



Pulmonary Artery Pressure Changes Differentially Effect Survival in Lung Transplant Patients with COPD and Pulmonary Hypertension: *An Analysis of the UNOS Registry*

**Kathryn L. O'Keefe MD, Ahmet Kilic MD, Amy Pope-Harman MD,
Donald Hayes, Jr. MD, Stephen Kirkby MD,
Robert S.D. Higgins MD, MPH, Bryan A. Whitson MD, PhD**



Wexner
Medical
Center

AATS
ANNUAL
MEETING
2013

93RD



AMERICAN ASSOCIATION
FOR THORACIC SURGERY
We Model Excellence

We have no disclosures

Lung Transplantation

- **Effective treatment for end stage lung disease**
- **Shortage of organs**
- **High early mortality rates**



- **Predictors of primary graft dysfunction?**
- **Factors in long term survival?**

Background

- Pulmonary hypertension and right ventricular dysfunction can complicate lung transplant procedures¹⁻³
- What about changes in pulmonary artery pressure (PAP)?

1. Whitson BA et al, "Risk Factors for Primary Graft Dysfunction after Lung Transplantation," *JTCVS*; 131:1, 73-80.
2. Whelan TM et al, "Effect of Preoperative Pulmonary Artery Pressure on Early Survival After Lung Transplantation For Idiopathic Pulmonary Fibrosis," *J Heart Lung Transplant*, 24:9, 1269-74.
3. Diamond JM et al, "Clinical Risk Factors for Primary Graft Dysfunction after Lung Transplantation," *Am J Respir Crit Care Med*, 187:5, 527-534.

Study Objective:

To evaluate the effect of changes in waitlist pulmonary artery pressures on survival after lung transplantation

Methods

- **United Network for Organ Sharing (UNOS)/ Standard Transplant Analysis and Research (STAR) Registry**
- **Data indexed at listing (aka candidacy) and at transplant (aka recipient)**
- **All solid organ transplants**
- **Donor and recipient characteristics**
- **Outcomes data**

Methods

- **UNOS/STAR Registry Thoracic Dataset**
 - **413 pre- and post-transplant data elements**
- **Lung transplant recipients**
 - **1987 – 2012**
 - **Ages > 18**
 - **Cadaveric donors**
 - **Re-transplants excluded**

Study Definitions

- **Included records required mean PAP (mPAP):**
 - **Listing time**
 - **Transplant time**
 - **Unique values**

Study Definitions

$$\text{mPAP change} = \text{mPAP}_{\text{listing}} - \text{mPAP}_{\text{transplant}}$$

$$\Delta + 5\text{mmHg} \geq$$

Increase

0

Unchanged

$$\leq - 5\text{mmHg}$$

Decrease

Statistical Analysis

- **SAS version 9.1 (SAS Institute, Cary, NC)**
- **Chi-square test for between-group comparisons**
- **Unadjusted all-cause mortality and survival compared with the Kaplan-Meier method**
- **Cox proportional hazards regression model**
- **$P < 0.05$ deemed significant**

Study Results

21,924 lung transplants registered

1,677 met inclusion criteria

Indication for Lung Transplantation

Indication for Lung Transplantation	Entire Registry		Study Cohort	
	Frequency Total Recipients	Percent	Frequency Mean PAP Dataset	Percent
Chronic Obstructive Pulmonary Disease	7690	35.08 %	616	36.73 %
Idiopathic Pulmonary Fibrosis	5596	25.52 %	464	27.67 %
Primary Pulmonary Hypertension	795	3.63 %	109	6.5 %
Cystic Fibrosis	2893	13.2 %	89	5.31 %
Alpha-1	1376	6.28 %	76	4.53 %
Sarcoidosis	646	2.95 %	64	3.82 %
Re-transplantation	39	0.18 %	NA	NA
Other	2889	13.18 %	259	15.44 %
Total	21924	100 %	1677	100 %

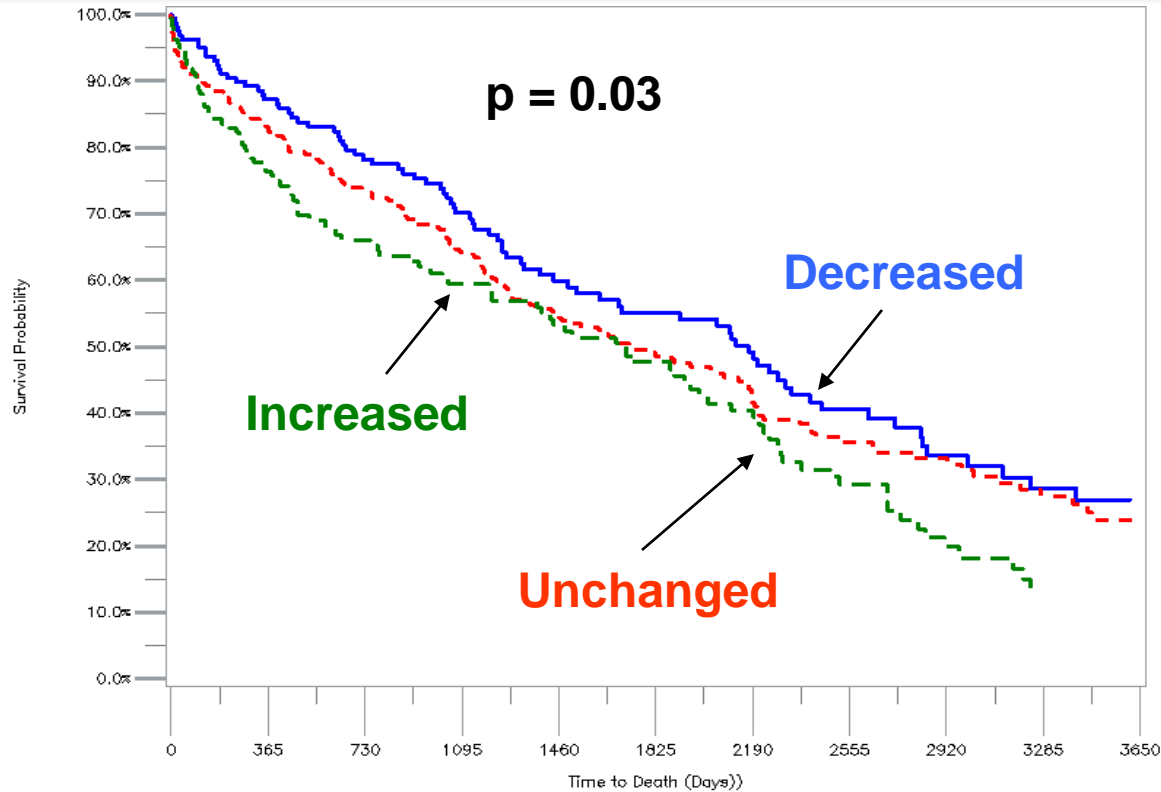
Waitlist mPAP Measurements

	Frequency	Percent
mPAP Decrease	385	23 %
mPAP Unchanged	737	44 %
mPAP Increase	555	33 %
Total	1677	100 %

Waitlist mPAP Measurements by Diagnosis

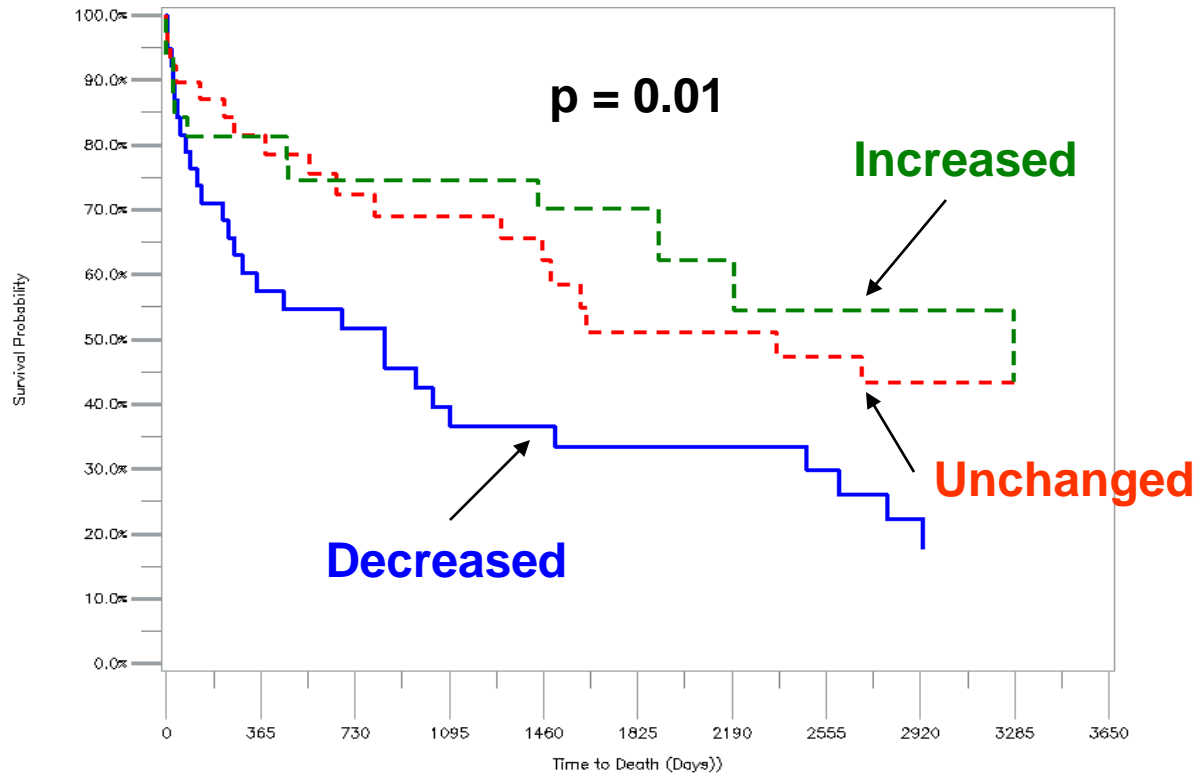
Diagnosis	Frequency mPAP Decrease	Frequency mPAP Unchanged	Frequency mPAP Increase	Frequency Total	P value
Chronic Obstructive Pulmonary Disease	161 (26.1%)	292 (47.4%)	163 (26.5%)	616	< 0.01
Idiopathic Pulmonary Fibrosis	74 (15.9%)	205 (44.2%)	185 (39.8%)	464	< 0.01
Primary Pulmonary Hypertension	38 (34.8%)	39 (35.8%)	32 (29.4%)	109	< 0.01
Cystic Fibrosis	15 (16.8%)	45 (50.6%)	29 (32.6%)	89	< 0.01
Alpha-1	12 (15.8%)	41 (53.9%)	23 (30.3%)	76	< 0.01
Sarcoidosis	14 (21.8%)	21 (32.8%)	29 (45.3%)	64	< 0.01
Other	71 (27.4%)	94 (36.3%)	94 (36.3%)	259	< 0.01
Total (%)	385 (23%)	737 (44%)	555 (33%)	1677 (100%)	

COPD Recipients: Waitlist Mean PAP Values



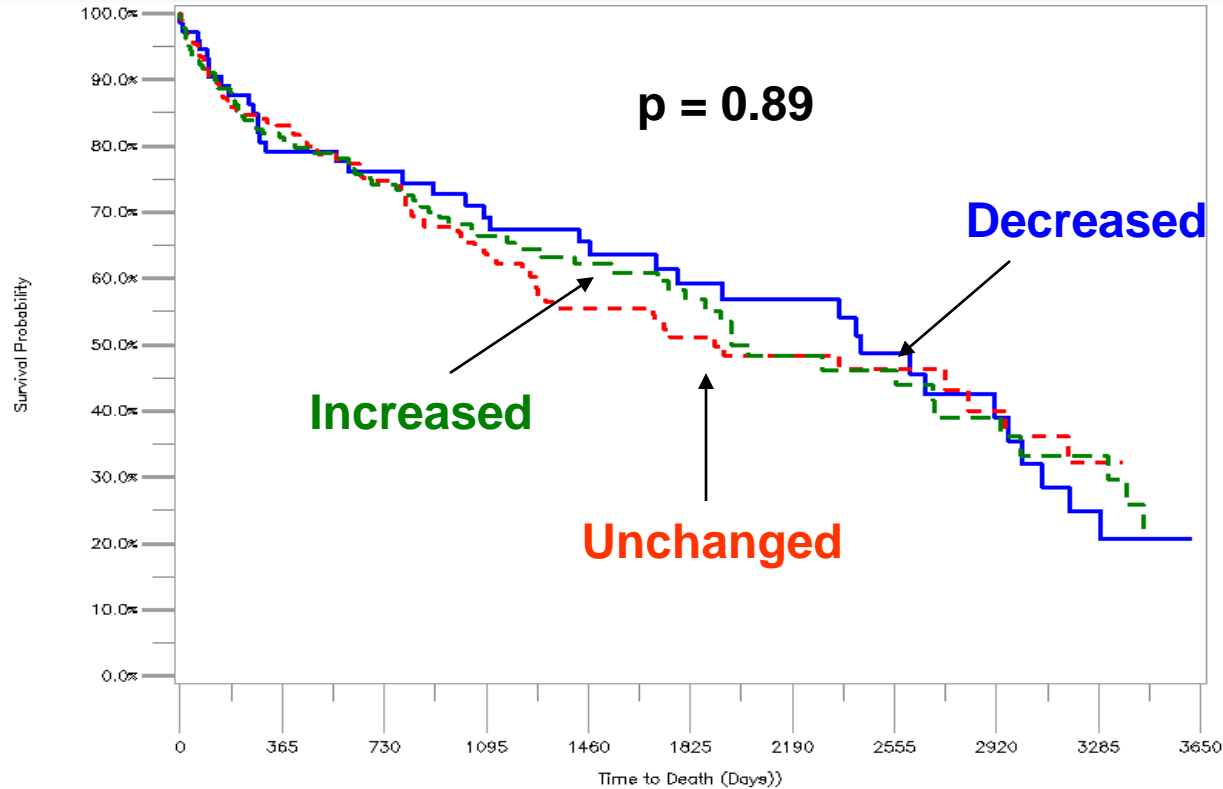
Number at Risk											
Group	Time (Days)										
	0	365	730	1095	1460	1825	2190	2555	2920	3285	3650
Increased	163	112	86	69	59	48	40	32	14	8	8
Decreased	161	132	112	89	67	56	49	32	23	17	15
Unchanged	292	226	187	153	116	96	64	47	37	25	19

PPH Recipients: Waitlist mPAP Values



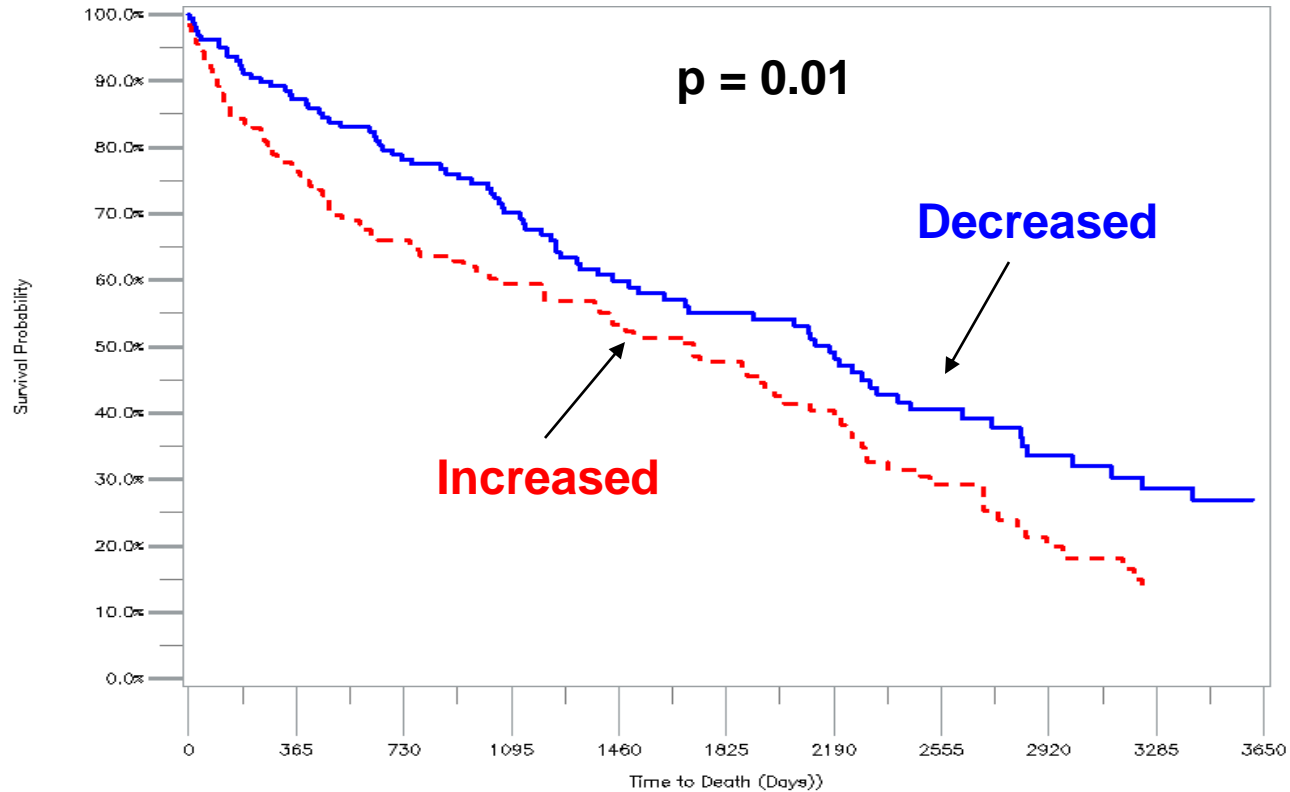
Number at Risk											
Group	Time (Days)										
	0	365	730	1095	1460	1825	2190	2555	2920	3285	3650
Increased	32	24	19	17	16	12	8	6	5	5	4
Decreased	38	21	17	13	12	10	9	8	5	3	0
Unchanged	39	29	22	20	18	14	13	12	10	9	6

IPF Recipients: mPAP Values



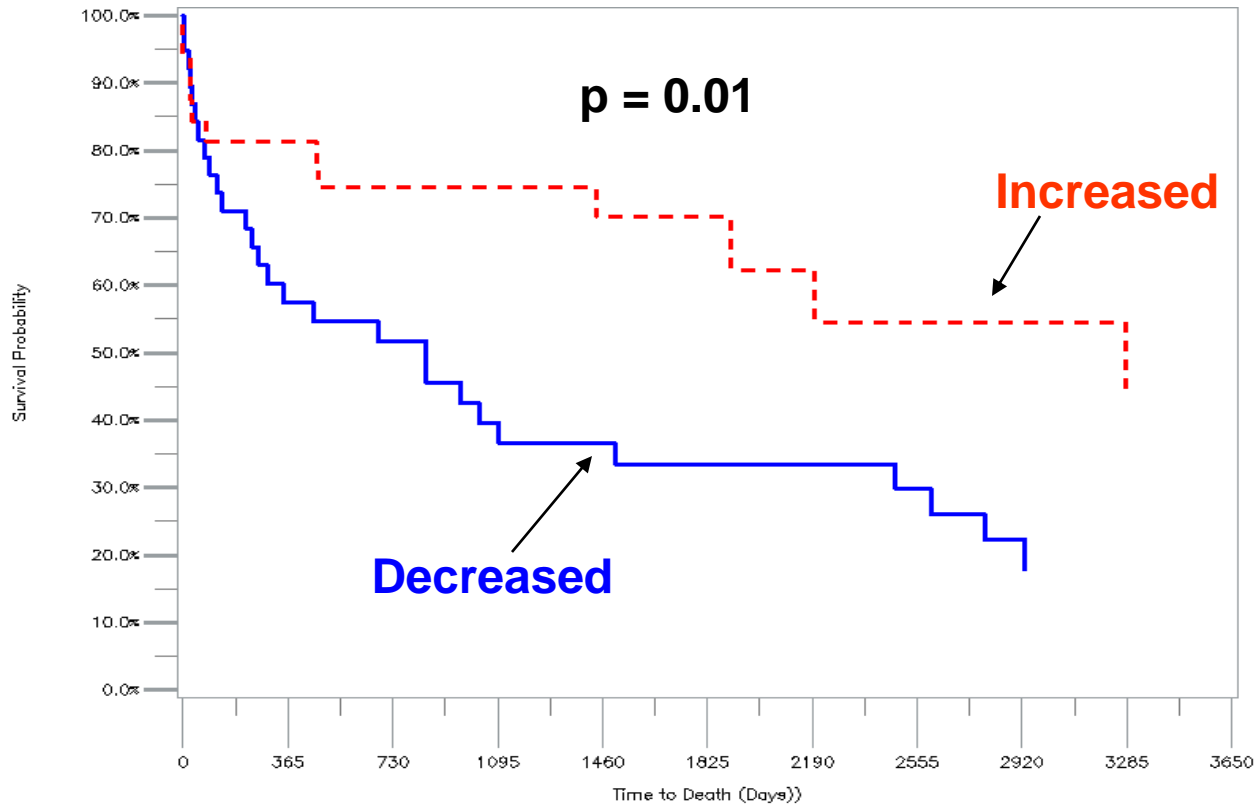
		Number at Risk										
Group	Time (Days)											
	0	365	730	1095	1460	1825	2190	2555	2920	3285	3650	
Increased	185	117	92	69	54	38	26	21	15	10	6	
Decreased	0	55	44	39	34	25	21	17	11	6	3	
Unchanged	205	143	109	77	53	42	27	20	12	7	4	

COPD Recipients: mPAP Change ONLY



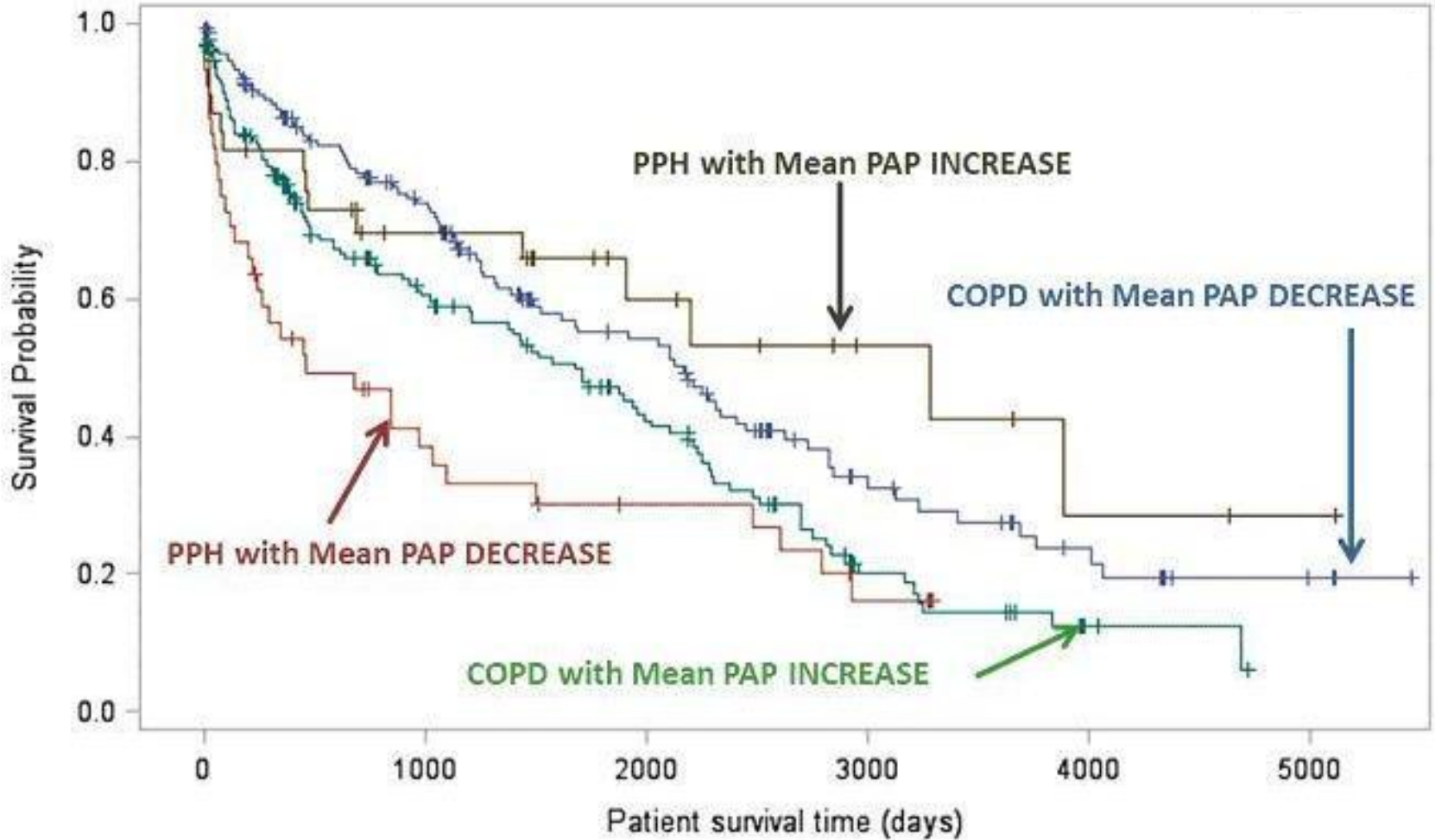
Number at Risk											
Group	Time (Days)										
	0	365	730	1095	1460	1825	2190	2555	2920	3285	3650
Increased	163	112	86	69	59	48	40	32	14	8	8
Decreased	161	132	112	89	67	56	49	32	23	17	15

PPH Recipients: mPAP Changes ONLY



Group	Number at Risk										
	Time (Days)										
	0	365	730	1095	1460	1825	2190	2555	2920	3285	3650
Increased	32	24	19	17	16	12	8	6	5	5	4
Decreased	38	21	17	13	12	10	9	8	5	3	0

Survival in PPH or COPD with mPAP change



Proportional Hazard Analysis: Factors Associated With Long-Term Survival

Covariate	P-value	Hazard Ratio	95% Hazard Ratio Confidence Limits
Mean Pulmonary Artery Pressure - Unchanged		Reference	
Mean Pulmonary Artery Pressure - Decrease	0.70	0.96	0.79 – 1.18
Mean Pulmonary Artery Pressure - Increase	0.021	0.78	0.62 – 0.96
Diagnosis - Sarcoidosis		Reference	
Diagnosis - Alpha-1 Antitrypsin	0.37	1.38	0.68 – 2.80
Diagnosis - Cystic Fibrosis	0.26	1.53	0.74 – 3.17
Diagnosis - Chronic Obstructive Pulmonary Disease	0.082	1.73	0.93 – 3.21
Diagnosis - Idiopathic Pulmonary Fibrosis	0.17	1.54	0.83 – 2.88
Diagnosis - Pulmonary Hypertension	0.054	1.94	0.99 – 3.82
Diagnosis - Other	0.15	1.6	0.85 – 3.02
Recipient Race - Caucasian		Reference	
Recipient Race - African-American	0.90	1.02	0.73 – 1.43
Recipient Race - Other	0.045	0.68	0.47 – 0.99
Recipient Gender – Male		Reference	
Recipient Gender – Female	0.97	1.00	0.84 – 1.20
Donor Race - Caucasian		Reference	
Donor Race - African-American	0.0043	1.36	1.10 – 1.67
Donor Race - Other	0.83	1.03	0.81 – 1.31
Donor Gender – Male		Reference	
Donor Gender - Female	0.56	0.95	0.79 – 1.14
Transplant Type – Single Lung Transplant		Reference	
Transplant Type – Bilateral Lung Transplant	0.57	0.95	0.79 – 1.14
Increasing Donor Age (Years)	0.0053	1.01	1.00 – 1.01
Increasing Waitlist Time (Days)	0.014	1.00	1.00 – 1.00
Increasing Recipient Age (Years)	0.038	1.01	1.00 – 1.02
Increasing Ischemic Time (Hours)	0.30	0.98	0.93 – 1.02
Prostacyclin Use	0.44	0.46	0.062 – 3.39
Inhaled Nitric Oxide	0.62	0.61	0.084 – 4.41

Mean Waitlist Time by Group

	Number of Patients	Mean Waitlist Time (Days \pm STD Dev)
mPAP Decrease	385	423 \pm 467
mPAP Unchanged	738	492 \pm 567
mPAP Increase	558	546 \pm 619

$p = 0.004$

Study Limitations

- **Retrospective review**
 - **Selection bias**
- **Incomplete datasets**
- **2 time points in data collection**
- **Variability between centers**

Study Strengths

- **Large cohort**
- **Multi-institutional**
- **Population based data**

Conclusions

Changes in waitlist mPAP can have an effect on survival after lung transplantation

COPD: *Increased* mPAP → *decreased* survival

PPH: *Decreased* mPAP → *decreased* survival

Future Directions

- **Emphasis on collection and accurate entry of database parameters**
- **Standardize hemodynamic measurements in transplant patients?**
- **Further evaluation of waitlist mPAP data**

