

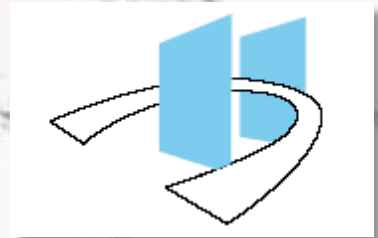
Trasplante pulmonar

Control y seguimiento del trasplantado pulmonar

Félix Heras Gómez

Universidad de Valladolid

Hospital Clínico Universitario de Valladolid



Complicaciones



- **Generales**
- **De la anastomosis de la vía aérea**
- **Infecciosas**
- **Rechazo**

- **Bronquiolitis obliterante**
- **Arteritis coronaria en Tx CP**
- **Procesos linfoproliferativos**

An anatomical diagram of the human respiratory system. It shows the trachea (windpipe) at the top, branching into the left and right bronchi. The bronchi further divide into smaller bronchioles, which lead to the lungs. The lungs are depicted with a pinkish-red color, and the bronchi and bronchioles are shown in a light blue color. The diagram is centered on a white background.

Complicaciones generales

Complicaciones

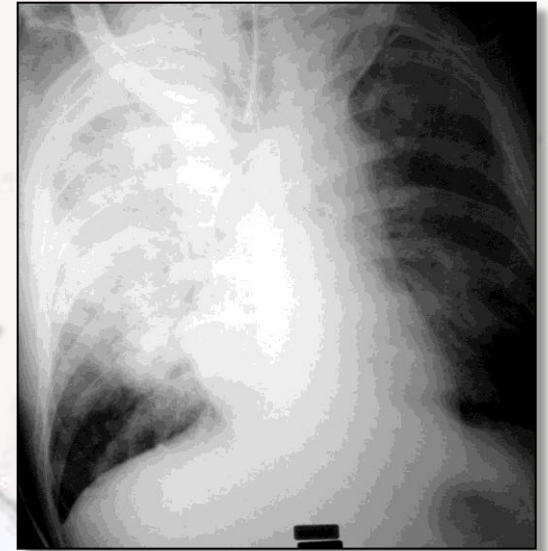
Generales

hemorrágicas
hemodinámicas
renales

...

Edema

(respuesta a la reimplantación)



Complicaciones

Isquemia-reperfusión



Disfunción precoz del injerto

Leve – LPA – DRA



Complicaciones de la vía aérea



Complicaciones

De la vía aérea

Primeras semanas del postoperatorio

Disrupción anastomosis (fuga aérea)

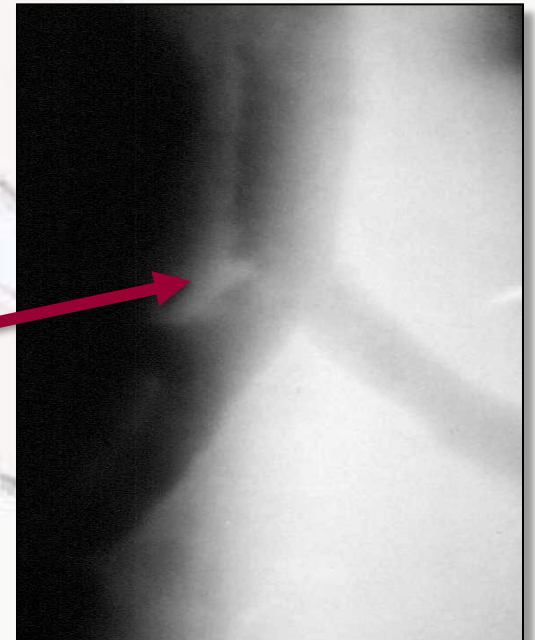
Infección

Hemorragia

Necrosis mucosa

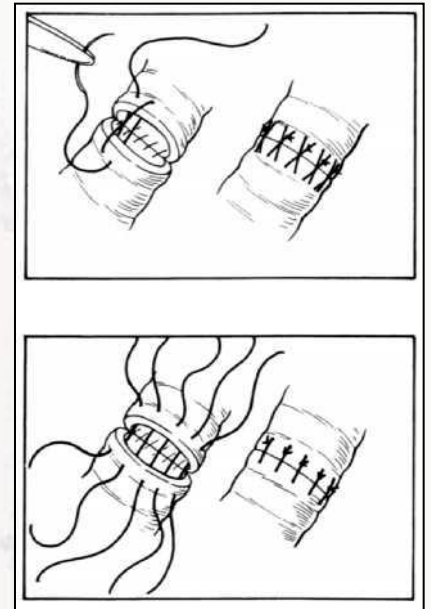
A distancia

Estenosis



Profilaxis

De la vía aérea



Técnicas operatorias

Refuerzo anastomosis

con tejidos adyacentes

Acortamiento bronquio “donante”

Anastomosis telescopada

Revascularización bronquial directa

Complicaciones infecciosas

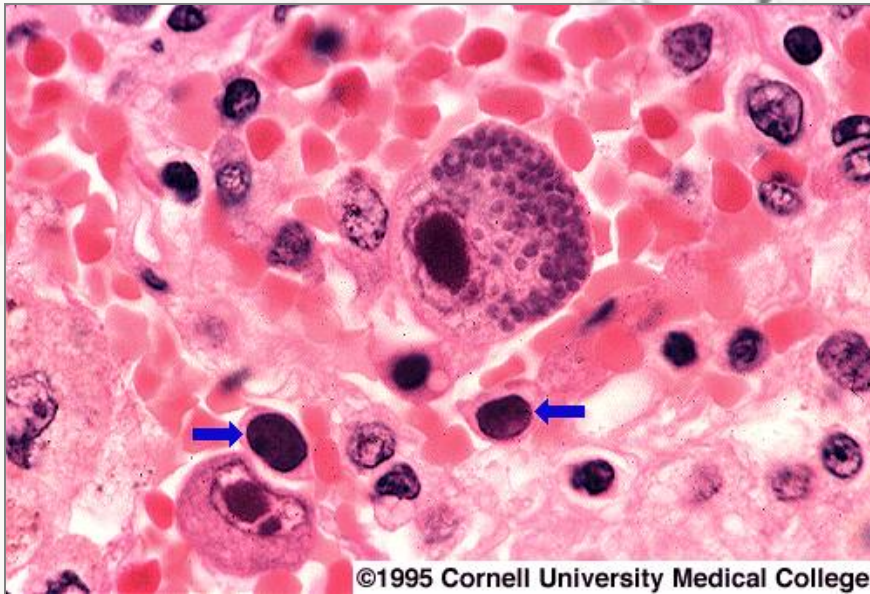


Complicaciones infecciosas

- Bacterianas 60 %
- Víricas 25 %

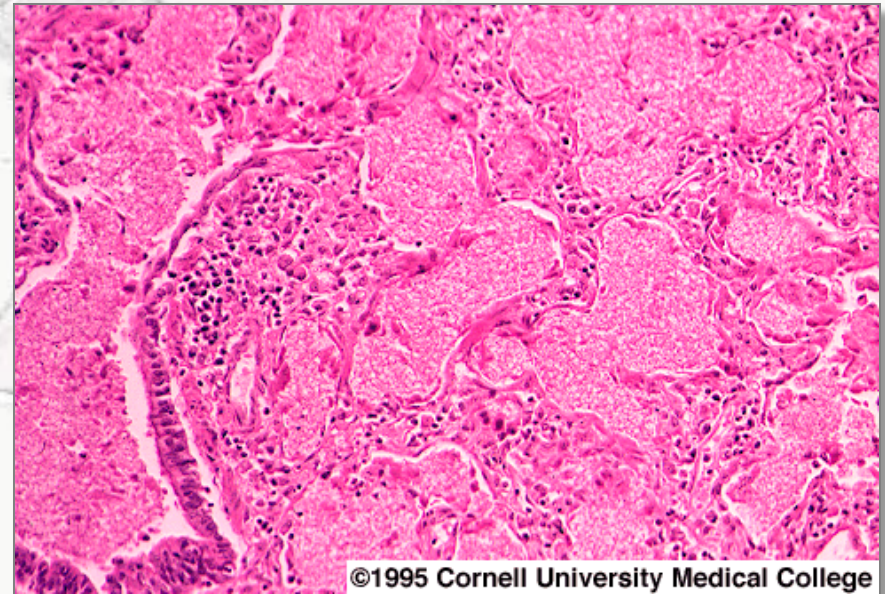
- Fúngicas 10 %
- Otras 5 %

Citomegalovirus



©1995 Cornell University Medical College

Pneumocystis



©1995 Cornell University Medical College

Complicaciones infecciosas



Bacterianas:

pseudomonas
estafilococo
estreptococo
legionella

Víricas:

citomegalovirus
herpes simple
Epstein Barr

Fúngicas:

cándida
aspergillus
histoplasma
criptococo

Otras:

pneumocystis
toxoplasma
nocardia

Profilaxis

Si cultivo de “donante” estéril

Cefazolina o vancomicina 48 horas

Antibioterapia 5 días

Exclusión de donantes CMV+

En receptores CMV-

Inmunoglobulina anti-CMV

Aciclovir

Trimetoprim-sulfametoxazol

Aerosoles de Pentamidina

Fluconazol

Profilaxis



- **Preoperatorio**

Antibacteriana

- **Postoperatorio inmediato (10 días)**

Antibacteriana y antifúngica

- **Postoperatorio (> 10 días)**

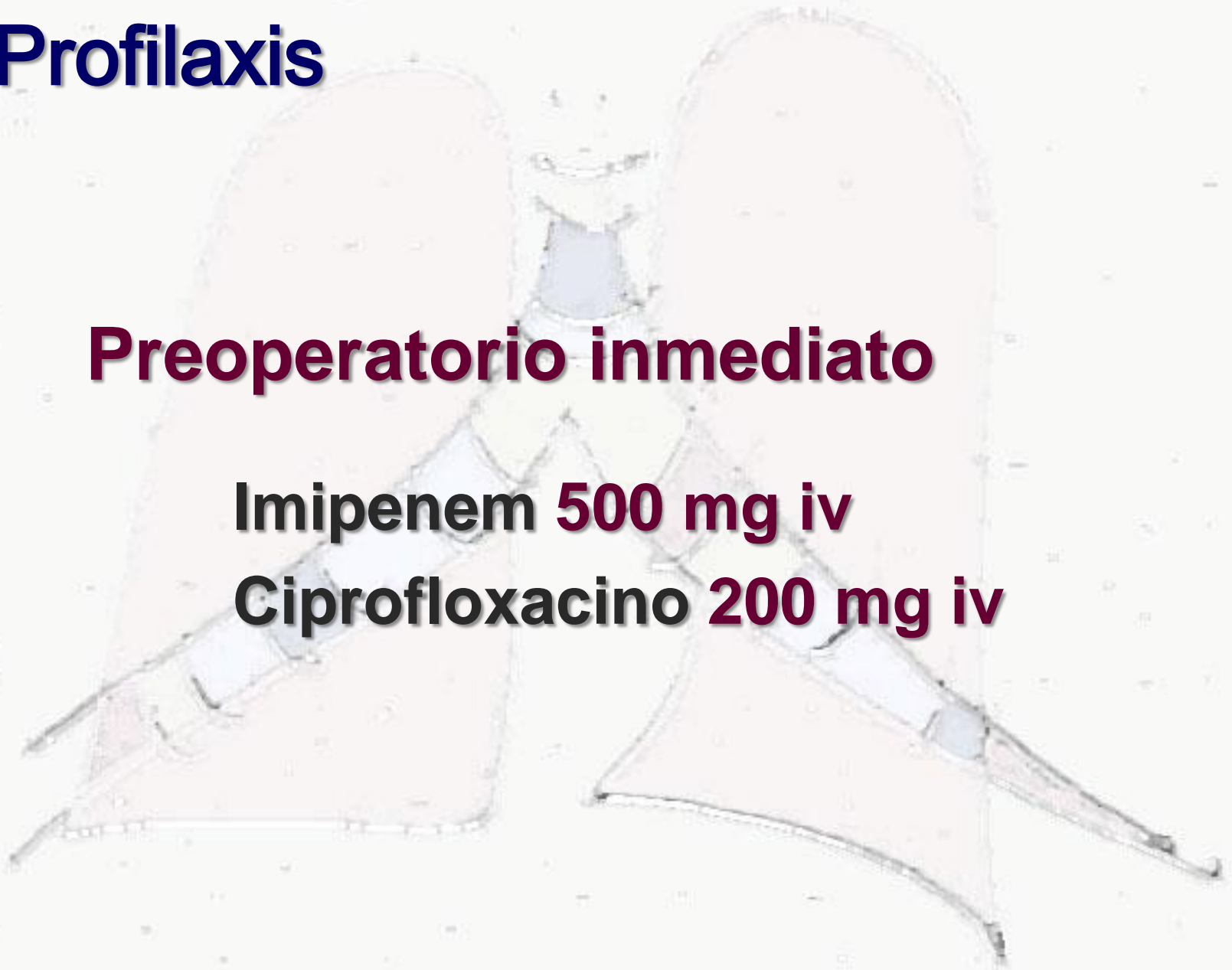
Antibacteriana, antifúngica, antiviral y antiprotozoos

Profilaxis

Preoperatorio immediato

Imipenem 500 mg iv

Ciprofloxacino 200 mg iv



Profilaxis

Postoperatorio: primeros 10 días

Imipenem 500 mg/8 h iv

Ciprofloxacino 200 mg/12 h iv

Colimicina aerosol 1 millón U/12 h, patología séptica

Tobramicina aerosol 50-100 mg/8-12 h, resto pacientes

Anfotericina aerosol/8 h

(1.5 mg/2 ml solución de 50 mg en 20 ml agua destilada)

Fluconazol 100 mg/12 h, oral

Nistatina colutorios/8 h

Clorhexidina colutorios, tras comidas y fisioterapia

Nistatina óvulos vaginales/8 h, 10 primeros días

Mupirocina crema nasal/8 h

Profilaxis

Postoperatorio: después de 10 d

Cotrimoxazol 100/12 h oral, a partir del 20º día

Ganciclovir 5 mg/kg/12 h iv, a partir del 10º día

(21 días en receptor CMV+,

3 meses en receptor CMV- con donante CMV+)

Ganciclovir 1 g/8 h oral

(2 meses adicionales tras tratamiento iv)

Complicaciones por rechazo



Rechazo

Tipos

- **Hiperagudo** Debido a Ac presentes en el receptor: Sistema ABO, Ac citotóxicos, etc.
- **Agudo** Inflamación mediada por células. Disparidad en el sistema HLA entre donante y receptor. Activación células T
- **Crónico** Obliteración de la vía aérea y fibrosis del injerto. Bronquiolitis obliterante. Menor supervivencia a largo plazo

Rechazo



Histología

Agudo

- Infiltrado linfocitario perivascular que se extiende a septos alveolares y paredes bronquiolares
- Exudado inflamatorio alveolar

Crónico

- Inflamación y fibrosis de la lámina propia de la vía aérea cartilaginosa. Bronquiectasias. Bronquiolitis obliterante

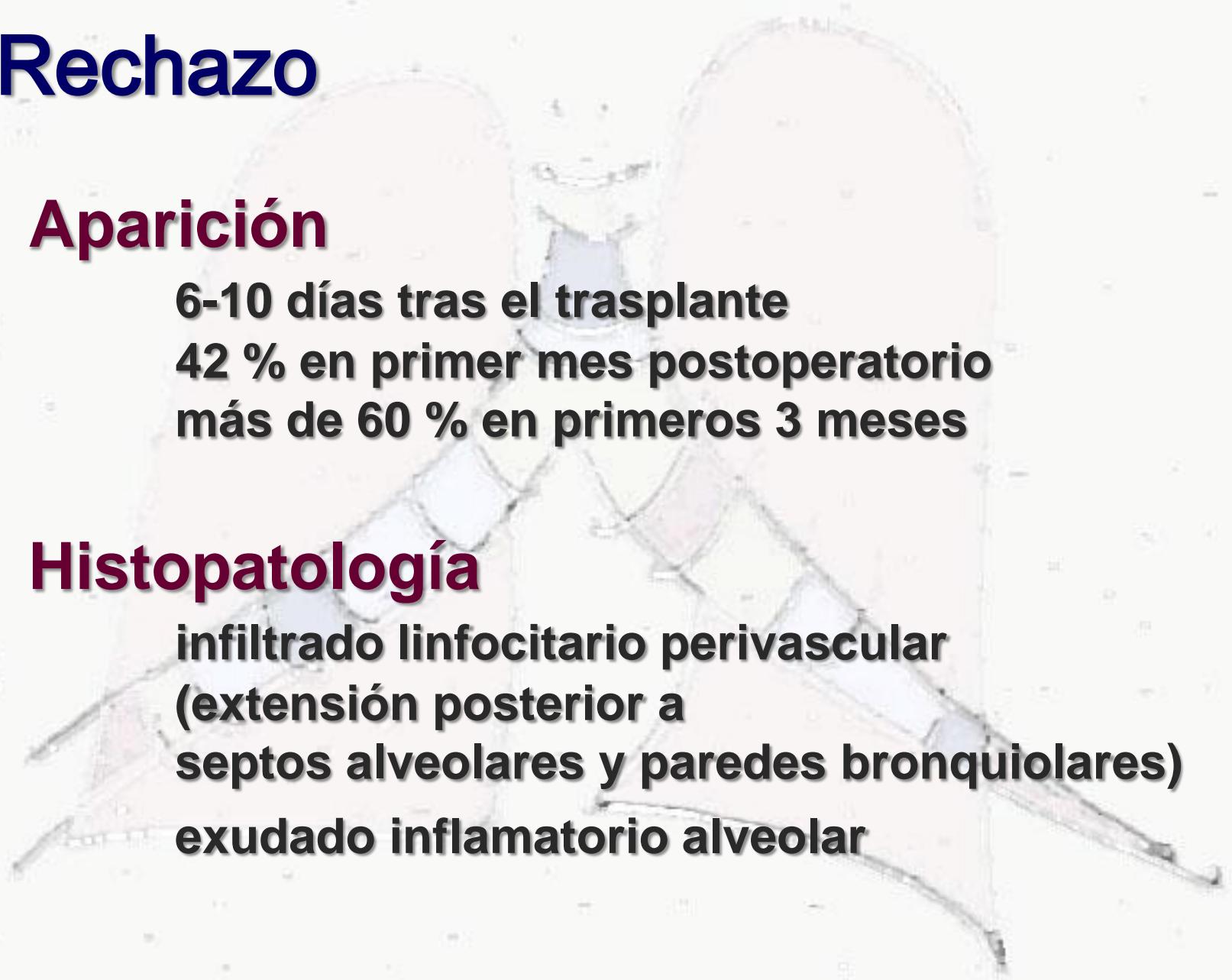
Rechazo

Aparición

6-10 días tras el trasplante
42 % en primer mes postoperatorio
más de 60 % en primeros 3 meses

Histopatología

infiltrado linfocitario perivascular
(extensión posterior a
septos alveolares y paredes bronquiolares)
exudado inflamatorio alveolar



Rechazo

Diagnóstico

Clínico: fiebre, disnea, crepitantes

Rx: difuminación hiliar y/o infiltrado basal

Funcional: caída del VEMS, hipoxemia

Gammagrafía perfusión: descenso de flujo en pulmón Tx y ascenso en el propio

LBA / Biopsia transbronquial

Biopsia

sensibilidad 84 %

especificidad 100 %

Respuesta a metilprednisolona

1 g - 3 días seguidos

Rechazo

Inmunosupresión

- **Ciclosporina**

300 mg oral preoperatorio

2-5 mg/kg/d iv → 5-10 mg/kg/d oral

→ 2-8 mg/kg/d oral

(75-200 ng/ml plasma, 200-400 ng/ml sangre)

- **Azatioprina**

2 mg/kg iv preoperatorio

1-2 mg/kg/d (linfocitos > 4000/mm³)

- **Prednisona**

1-2 mg/kg/d

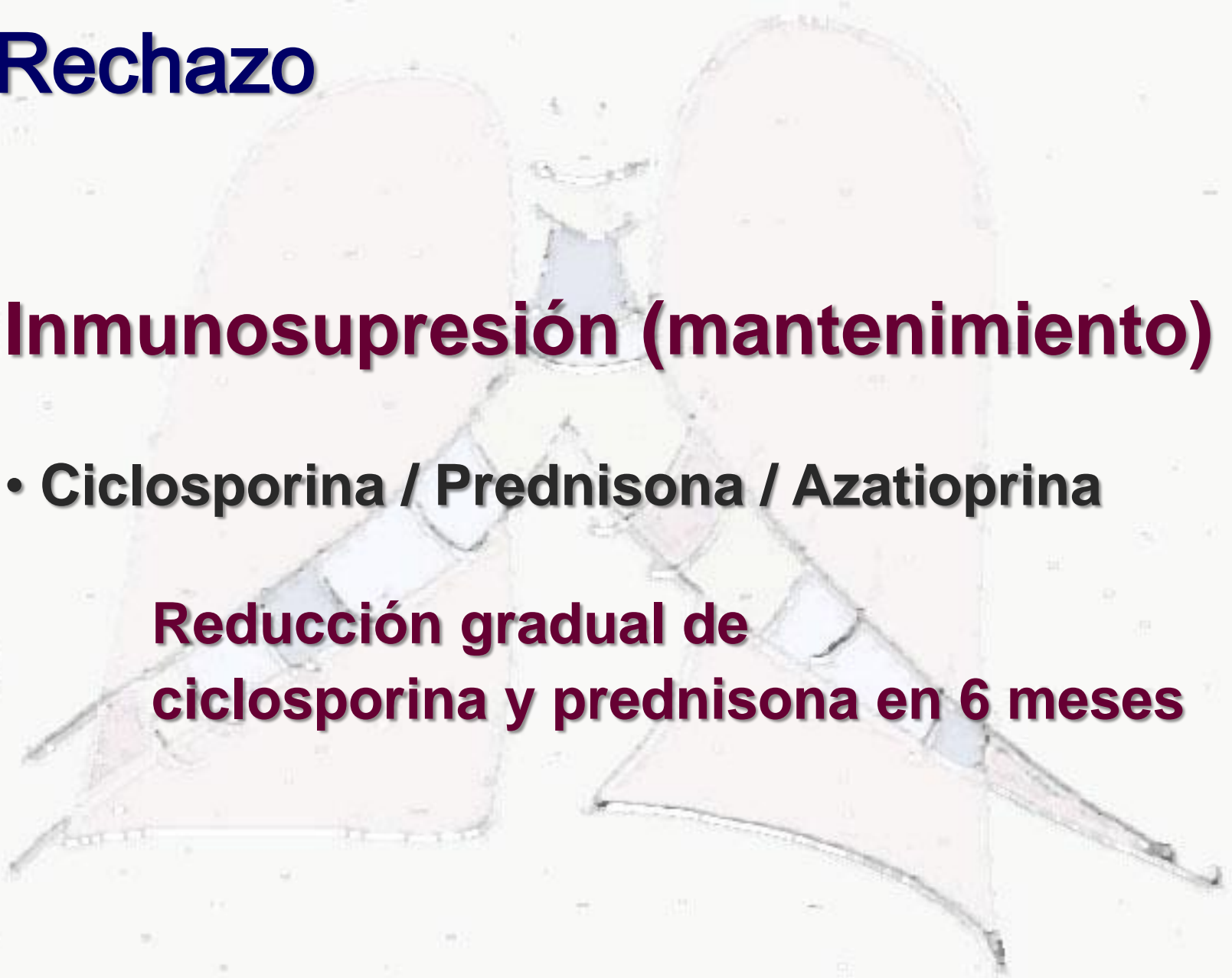
- **Globulina antitimocítica**

Rechazo

Inmunosupresión (mantenimiento)

- **Ciclosporina / Prednisona / Azatioprina**

**Reducción gradual de
ciclosporina y prednisona en 6 meses**



Fármacos inmunosupresores

- **Ciclosporina (Sandimmun Neoral ®)**
2-5 mg/kg/d, oral, repartidos/12 h
- **Azatioprina (Immurel ®)**
1-3 mg/kg/d, oral
- **Prednisona (Dacortin ®)**
0.5 mg/kg/d, oral 3-6 m, reducción posterior
- **Tacrolimus (FK 506 o Prograf ®)**
0.1-0.2 mg/kg/d, oral, repartidos/12 h
0.01-0.05 mg/kg, infusión continua/24 h
- **Micofenolato Mofetil (CellCept ®)**
1 g/12 h

Sustitución de CS por TA y AZ por MM

Complicaciones tardías



Complicaciones tardías

- Bronquiolitis obliterante

Expresión de rechazo crónico
Descenso de VEMS

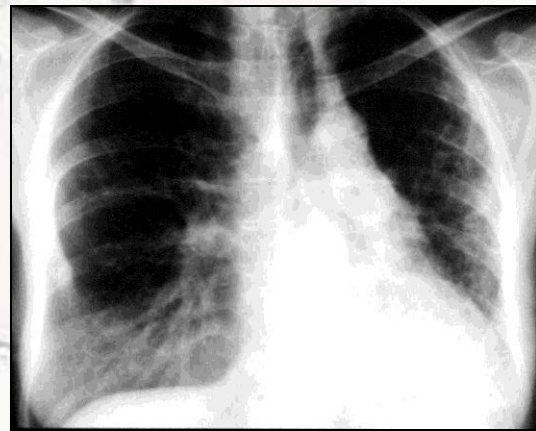
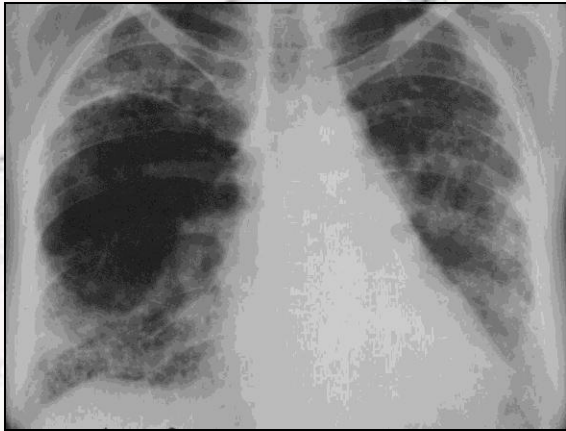
- Arteritis coronaria en Tx CP

Favorecida por
incompatibilidad antigénica y dislipemia

- Procesos linfoproliferativos

Epifenómeno infección virus Epstein-Barr

Trasplante pulmonar (UP y BP) en el adulto





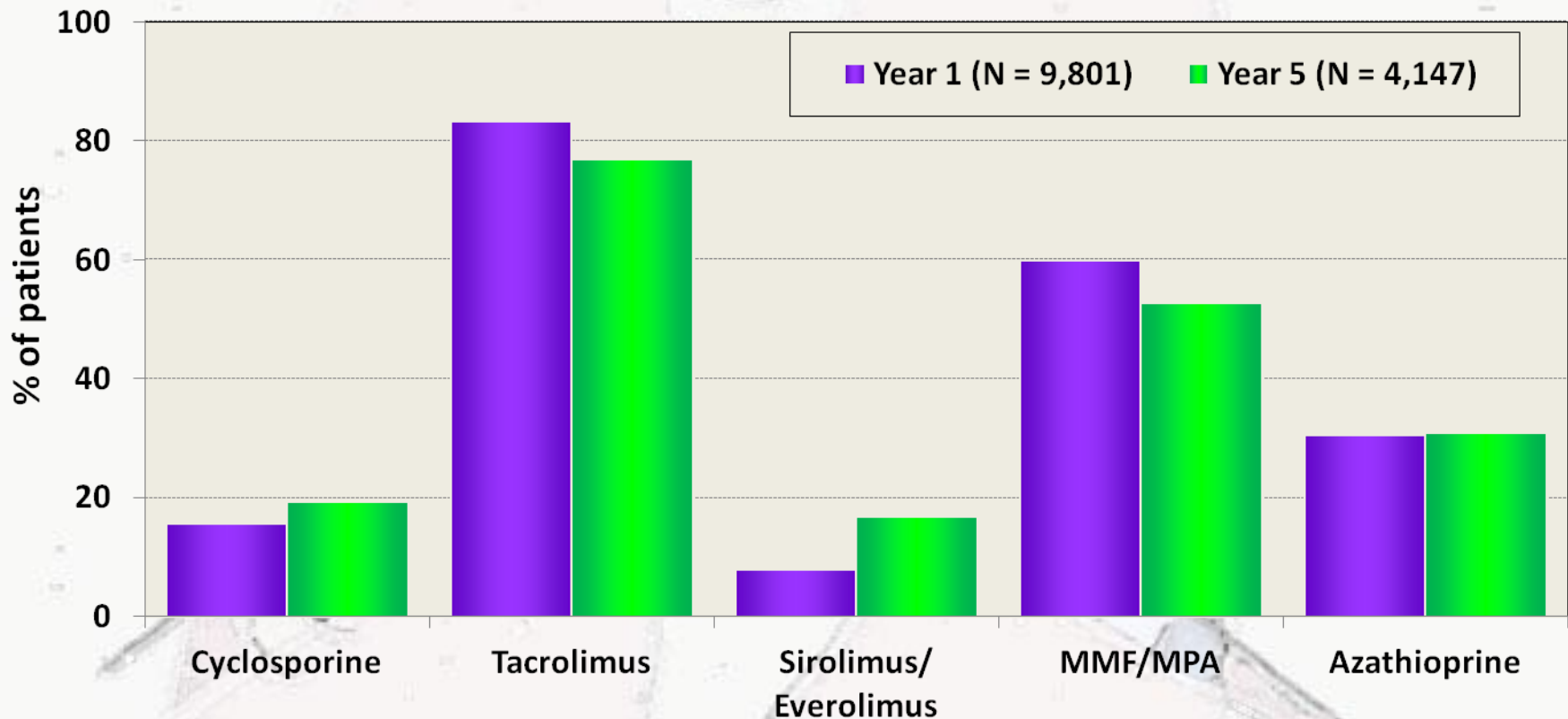
Mantenimiento de la inmunosupresión

ADULT LUNG RECIPIENTS

Maintenance Immunosuppression at Time of Follow-up

Analysis limited to patients receiving prednisone

(Follow-ups: January 2002 – June 2012)



NOTE: Different patients are analyzed in Year 1 and Year 5

An anatomical drawing of a human torso, showing the ribcage and lungs. The drawing is rendered in a light, sketchy style with some color shading. The ribcage is shown in a light blue/grey color, and the lungs are shown in a light pink color. The text "Morbilidad y mortalidad" is overlaid in the center of the image in a bold, dark blue font.

Morbilidad y mortalidad

Adult Lung Transplants

Cumulative Morbidity Rates in Survivors within 1 Year Post-Transplant (Follow-ups: April 1994 – June 2012)

Outcome	Age: 18-65 years		Age: >65 years	
	<u>Within 1 Year</u>	Total number with <u>known response</u>	<u>Within 1 Year</u>	Total number with <u>known response</u>
Hypertension	51.4%	(N = 14,128)	55.7%	(N = 1,139)
Renal Dysfunction	23.3%	(N = 15,856)	23.6%	(N = 1,435)
<i>Abnormal Creatinine ≤ 2.5 mg/dl</i>	16.3%		16.1%	
<i>Creatinine > 2.5 mg/dl</i>	5.3%		4.5%	
<i>Chronic Dialysis</i>	1.6%		2.9%	
<i>Renal Transplant</i>	0.1%		0.0%	
Hyperlipidemia	24.5%	(N = 14,778)	38.1%	(N = 1,197)
Diabetes	24.9%	(N = 15,798)	21.3%	(N = 1,429)
Bronchiolitis Obliterans Syndrome	9.7%	(N = 14,896)	7.3%	(N = 1,368)

Adult Lung Transplants

Cumulative Morbidity Rates in Survivors within 1 and 5 Years Post-Transplant (Follow-ups: April 1994 – June 2012)

Outcome	Within 1 Year	Total number with <u>known response</u>	Within 5 Years	Total number with <u>known response</u>
Hypertension	51.7%	(N = 15,267)	82.4%	(N = 4,503)
Renal Dysfunction	23.3%	(N = 17,291)	55.4%	(N = 5,571)
<i>Abnormal Creatinine ≤ 2.5 mg/dl</i>	16.2%		36.5%	
<i>Creatinine > 2.5 mg/dl</i>	5.2%		15.0%	
<i>Chronic Dialysis</i>	1.7%		3.2%	
<i>Renal Transplant</i>	0.1%		0.7%	
Hyperlipidemia	25.5%	(N = 15,975)	58.4%	(N = 4,856)
Diabetes	24.6%	(N = 17,227)	40.5%	(N = 5,498)
Bronchiolitis Obliterans Syndrome	9.5%	(N = 16,264)	39.7%	(N = 4,701)

Adult Lung Transplants

Morbidity Rates in Survivors within 10 Years Post-Transplant (Follow-ups: April 1994 – June 2012)

Outcome	<u>Within 10 Years</u>	<u>Total number with known response</u>
Renal Dysfunction	74.1%	(N = 1,059)
<i>Abnormal Creatinine \leq 2.5 mg/dl</i>	40.3%	
<i>Creatinine > 2.5 mg/dl</i>	19.8%	
<i>Chronic Dialysis</i>	8.7%	
<i>Renal Transplant</i>	5.3%	
Bronchiolitis Obliterans Syndrome	61.6%	(N = 774)

Adult Lung Transplants

Post Transplant Malignancy (Follow-ups: April 1994 – June 2012) Cumulative Morbidity Rates in Survivors

Malignancy/Type		1-Year Survivors	5-Year Survivors	10-Year Survivors
No Malignancy		17,068 (96.4%)	5,040 (85.3%)	883 (73.2%)
Malignancy (all types combined)		630 (3.6%)	871 (14.7%)	324 (26.8%)
<i>Malignancy Type*</i>	<i>Skin</i>	199	590	226
	<i>Lymphoma</i>	243	94	38
	<i>Other</i>	164	227	93
	<i>Type Not Reported</i>	24	9	0

Other malignancies reported include: adenocarcinoma (2; 2; 1), bladder (2; 1; 0), lung (2; 4; 0), breast (1; 5; 2); prostate (0; 5; 1), cervical (1; 1; 0); liver (1; 1; 1); colon (1; 1; 0). Numbers in parentheses represent the number of reported cases within each time period.

Adult Lung Transplants

Cause of Death (Deaths: January 1992 – June 2012)

Cause of Death	0-30 Days (N = 2,725)	31 Days - 1 Year (N = 4,737)	>1 Year - 3 Years (N = 4,315)	>3 Years - 5 Years (N = 2,449)	>5 Years – 10 Years (N = 2,892)	>10 Years (N = 899)
Bronchiolitis	8 (0.3%)	216 (4.6%)	1,119 (25.9%)	710 (29.0%)	734 (25.4%)	188 (20.9%)
Acute Rejection	94 (3.4%)	85 (1.8%)	63 (1.5%)	16 (0.7%)	17 (0.6%)	2 (0.2%)
Lymphoma	1 (0.0%)	110 (2.3%)	78 (1.8%)	36 (1.5%)	56 (1.9%)	31 (3.4%)
Malignancy, Non-Lymphoma	5 (0.2%)	134 (2.8%)	329 (7.6%)	266 (10.9%)	379 (13.1%)	113 (12.6%)
CMV	0	112 (2.4%)	42 (1.0%)	7 (0.3%)	4 (0.1%)	1 (0.1%)
Infection, Non-CMV	535 (19.6%)	1,687 (35.6%)	971 (22.5%)	471 (19.2%)	523 (18.1%)	154 (17.1%)
Graft Failure	672 (24.7%)	790 (16.7%)	807 (18.7%)	440 (18.0%)	515 (17.8%)	156 (17.4%)
Cardiovascular	298 (10.9%)	228 (4.8%)	179 (4.1%)	120 (4.9%)	148 (5.1%)	58 (6.5%)
Technical	301 (11.0%)	162 (3.4%)	38 (0.9%)	14 (0.6%)	24 (0.8%)	8 (0.9%)
Other	811 (29.8%)	1,213 (25.6%)	689 (16.0%)	369 (15.1%)	492 (17.0%)	188 (20.9%)

Adult Lung Transplants

Cause of Death Stratified by Age Group

(Deaths: January 1992 – June 2012)

Age Group	Cause of Death	0-30 Days	31 Days - 1 Year	>1 Year - 3 Years	>3 Years - 5 Years	>5 Years
18-65	Bronchiolitis	8 (0.3%)	201 (4.6%)	1,065 (26.4%)	691 (29.6%)	910 (24.5%)
	Malignancy	5 (0.2%)	220 (5.0%)	361 (8.9%)	275 (11.8%)	569 (15.3%)
	Infection	514 (19.7%)	1,686 (38.3%)	957 (23.7%)	450 (19.3%)	665 (17.9%)
	Graft Failure	644 (24.7%)	724 (16.5%)	757 (18.7%)	422 (18.1%)	661 (17.8%)
	Cardiovascular	280 (10.7%)	198 (4.5%)	161 (4.0%)	113 (4.8%)	200 (5.4%)
	Technical	290 (11.1%)	157 (3.6%)	38 (0.9%)	14 (0.6%)	32 (0.9%)
	All known causes	2,610	4,397	4,040	2,333	3,721
>65	Bronchiolitis	0	15 (4.4%)	54 (19.6%)	19 (16.4%)	12 (17.1%)
	Malignancy	1 (0.9%)	24 (7.1%)	46 (16.7%)	27 (23.3%)	10 (14.3%)
	Infection	21 (18.3%)	113 (33.2%)	56 (20.4%)	28 (24.1%)	17 (24.3%)
	Graft Failure	28 (24.3%)	66 (19.4%)	50 (18.2%)	18 (15.5%)	10 (14.3%)
	Cardiovascular	18 (15.7%)	30 (8.8%)	18 (6.5%)	7 (6.0%)	6 (8.6%)
	Technical	11 (9.6%)	5 (1.5%)	0	0	0
	All known causes	115	340	275	116	70

Mortalidad post-trasplante



Causas

Inmediata y primer año:

Rechazo agudo

Infecciones

Fallo del injerto

Complicaciones cardiacas

A partir del primer año:

Bronquiolitis obliterante

Infecciones

Gráficos de supervivencia



ADULT LUNG TRANSPLANTATION

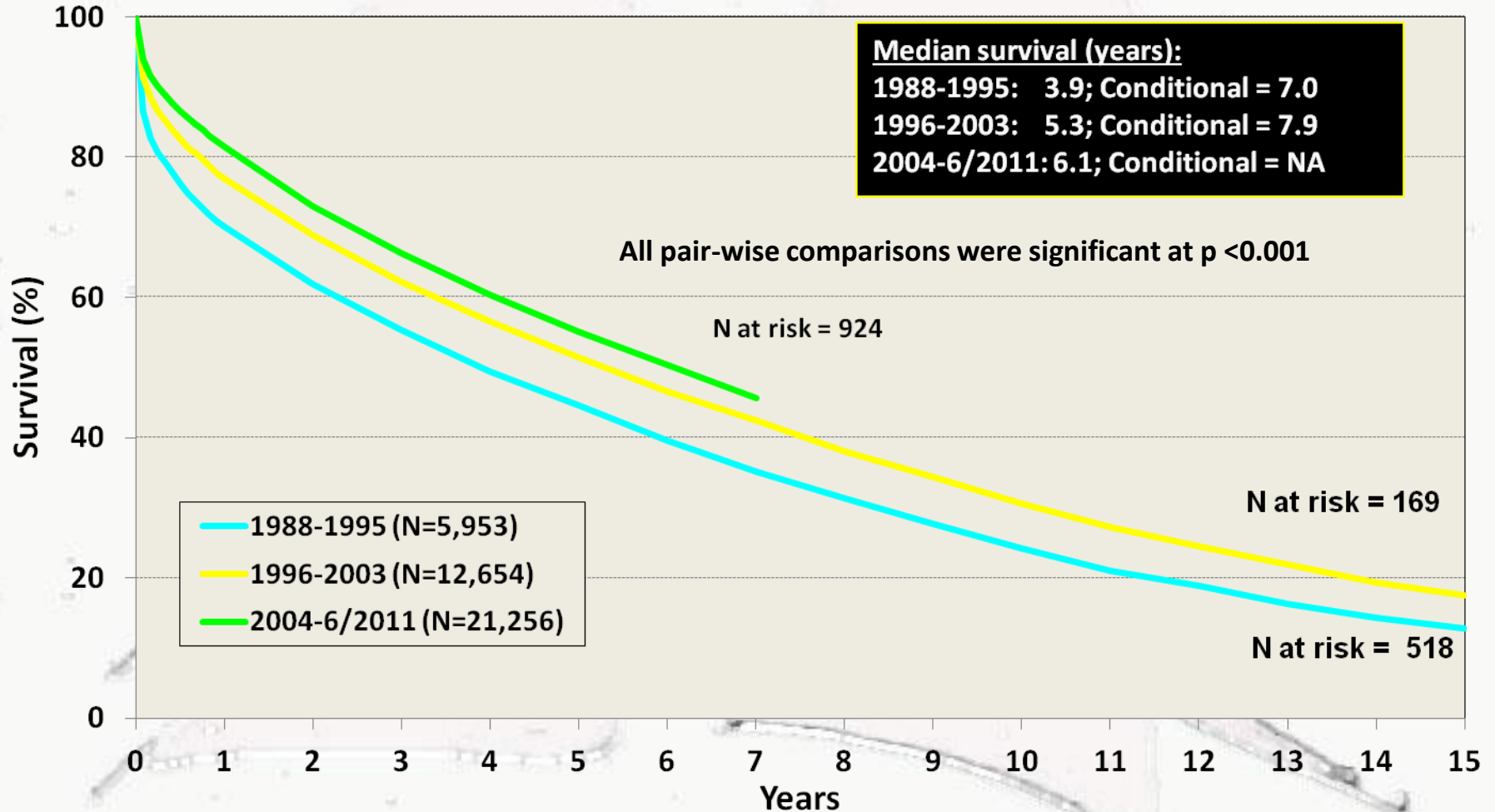
Kaplan-Meier Survival By Diagnosis (Transplants: January 1990 – June 2006)

Year	ALPHA-1 (N=1,925)	CF (N=3,275)	COPD (N=7,760)	IPF (N=3,931)	PPH (N=970)	SARCOIDOSIS (N=506)
1	77.9	81.8	82.1	72.5	67.2	69.9
3	63.9	66.2	65	57.1	57	56.5
5	54.1	56	50	44.6	48.5	50.8
7	44	48.3	37.4	33.8	41.5	42.7
10	31.2	38.6	21.8	21.1	30	31

Adult Lung Transplants

Kaplan-Meier Survival by Era

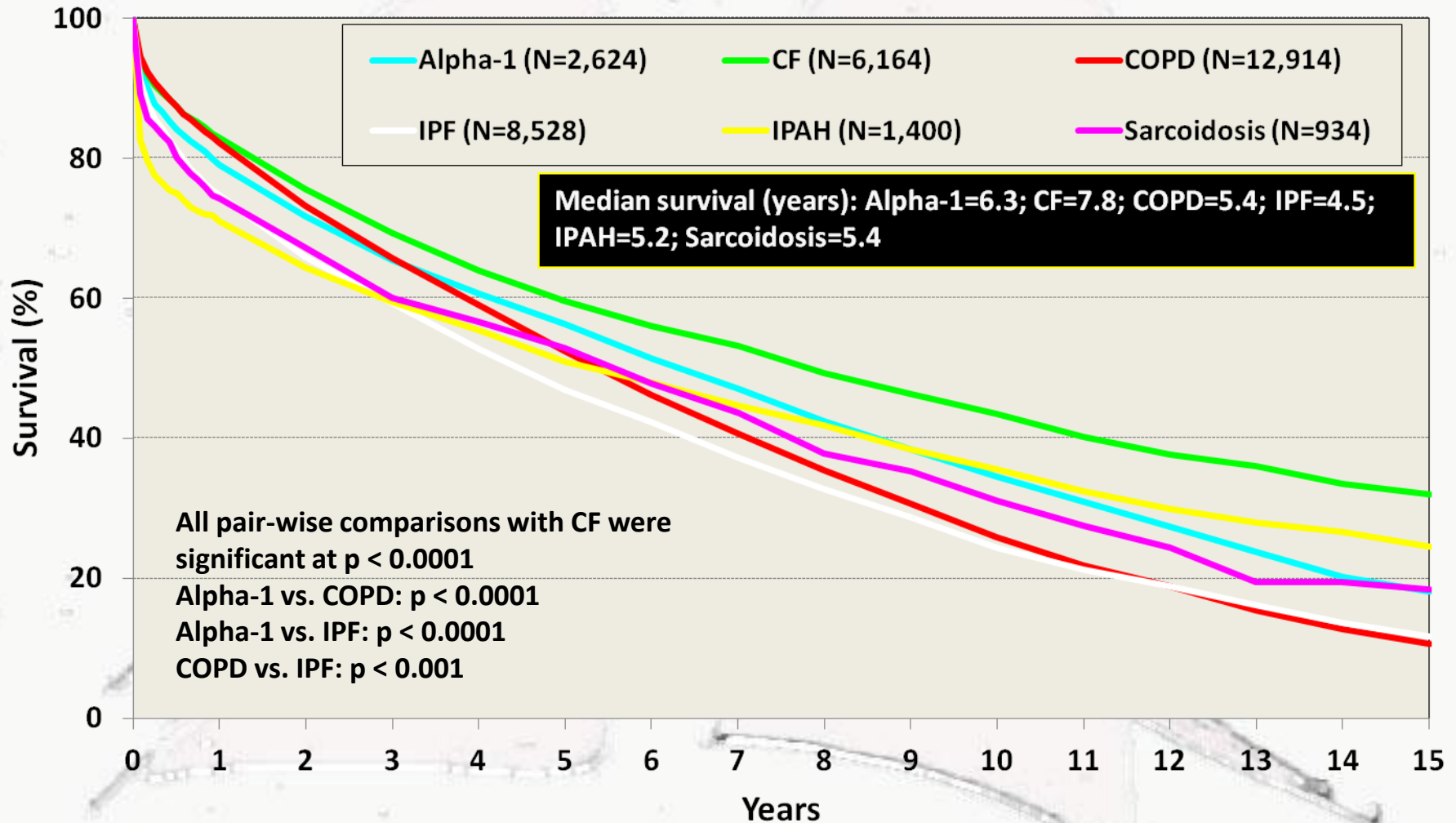
(Transplants: January 1988 – June 2011)



Adult Lung Transplants

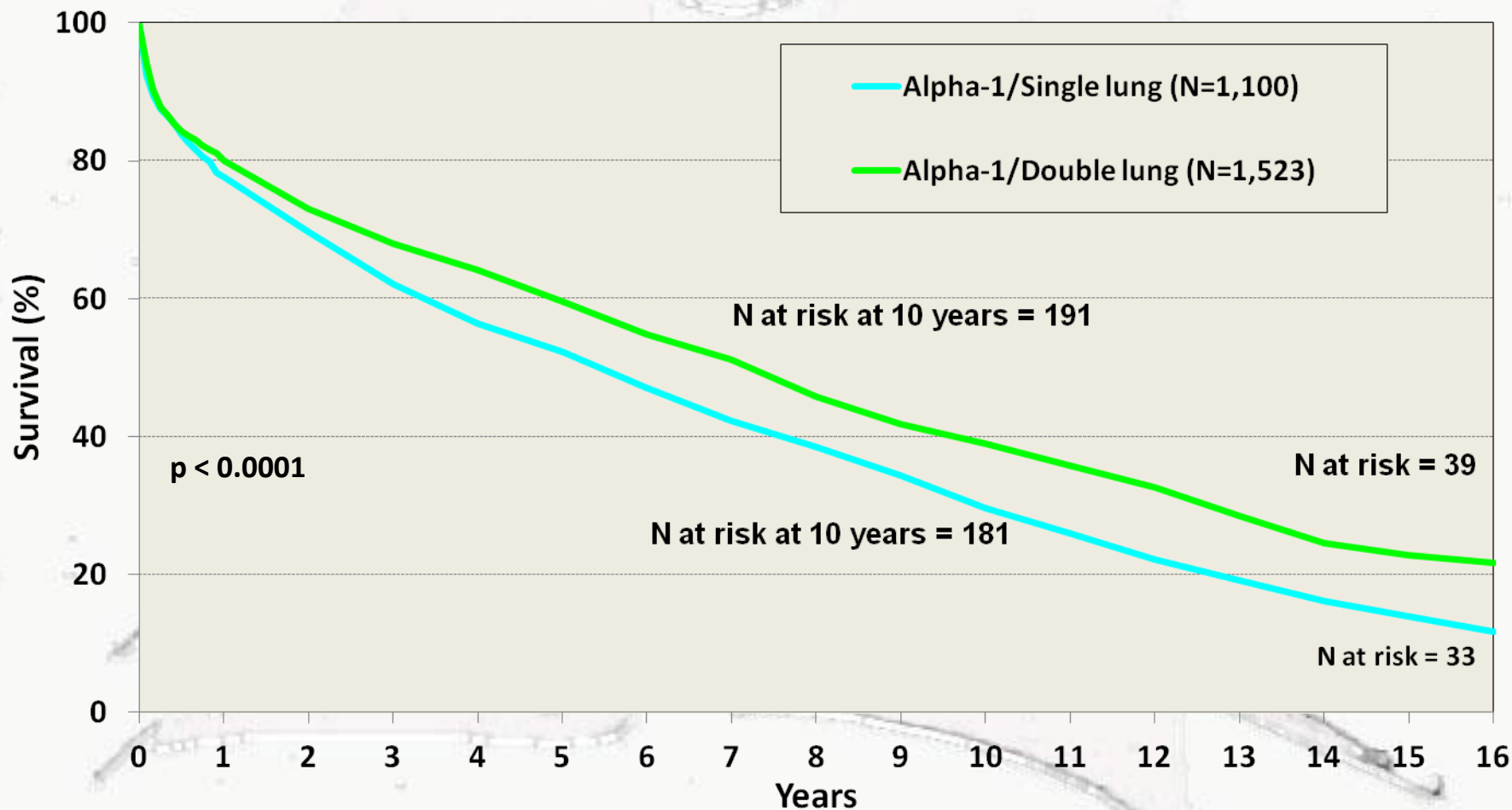
Kaplan-Meier Survival by Diagnosis

(Transplants: January 1990 – June 2011)



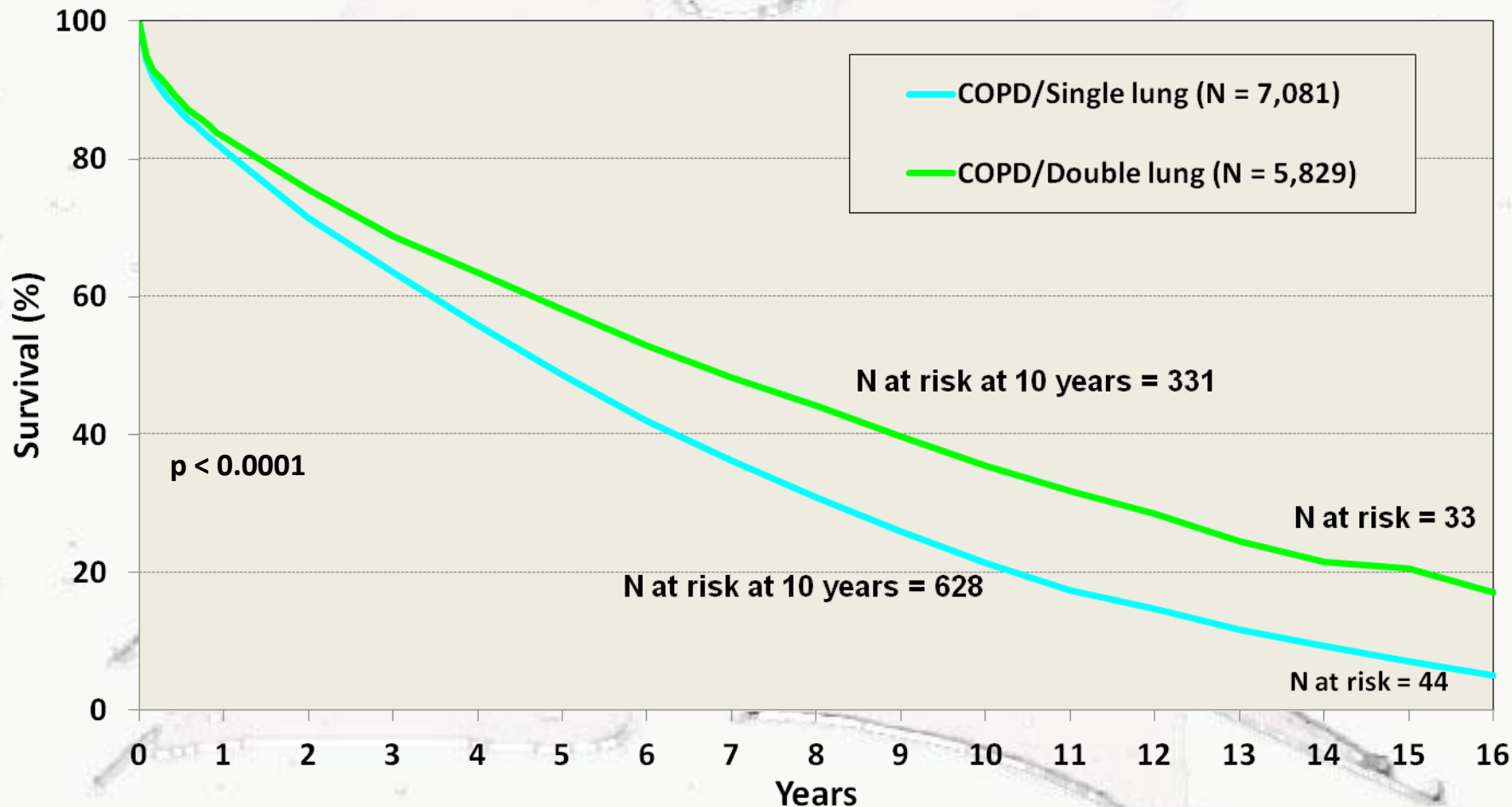
Adult Lung Transplants

Kaplan-Meier Survival By Procedure Type (Transplants: January 1990 – June 2011) Diagnosis: Alpha-1 Antitrypsin Deficiency



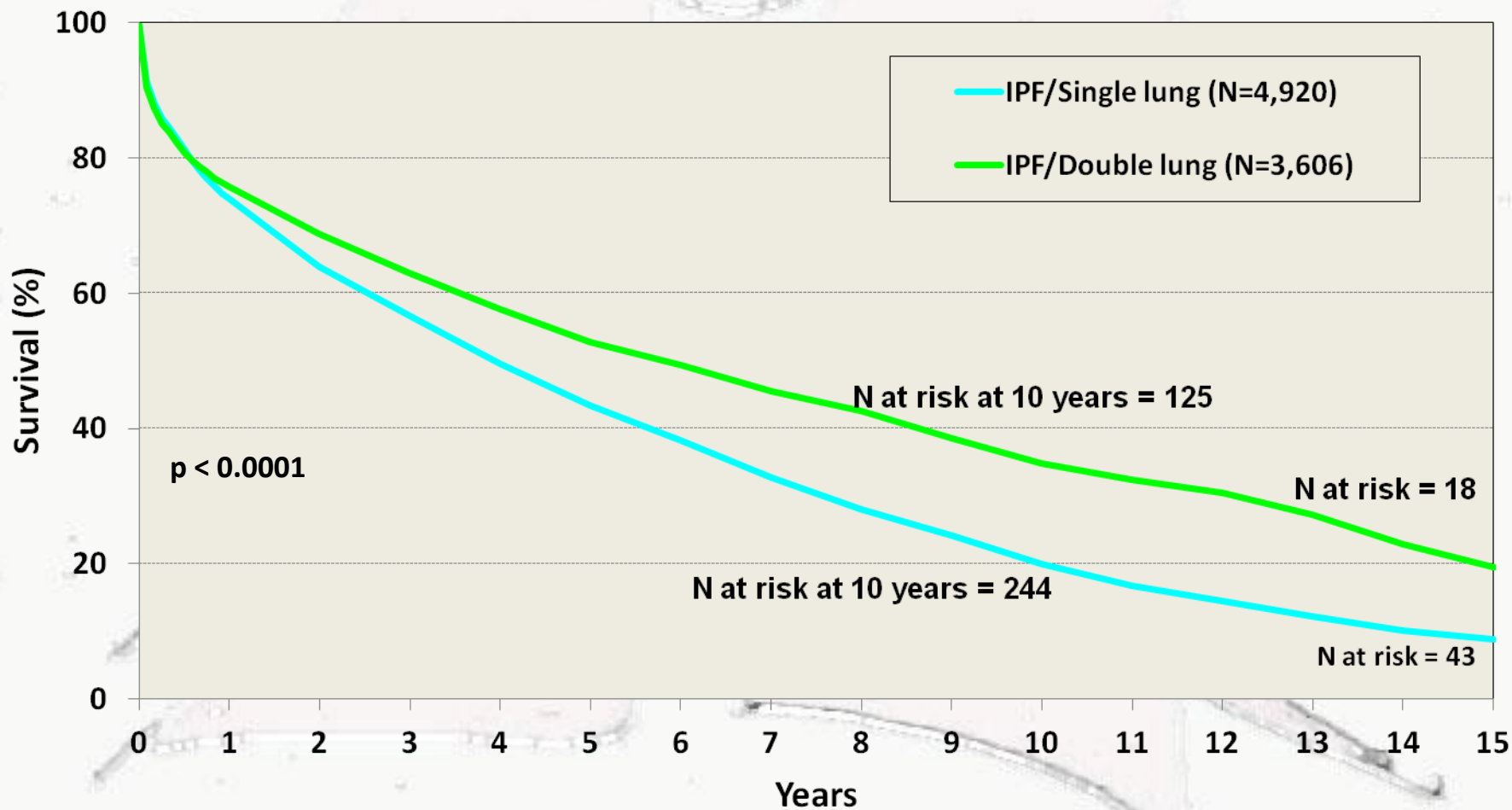
Adult Lung Transplants

Kaplan-Meier Survival By Procedure Type (Transplants: January 1990 – June 2011) Diagnosis: COPD/Emphysema



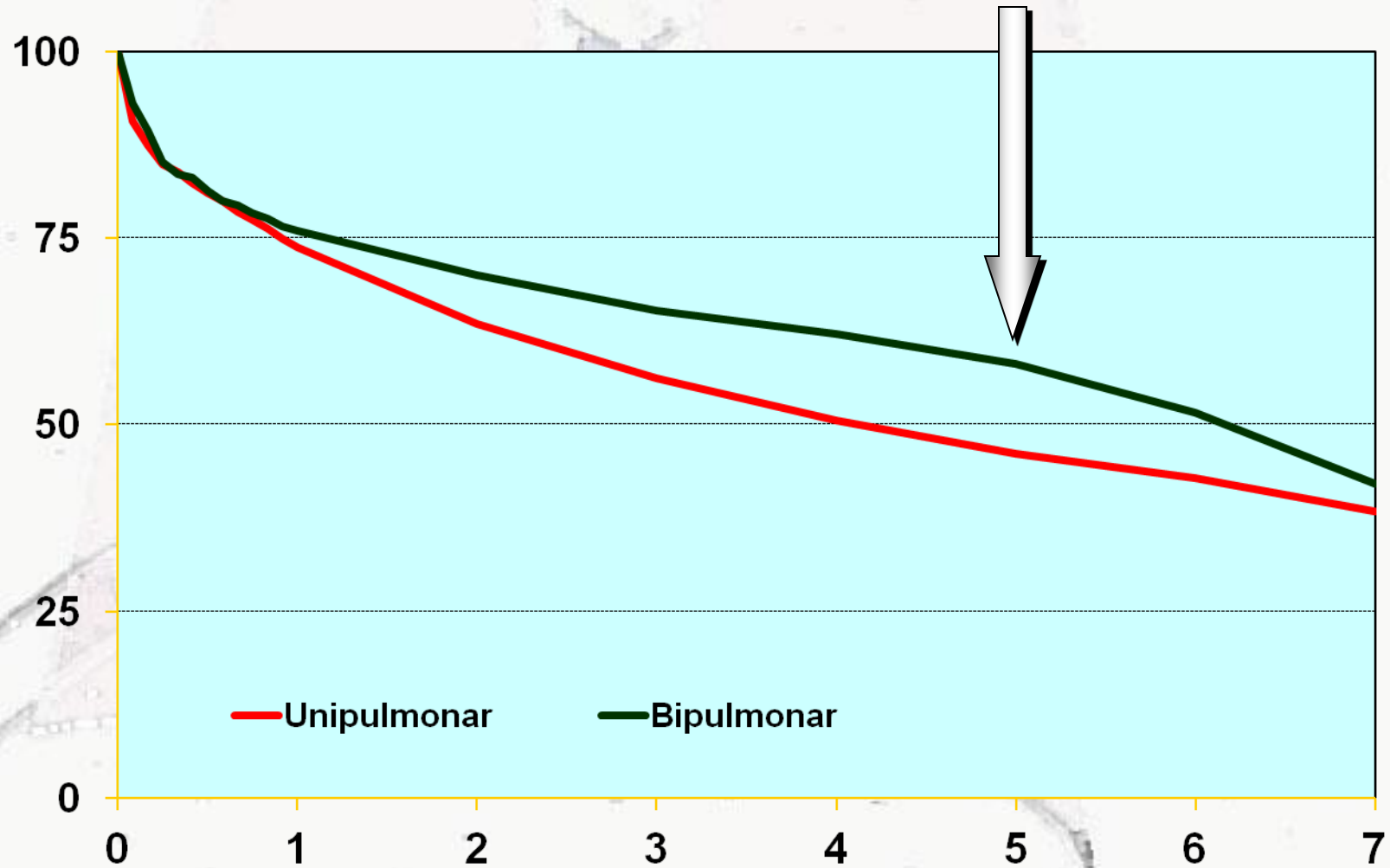
Adult Lung Transplants

Kaplan-Meier Survival By Procedure Type (Transplants: January 1990 – June 2011) Diagnosis: Idiopathic Pulmonary Fibrosis



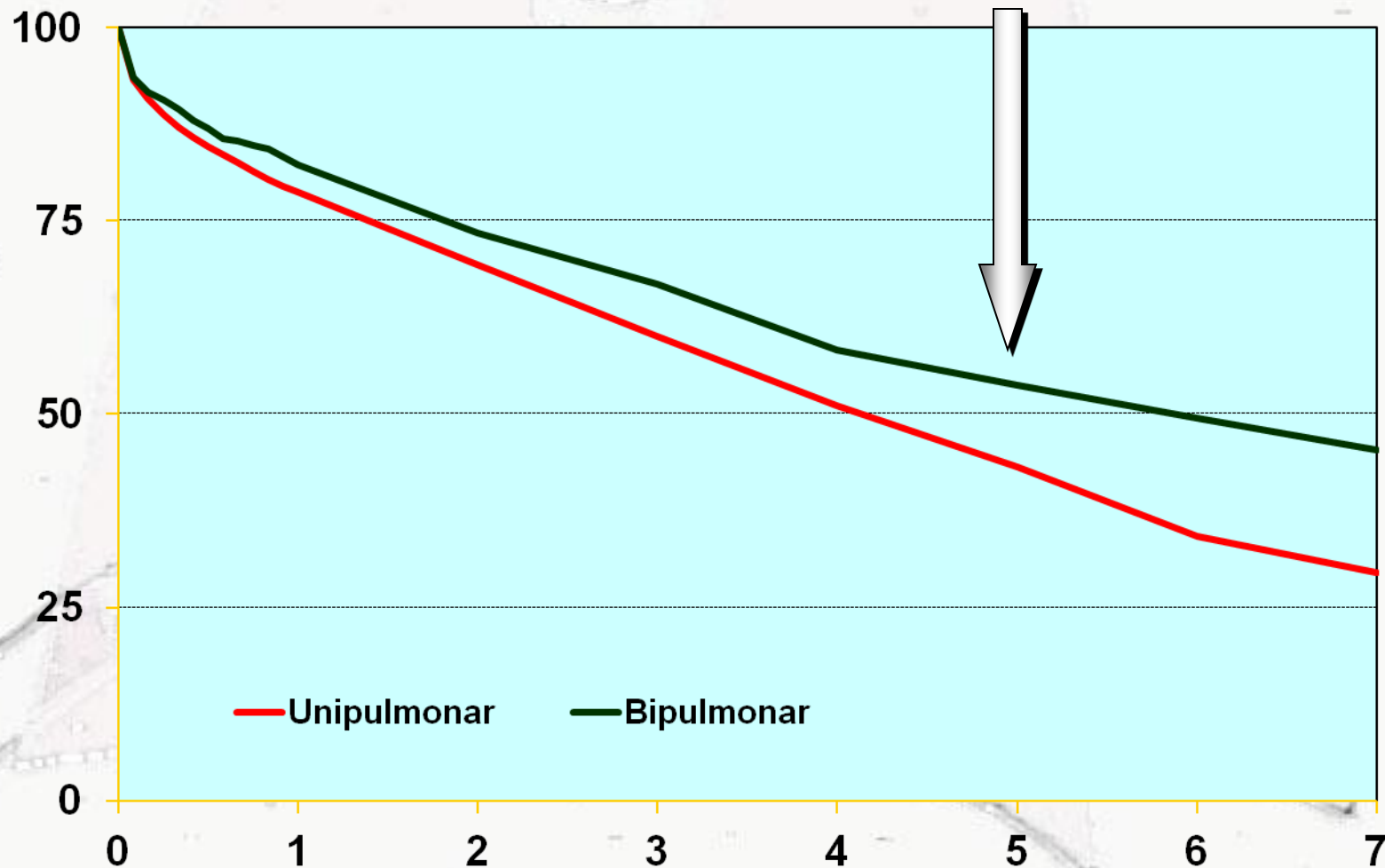
Supervivencia

Déficit alfa1 antitripsina



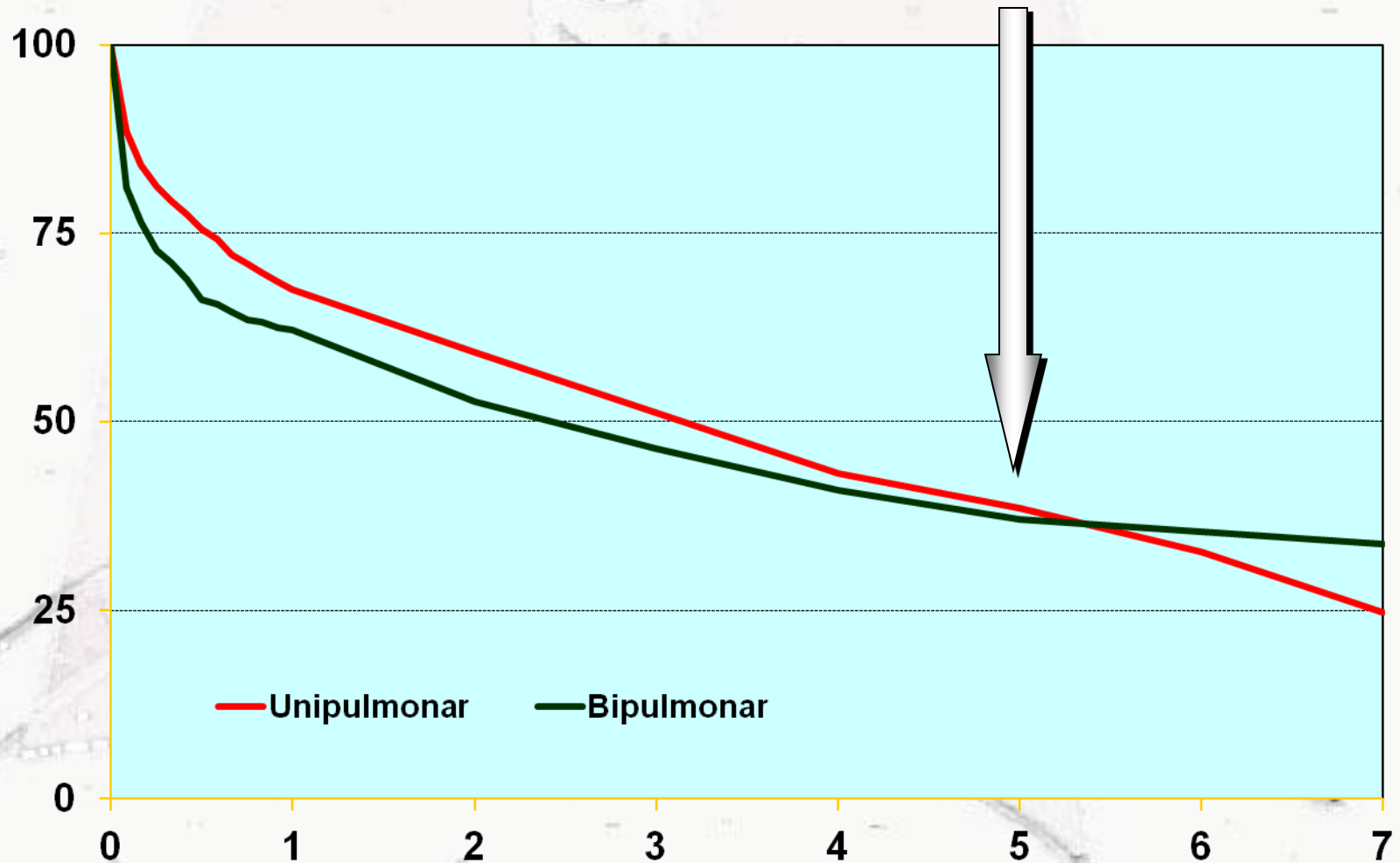
Supervivencia

Enfisema / EPOC



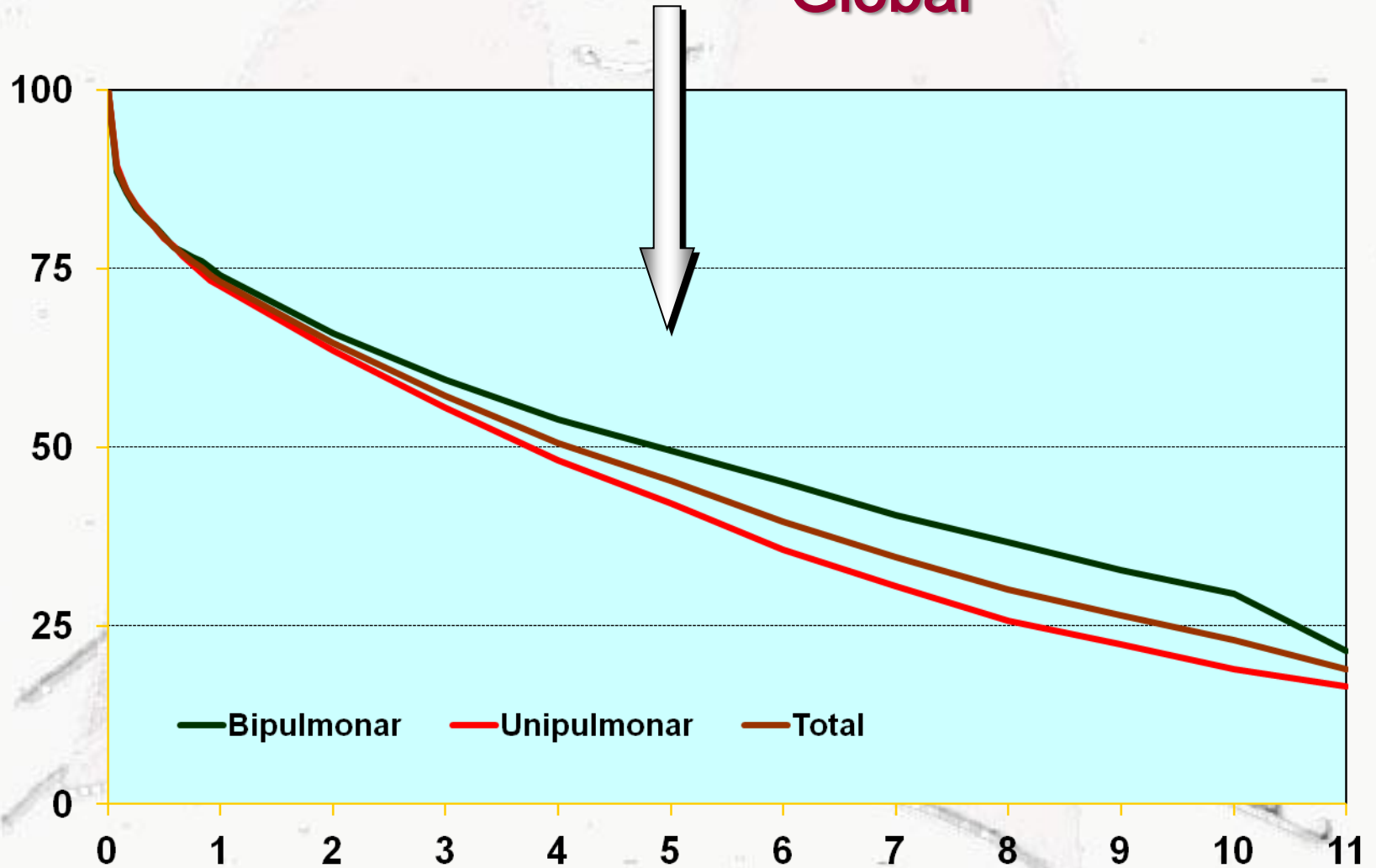
Supervivencia

Fibrosis pulmonar



Supervivencia

Global



Trasplante pulmonar

Control y seguimiento del trasplantado pulmonar

Félix Heras Gómez

Universidad de Valladolid

Hospital Clínico Universitario de Valladolid

