



# The Effect of the Cystic Fibrosis Care Center on Lung Transplant Outcomes

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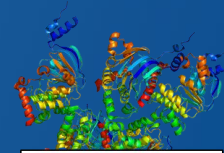
Presented by: Aravind Krishnan

# Disclosures

- I have no disclosures
- CM and PS receive research funding from the Cystic Fibrosis Foundation
- This funding was not used directly for the purposes of this research

# Cystic Fibrosis

- Most common lethal genetic mutation in Caucasian population
- Results in:
  - respiratory failure
  - pancreatic insufficiency
  - liver disease
  - failure to thrive
- Patients with CF account for ~10% of US adult lung transplant volume

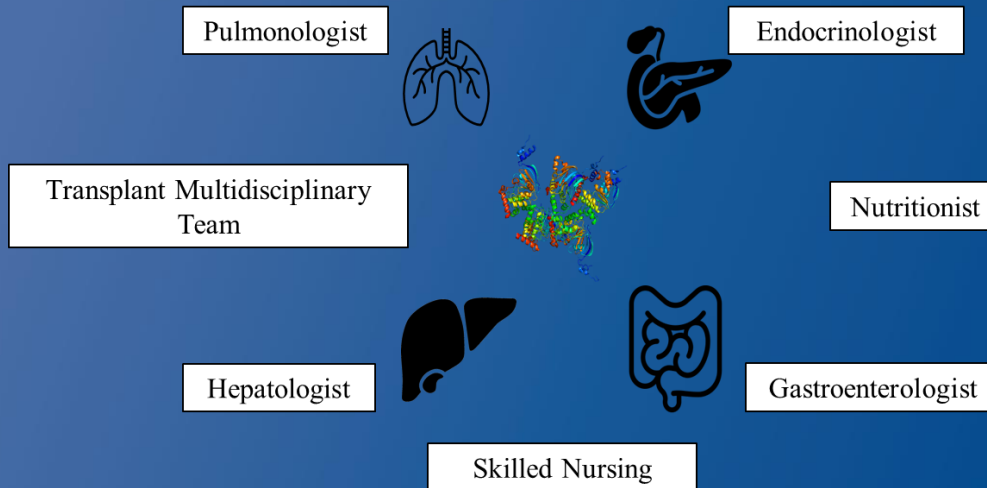


CFTR Protein  
disrupted in CF



# Multidisciplinary Care for Cystic Fibrosis

- Cystic Fibrosis Care Centers (CFCCs) are accredited by the Cystic Fibrosis Foundation based on their ability to provide comprehensive care for CF patients



# Purpose

- It is unclear how outcomes after lung transplant for CF patients at CFCCs compare to non-CFCCs
- We hypothesize that CF patients who receive a lung transplant at CFCCs experience superior graft survival compared to those transplanted at non-CFCCs

# Methods

- Scientific Registry of Transplant Recipients used to identify all first-time, adult (18 years and older) double lung-transplant recipients for a diagnosis of CF, from May 2005 to June 2018 (LAS era).
- Primary Exposure: Transplantation at a CFCC
- Primary Outcome: Graft Failure (death or re-transplantation for graft dysfunction)

# Analysis

- Multivariate model included all variables that demonstrated univariate association with primary outcome ( $P < 0.20$ ), and then optimized using AIC
- Adjusted 2-tiered mixed-effects parametric survival analysis used to assess outcomes
  - 1<sup>st</sup> tier: Center-level factors— status as a CFCC, annual volume of lung transplants for CF, and use of induction immunosuppression
  - 2<sup>nd</sup> tier: Patient-level factors— recipient: race, age, sex, functional status, total bilirubin, use of ECMO prior to transplant, FEV<sub>1</sub>, BMI; donor: age, high creatinine

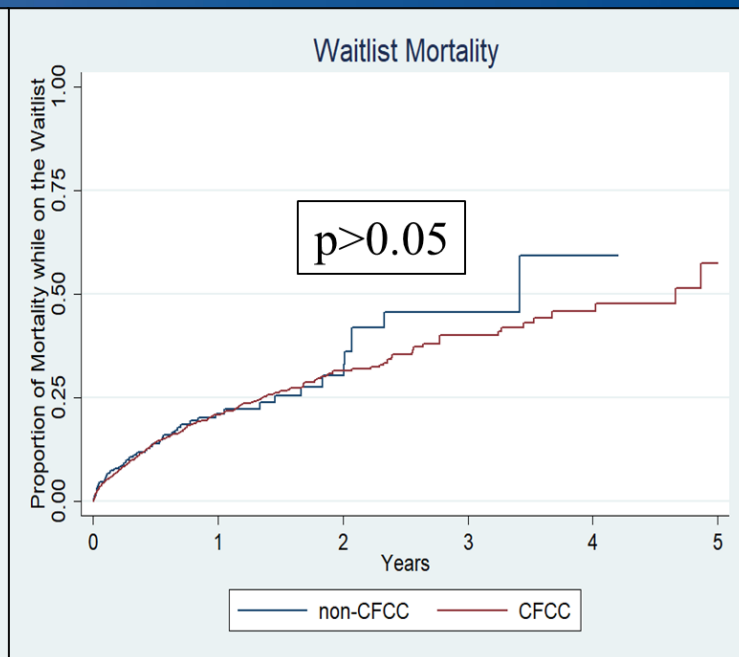
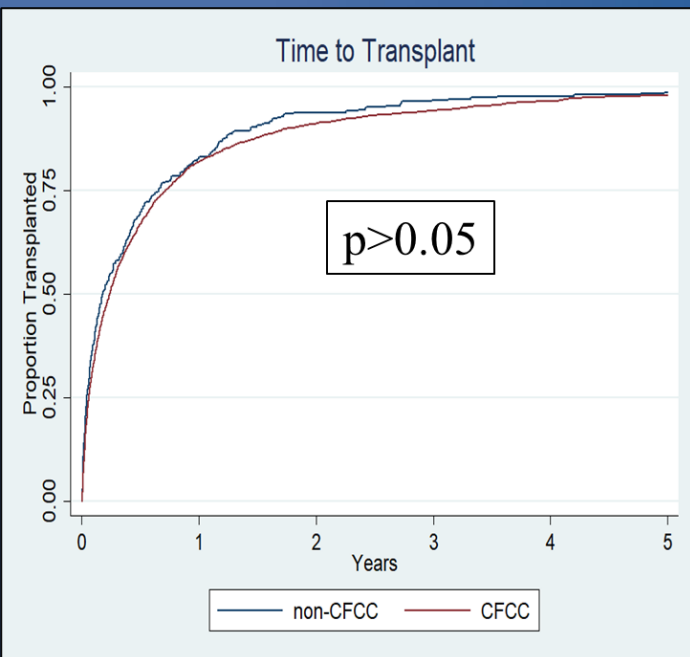
# Patients

- 2,573 patients transplanted at 68 centers
- 50/68 centers were CFCCs (73.5%)
- Majority of patients transplanted at CFCCs (87.9%)
- At baseline, patients were similar

Characteristic	CFCC (n=2263)	non-CFCC (n=310)	p Value
<b>Recipient Characteristics</b>			
Age at Transplant: mean (SD)	32.2 (9.8)	30.9 (10.5)	<b>0.014</b>
Male: N (%)	1153 (51.0)	168 (54.2)	0.28
Ethnicity: N (%)			<b>0.003</b>
Caucasian	2158 (95.4)	285 (91.9)	
African American	40 (1.8)	4 (1.3)	
Hispanic	61 (2.7)	19 (6.1)	
Other (including Asian, mixed race, Native American)	4 (0.2)	2 (0.6)	
BMI: mean (SD)	19.8 (3.0)	19.6 (3.2)	0.21
Lung Allocation Score: mean (SD)	49.9 (18.1)	48.9 (18.2)	0.36
Total Bilirubin: mean (SD)	0.45 (0.8)	0.45 (0.5)	0.88
FEV1 at Transplant: mean (SD)	24.9 (13.6)	24.8 (12.3)	0.88
Average Functional Capacity at Transplant: Median (IQR)	50% (30%-60%)	50% (30%-60%)	0.18
ECMO prior to Transplantation: N (%)	136 (6.0%)	15 (4.8%)	0.41
Waitlist Time (days): Median (IQR)	87 (22-262)	65.5 (16-240)	0.10
<b>Donor Characteristics</b>			
Age: mean (SD)	32.5 (13.4)	31.1 (11.8)	0.10
High Creatinine: N (%)	400 (17.7)	73 (23.6)	<b>0.012</b>
<b>Center Characteristics</b>			
Annual Volume: median (IQR)	5.6 (3.4-9.7)	2.5 (1.8-3.0)	<b>&lt;0.001</b>
Induction N (%)	1386 (61.3)	192 (61.9)	0.82
Region: N (%)			<b>&lt;0.0001</b>
Northeast	482 (21.3)	18 (5.8)	
Midwest	482 (21.3)	17 (5.5)	
South	903 (39.9)	203 (65.5)	
West	396 (17.5)	72 (23.2)	



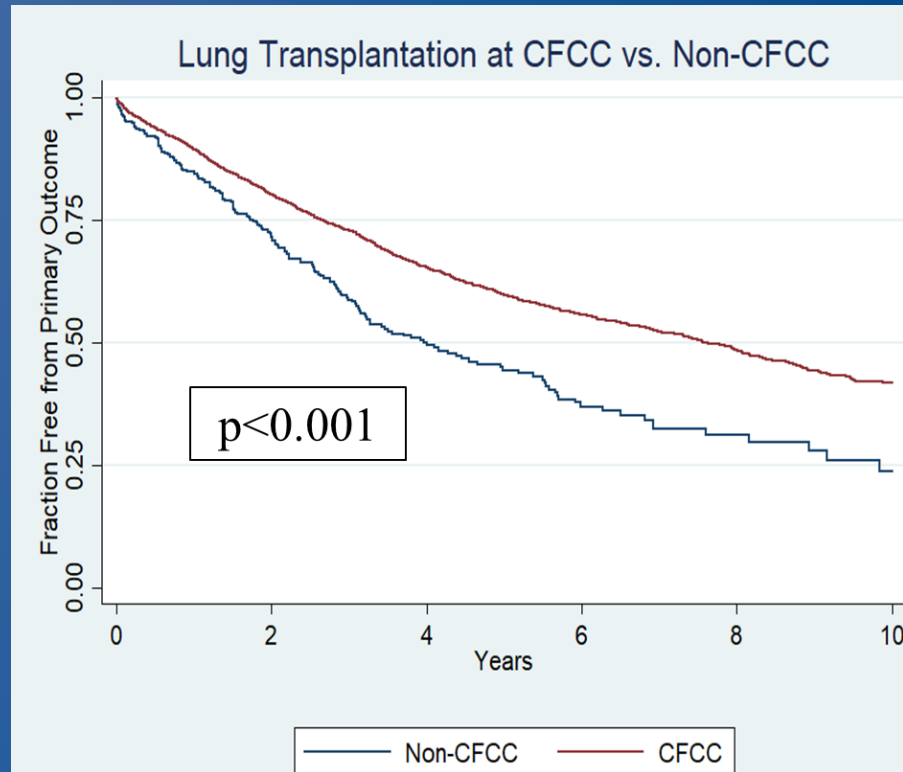
# Waitlist Survival and Time-to-Transplant Similar at CFCCs and non-CFCCs



# Graft Survival- Unadjusted Kaplan Meier Analysis



- Median survival
  - CFCC: 8 years
  - Non-CFCC: 4 years

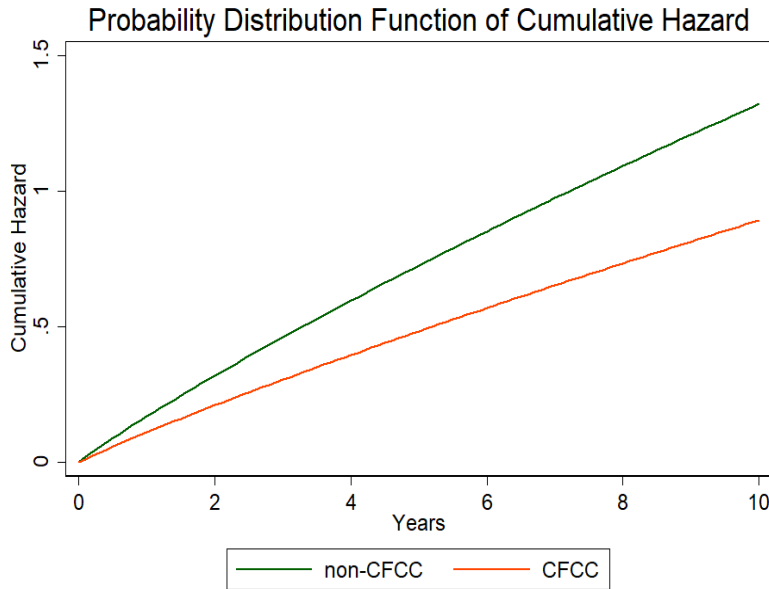


# Adjusted Parametric Survival Analysis

Transplantation at a CFCC is associated with a 33% reduced risk of mortality (p<0.001)

	Hazard Ratio	P Value	95% CI
<b>Tier 1 Center Level</b>			
Cystic Fibrosis Care Center	0.67	<0.001	0.56-0.82
Annual Volume	0.98	0.200	0.97-1.01
Induction	0.87	0.023	0.77-0.98
<b>Tier 2 Patient Level</b>			
Race			
Caucasian	REF		
African American	1.58	0.027	1.05-2.38
Hispanic	0.87	0.459	0.59-1.26
Other	1.66	0.60	0.41-6.7
Male Sex	1.06	0.34	0.94-1.20
Donor Age	1.01	0.031	1.00-1.01
Donor High Creatinine	0.90	0.23	0.76-1.07
Recipient BMI	0.98	0.20	0.96-1.01
Recipient Age at Transplant	0.97	<0.001	0.96-0.98
ECMO prior to Transplantation	1.06	0.74	0.75-1.49
Recipient Functional Status	0.99	0.058	0.99-1.00
Recipient Total Bilirubin	1.09	0.006	1.03-1.16
Recipient FEV1 at Transplant	0.99	0.044	0.99-1.00

# Cumulative Hazard after Lung Transplant at a CFCC vs. non-CFCC



- Weibull distribution function used to generate cumulative hazard of loss of graft after transplantation at a CFCC vs. non-CFCC.
- Cumulative hazard is consistently lower at CFCCs ( $P < 0.001$ )

# Sub-Analysis: Hypothesis Generation

- Examined transfer from transplant center to another center during follow-up as an exposure variable
- 108 patients included
- Limited by small numbers, and no indication for reason for transfer

	Hazard Ratio	P value	95% CI
Interfacility Transfer			
CFCC to CFCC	Ref		
non-CFCC to CFCC	1.15	0.74	0.50-2.61
non-CFCC to non-CFCC	3.15	0.057	0.97-10.24
CFCC to non-CFCC	2.06	0.035	1.05-4.05
Race			
Caucasian	Ref		
African American	0.83	0.86	0.10-7.16
Hispanic	1.39	0.68	0.29-6.7
Male Sex	1.15	0.64	0.63-2.09
LAS	1.003	0.77	0.98-1.03
Donor Age	0.98	0.16	0.96-1.01
Donor High Creatinine	0.69	0.34	0.33-1.46
Recipient BMI	0.95	0.47	0.84-1.08
Recipient Age at Transplant	0.97	0.087	0.94-1.00
Recipient Functional Status	0.99	0.081	0.97-1.01
Recipient Total Bilirubin	1.17	0.461	0.77-1.78
Recipient FEV1 at Transplant	1.00	0.727	0.98-1.03

# Conclusion

- Transplantation at a CFCC is associated with improved survival after lung transplant for cystic fibrosis
- CFCCs provide comprehensive, CF-specific expertise, which may contribute to improved graft survival
- Post-transplant follow-up at a CFCC may play a role in improved graft survival