0.808
Other	0.59 (0.97-1.00)	0.060
Intraoperative Characteristics		
Concomitant Cardiac Surgery	1.21 (0.98-1.49)	0.075
Ischemia Time (min)	1.00 (0.99-1.00)	0.354
Cardiopulmonary Bypass Time (min)	1.00 (1.00-1.01)	0.470

Univariate Cox Regression Modeling



BOS-Free Survival at 5 Years

Variables	Odds Ratio [95% CI]	p-value	Score
Single Lung Transplant	1.47 (1.13-1.92)	0.004	1
BMI ≥ 35 kg/m^2	7.69 (2.40-2.46)	0.001	8
Albumin ≤ 3 g/dL	1.93 (1.01-3.69)	0.045	2
Donor Age ≥ 45 years	1.30 (0.99-1.70)	0.061	1
Donor Smoking History	1.44 (1.11-1.87)	0.006	1
Donor CMV	1.32 (0.99-1.75)	0.055	1

Multivariable Model and Scoring System

Discussion

- BOS remains a prevalent cause of mortality following lung transplantation, with a pooled incidence of approximately 50% among long-term survivors.
- Of all factors, recipient BMI was the strongest predictor of BOS.
- The developed model strongly stratifies patients by risk of post-transplant BOS with good predictive power.
- Subsequent prophylactic prevention strategies and early intervention may improve outcomes in high risk cohorts.

<u>Limitations</u>:

- Retrospective, single-center design without validation.
- Prolonged follow-up time with inability to capture subtle changes in treatment practices over time.

Conclusions

The developed BOS predictive model can be utilized to help identify lung transplant recipients at high-risk for BOS development post-transplant.

Further studies are needed to provide external validation and include post-transplant acute rejection and infection episodes.

Disclosures

No authors for this presentation have relevant financial interests to disclose.