INDICAZIONI AL TRAPIANTO POLMONARE E LA SCELTA DEL RICEVENTE

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ORIGINAL ARTICLE

Extended recipients but not extended donors are associated with poor outcomes following lung transplantation†

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Abstract

OBJECTIVES: Extended donors (EDs) are safely used to increase the donor pool in lung transplantation (LT), but their influence in critically ill patients (extended recipients [ERs]) remains controversial. We compared LT outcomes matching optimal donors (ODs) or EDs with optimal recipients (ORs) or ERs.

METHODS: Three hundred and sixty-five LTs were reviewed. ED criteria: age >55, PaO_2/FiO_2 < 350 mmHg, pulmonary infiltrates/purulent secretions and ischaemic times >6 h (single LT [SLT]) and >9 h (double LT [DLT]). ER criteria: pulmonary fibrosis or pulmonary hypertension, pretransplant intubation, age >60 years and bypass >2 h. Four groups were created: Group 1 (OD/OR), Group 2 (OD/ER), Group 3 (ED/OR) and Group 4 (ED/ER). Thirty-day mortality, primary graft dysfunction (PGD), onset of bronchiolitis obliterans syndrome (BOS), long-term survival and other transplant outcomes were compared between OD and ED, OR and ER and among the four groups of study.

RESULTS: There were 151 SLTs and 214 DLTs. *Donors*: OD (n = 229) vs ED (n = 136); PGD 8 vs 10% (P = 0.43); 30-day mortality 19 vs 20% (P = 0.53) and survival (1, 5, 10 and 15 years) 67, 47, 34, 26 vs 69, 53, 46 and 29% (P = 0.33). *Recipients*: OR (n = 182) vs ER (n = 183); PGD 7 vs 10% (P = 0.10); 30-day mortality 15 vs 23% (P = 0.04) and survival (1, 5, 10 and 15 years): 73, 57, 46, 30 vs 61, 42, 29 and 23% (P = 0.002). *Four donor/recipient (D/R) groups*: Group 1 (n = 122), Group 2 (n = 106), Group 3 (n = 61), Group 4 (n = 76); PGD 10, 6, 3 and 16% (P = 0.05); 30-day mortality 13, 26, 19 and 20%, respectively (P = 0.13); survival (1, 5, 10 and 15 years) 74, 55, 44 and 35% (Group 1), 55, 39, 22 and 16% (Group 2), 70, 59, 48 and 26% (Group 3) and 68, 47, 37 and 22% (Group 4) (P = 0.004). No differences in the onset of BOS were observed among the four study groups.

CONCLUSIONS: LT in critically ill recipients is associated with poor early and long-term outcomes, irrespective of the quality of the donor and length of ischaemic times.

Keywords: Lung transplantation • Lung donor criteria • Marginal donor lungs • Extended donors • Extended recipients • Lung donor pool

Iter della valutazione trapianto

1°: specialista o centro specialistico (pneumologico/cardiologico) che segue il paziente e lo riferisce al centro trapianti

2°: prima visita/colloquio con il paziente potenziale ricevente

3°: fase di screening

4°: valutazione se indicato l'inserimento in lista attiva

5°: rivalutazioni periodiche

6°: trapianto

7°: follow-up

Il trapianto di polmone deve essere preso in considerazione per quelle patologie respiratorie croniche/acute che stanno evolvendo verso una fase terminale di malattia e che non presentano altre alternative terapeutiche di tipo medico e/o chirurgico.

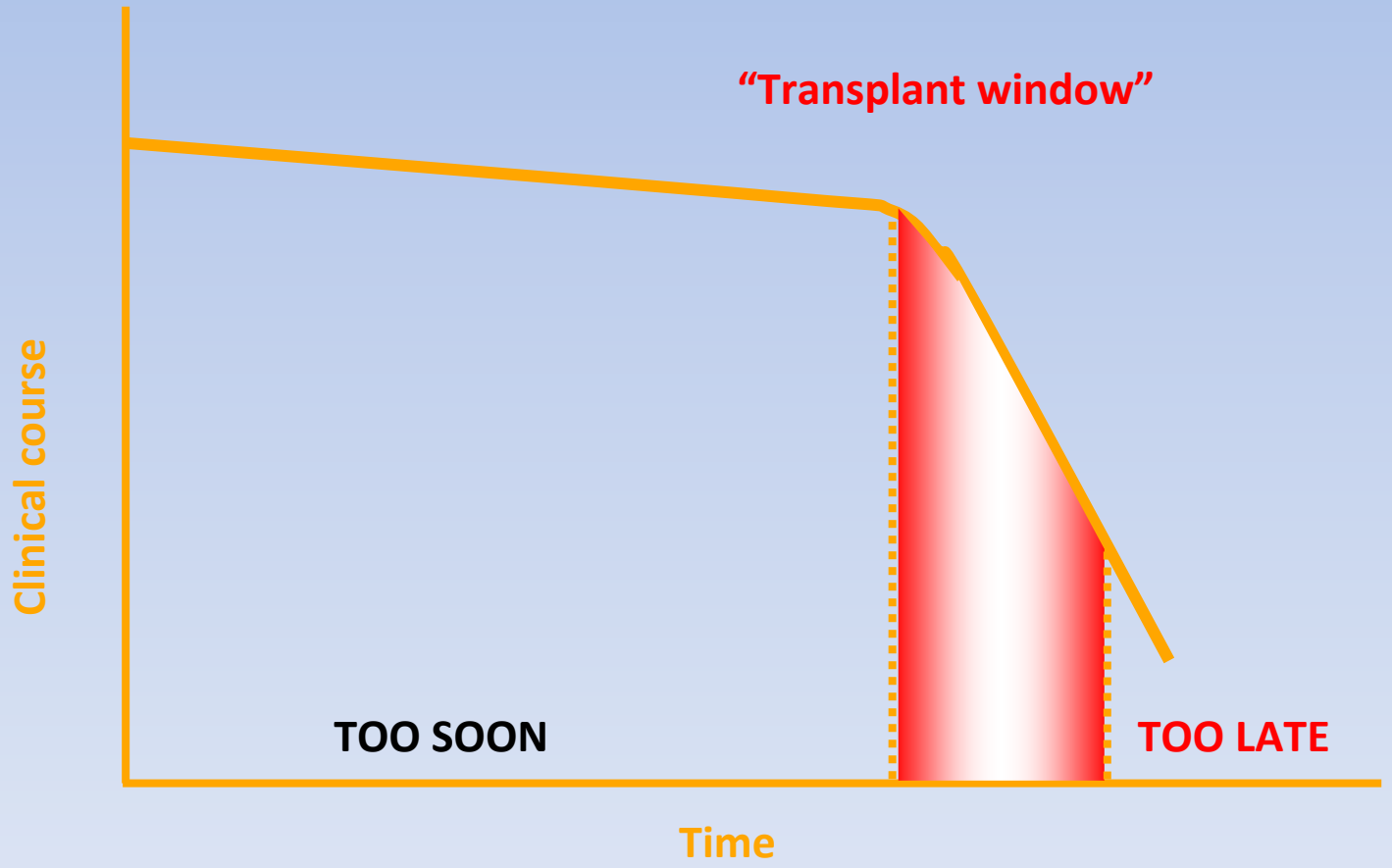
CRITERI GENERALI

- ***UNA MORTALITA' PREVISTA A 2 ANNI MAGGIORE DEL 50% SE IL TRAPIANTO NON VIENE ESEGUITO.***

- ***UNA PROBABILITA' DI SOPRAVVIVERE DOPO IL TRPAINTO >80% A 90 GIORNI.***

- ***UNA PROBABILITA' DI SOPRAVVIEVERE A 5-ANNI MAGGIORE DELL'80% AMMESSA LA BUONA FUNZIONALITA' DELL'ORGANO TRAPIANTATO .***

Transplantation Window of Opportunity



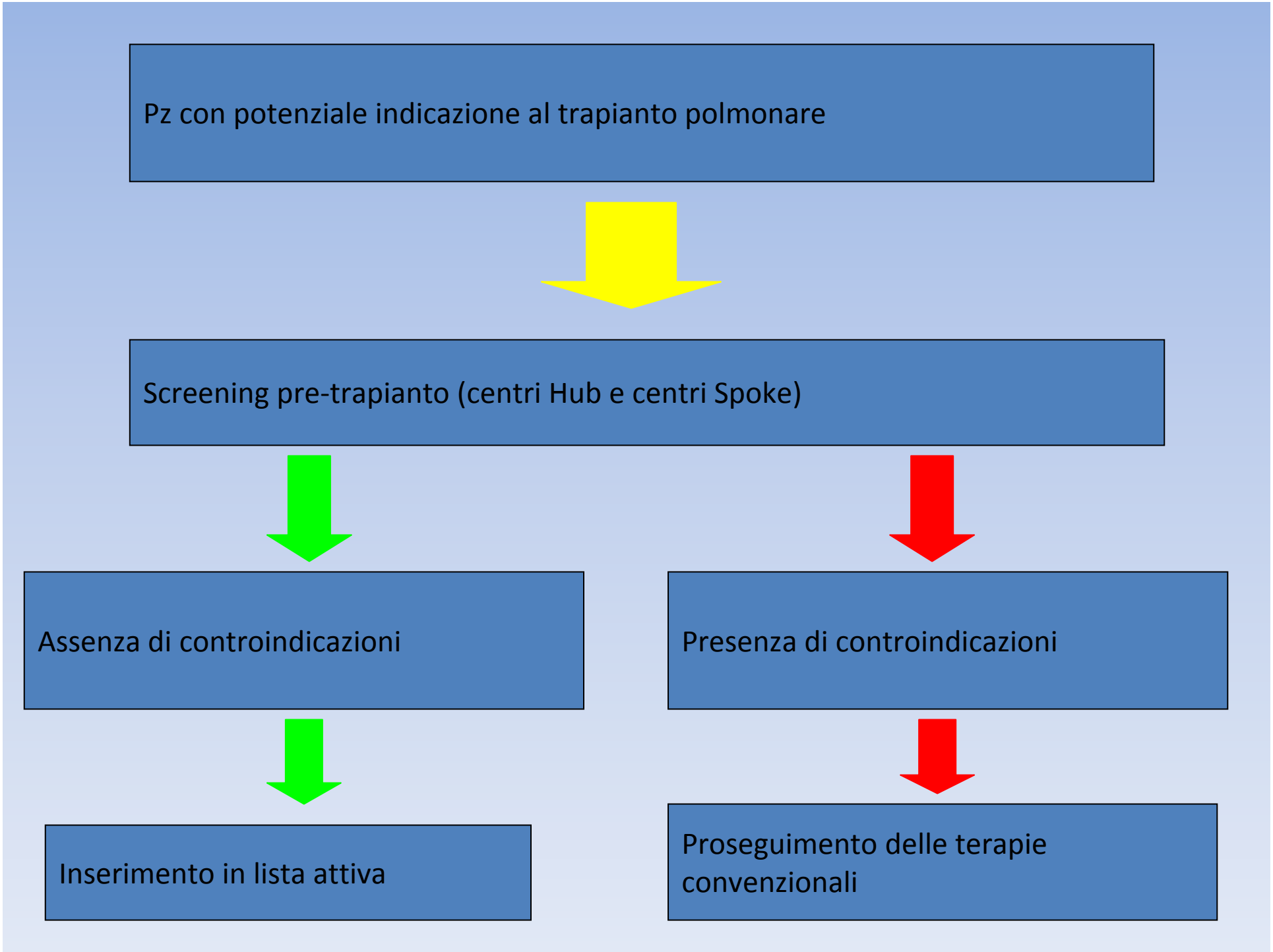
Marshall SE, et al. *Chest*. 1990.

CONTROINDICAZIONI ASSOLUTE:

- ASSENZA DI PREGRESSE PATOLOGIE NEOPLASTICHE (DISEASE FREE INTERVAL ???)
- UNA SIGNIFICATIVA ED INCORREGGIBILE DISFUNZIONE DI UN ALTRO ORGANO AMMESSA L'IMPOSSIBILITA' DI UN TRAPIANTO COMBINATO.
- SEVERA PATOLOGIA ATEROSCLEROTICA NON CORREGGIBILE O CON Già GRAVI SEGNI DI ISCHEMIA O DISFUNZIONE D'ORGANO
- PATOLOGIA MEDICA ACUTA ED INSTABILE (DISFUNZIONE EPATICA, IMA RECENTE, STROKE, ECC)
- SEPSI SISTEMICA
- INFEZIONI CRONICHE SCARSAMENTE CONTROLLATE DA PATOGENI MULTIRESTISTENTI ALLE ATTUALI TERAPIE MEDICHE
- TUBERCOLOSI ATTIVA
- GRAVE ED INCORREGGIBILE DIATESI EMORRAGICA
- SEVERE DEFORMITA' DELLA COLONNA/GABBIA TORACICA CON SINDROME RESTRITTIVA
- SEVERA OBESITA' BMI > 35 Kg/m2
- SCARSA O NO ADERENZA A TERAPIE MEDICHE PREGRESSE
- SERI DISTURBI PSICHIATRICI
- ASSENZA DI UN SUPPORTO FAMIGLIARE E/O SOCIALE AEDGUATO
- FUMO ATTIVO E/O ABUSO DI SOSTENZE STUPEFACENTI

CONTROINDICAZIONI RELATIVE :

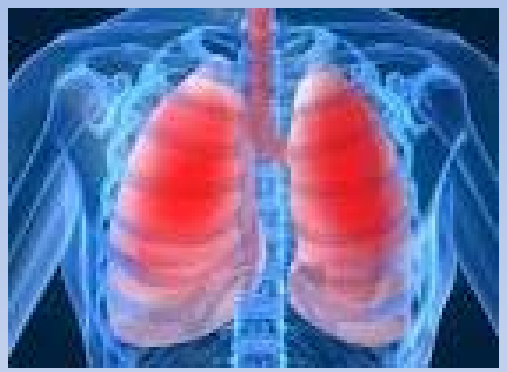
- ETA’ > 65 ANNI
- OBESITA’ DI TIPO I (BMI 30.0-34.9 Kg/m2)
- MALNUTRIZIONE
- SEVERA E SINTOMATICA OSTEOPOROSI
- PREGRESSI INTERVENTI DI RESEZIONE POLMONARE CHIRURGICA
- VENTILAZIONE MECCANICA O ECMO (ATTENZIONE !!!!!!)
- COLONIZZAZIONI BATTERICHE /VIRALI / FUNGINE
- EPATITI B EPATITE C (NON COMPLICATE)
- INFEZIONE DA HIV CON HIV-RNA NON DOSABILE (ATTENZIONE !!!!)
- INFEZIONI DA BURKORDELIA CENOCEPACEA E GLADIOLI MULTIRESISTENTI , MICOBATTERI ATIPICI (ASCESSUS, ECC)
- PATOLOGIA ATEROSCLEROTICA NON SEVERA O TRATTABILE (BY-PASS, PTCA , ECC)
- DIABETE
- REFLUSSO GASTROESOFAGEO
- ULCERA
- EPILESSIA , ECC


Pz con potenziale indicazione al trapianto polmonare
Screening pre-trapianto (centri Hub e centri Spoke)
Assenza di controindicazioni
Presenza di controindicazioni
Inserimento in lista attiva
Proseguimento delle terapie convenzionali

TIPO DI TRAPIANTO

Monopolmonare

- < 70 anni
- Patologie restrittive
- Enfisema polmonare
- Poor performance status



Bi-polmonare

- < 65 anni
- Patologie settiche
- Enfisema polmonare (pz giovani)
- Patologia vascolare polmonare

TRX cuore-polmone

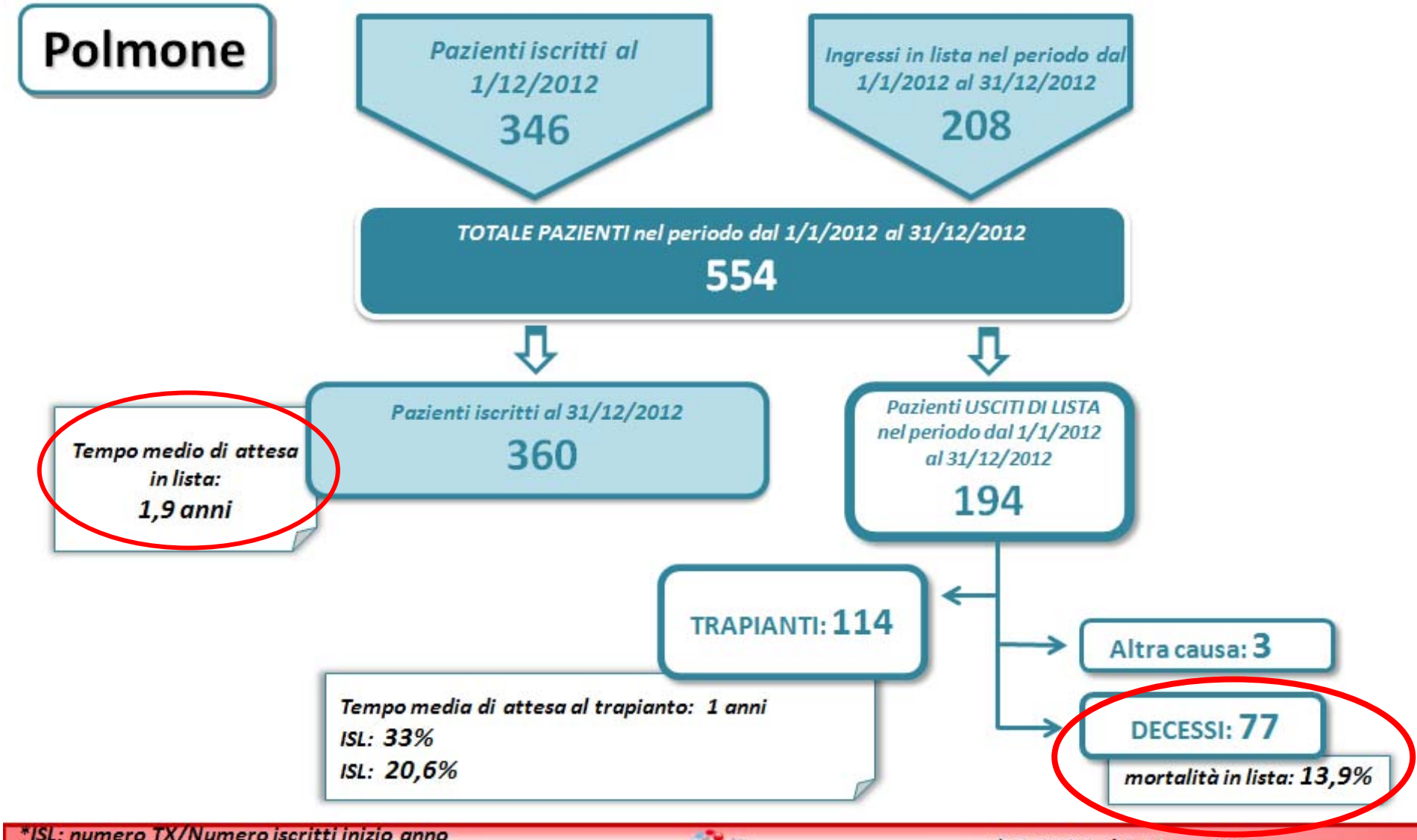
- < 60 anni
- Sn Eisenmenger con difetto cardiaco non correggibile
- Deficit ventricolare Dx refrattario
- Malattia cardiaca concomitante non chirurgica

LUNG ALLOCATION SCORE

UNOS (**United Network for Organ Sharing**) : ha adottato un sistema di score in grado di predire la severità della malattia, la prognosi e la velocità di evoluzione determinando così delle classi di rischio che vanno ad influenzare la priorità del paziente in lista di attesa.

Sistema recentemente adottato anche in Italia ma al momento “non vincolante”

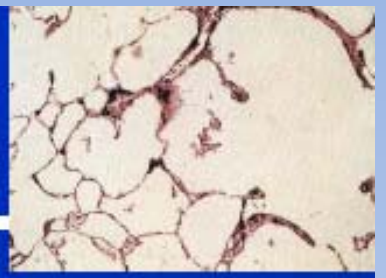
Flussi Lista di attesa 1/1/2012 – 31/12/2012



*ISL: numero TX/Numero iscritti inizio anno
**ISLT: numero TX/(Numero iscritti inizio anno+Ingressi)

* Dati SIT al 3 Marzo 2013

Patologie



RESTRITTIVE

-fibrosi e/o interstiziopatie primitive e secondarie

OSTRUTTIVE

-enfisema senza/con deficit di α1-antitripsina

VASCOLARI

-ipertensione polmonare primitiva o secondaria

SETTICHE

-fibrosi cistica, bronchiectasie

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ISHLT CONSENSUS

A consensus document for the selection of lung transplant candidates: 2014—An update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation

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Interstitial lung disease

Timing of referral:

- Histopathologic or radiographic evidence of usual interstitial pneumonitis (UIP) or fibrosing non-specific interstitial pneumonitis (NSIP), regardless of lung function.
- Abnormal lung function: forced vital capacity (FVC) <80% predicted or diffusion capacity of the lung for carbon monoxide (D_{LCO}) <40% predicted.
- Any dyspnea or functional limitation attributable to lung disease.
- Any oxygen requirement, even if only during exertion.
- For inflammatory interstitial lung disease (ILD), failure to improve dyspnea, oxygen requirement, and/or lung function after a clinically indicated trial of medical therapy.

Timing of listing:

- Decline in FVC ≥10% during 6 months of follow-up (note: a 5% decline is associated with a poorer prognosis and may warrant listing).
- Decline in D_{LCO} ≥15% during 6 months of follow-up.
- Desaturation to <88% or distance <250 m on 6-minute-walk test or >50 m decline in 6-minute-walk distance over a 6-month period.
- Pulmonary hypertension on right heart catheterization or 2-dimensional echocardiography.
- Hospitalization because of respiratory decline, pneumothorax, or acute exacerbation.

Cystic fibrosis

Timing of referral:

- FEV_1 that has fallen to 30% or a patient with advanced disease with a rapidly falling FEV_1 despite optimal therapy (particularly in a female patient), infected with non-tuberculous mycobacterial (NTM) disease or *B cepacia* complex (see previous comment on *B cenocepacia* and subsequently) and/or with diabetes.
- A 6-minute walk distance <400 m.
- Development of pulmonary hypertension in the absence of a hypoxic exacerbation (as defined by a systolic pulmonary arterial pressure (PAP) >35 mm Hg on echocardiography or mean PAP >25 mm Hg measured by right heart catheterization).
- Clinical decline characterized by increasing frequency of exacerbations associated with any of the following:
  - An episode of acute respiratory failure requiring non-invasive ventilation.
  - Increasing antibiotic resistance and poor clinical recovery from exacerbations.
  - Worsening nutritional status despite supplementation.
  - Pneumothorax.
  - Life-threatening hemoptysis despite bronchial embolization.

Timing of listing:

- Chronic respiratory failure.
  - With hypoxia alone (partial pressure of oxygen [Pao_2] <8 kPa or <60 mm Hg).
  - With hypercapnia (partial pressure of carbon dioxide [$Paco_2$] >6.6 kPa or >50 mm Hg).
- Long-term non-invasive ventilation therapy.
- Pulmonary hypertension.
- Frequent hospitalization.
- Rapid lung function decline.
- World Health Organization Functional Class IV.

COPD

Timing of referral:

- Disease is progressive, despite maximal treatment including medication, pulmonary rehabilitation, and oxygen therapy.
- Patient is not a candidate for endoscopic or surgical LVRS. Simultaneous referral of patients with COPD for both lung transplant and LVRS evaluation is appropriate.
- BODE index of 5 to 6.
- $Paco_2$ >50 mm Hg or 6.6 kPa and/or Pao_2 <60 mm Hg or 8 kPa.
- FEV_1 <25% predicted.

Timing of listing (presence of one criterion is sufficient):

- BODE index ≥7.
- FEV_1 <15% to 20% predicted.
- Three or more severe exacerbations during the preceding year.
- One severe exacerbation with acute hypercapnic respiratory failure.
- Moderate to severe pulmonary hypertension.

Pulmonary vascular diseases

Timing of referral:

- NYHA Functional Class III or IV symptoms during escalating therapy.
- Rapidly progressive disease (assuming weight and rehabilitation concerns not present).
- Use of parenteral targeted pulmonary arterial hypertension (PAH) therapy regardless of symptoms or NYHA Functional Class.
- Known or suspected pulmonary veno-occlusive disease (PVOD) or pulmonary capillary hemangiomatosis.

Timing of transplant listing:

- NYHA Functional Class III or IV despite a trial of at least 3 months of combination therapy including prostanoids.
- Cardiac index of <2 liters/min/m^2.
- Mean right atrial pressure of >15 mm Hg.
- 6-minute walk test of <350 m.
- Development of significant hemoptysis, pericardial effusion, or signs of progressive right heart failure (renal insufficiency, increasing bilirubin, brain natriuretic peptide, or recurrent ascites).[1,61,62]

Adenocarcinoma in situ and minimally invasive adenocarcinoma

Recommendations for referral and listing:

- Diffuse parenchymal tumor involvement causing lung restriction and significant respiratory compromise.
- Significantly reduced quality of life.
- Failure of conventional medical therapies.

Pediatric candidate selection

Timing of referral (similarities with adult candidates):

- A progressive lung disease on maximal medical therapy.
- A short predicted life expectancy.
- A poor quality of life.[94,95]
- Because the waiting times, particularly for smaller children, are longer, potential candidates should be referred to a transplant center as early as possible.
- Appropriate child and family support in place. It is essential that the child, in particular, commits to the transplant procedure and close long-term follow-up.[94]

LUNG TRANSPLANTATION

Adult Recipients

www.ISHLT.org

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Adult Lung Transplants

Indications (Transplants: January 1995 – June 2013)

Diagnosis	SLT (N = 15,321)	BLT (N = 26,579)	TOTAL (N = 41,900)
COPD/Emphysema	6,594 (43.0%)	7,078 (26.6%)	13,672 (32.6%)
Idiopathic Pulmonary Fibrosis	5,354 (34.9%)	4,825 (18.2%)	10,179 (24.3%)
Cystic Fibrosis	234 (1.5%)	6,628 (24.9%)	6,862 (16.4%)
Alpha-1	771 (5.0%)	1,572 (5.9%)	2,343 (5.6%)
Idiopathic Pulmonary Arterial Hypertension	92 (0.6%)	1,158 (4.4%)	1,250 (3.0%)
Pulmonary Fibrosis, Other	677 (4.4%)	970 (3.6%)	1,647 (3.9%)
Bronchiectasis	62 (0.4%)	1,069 (4.0%)	1,131 (2.7%)
Sarcoidosis	280 (1.8%)	776 (2.9%)	1,056 (2.5%)
Retransplant: Obliterative Bronchiolitis	312 (2.0%)	379 (1.4%)	691 (1.6%)
Connective Tissue Disease	177 (1.2%)	409 (1.5%)	586 (1.4%)
Obliterative Bronchiolitis (Not Retransplant)	105 (0.7%)	351 (1.3%)	456 (1.1%)
LAM	138 (0.9%)	302 (1.1%)	440 (1.1%)
Retransplant: Not Obliterative Bronchiolitis	205 (1.3%)	227 (0.9%)	432 (1.0%)
Congenital Heart Disease	58 (0.4%)	291 (1.1%)	349 (0.8%)
Cancer	7 (0.0%)	29 (0.1%)	36 (0.1%)
Other	255 (1.7%)	515 (1.9%)	770 (1.8%)

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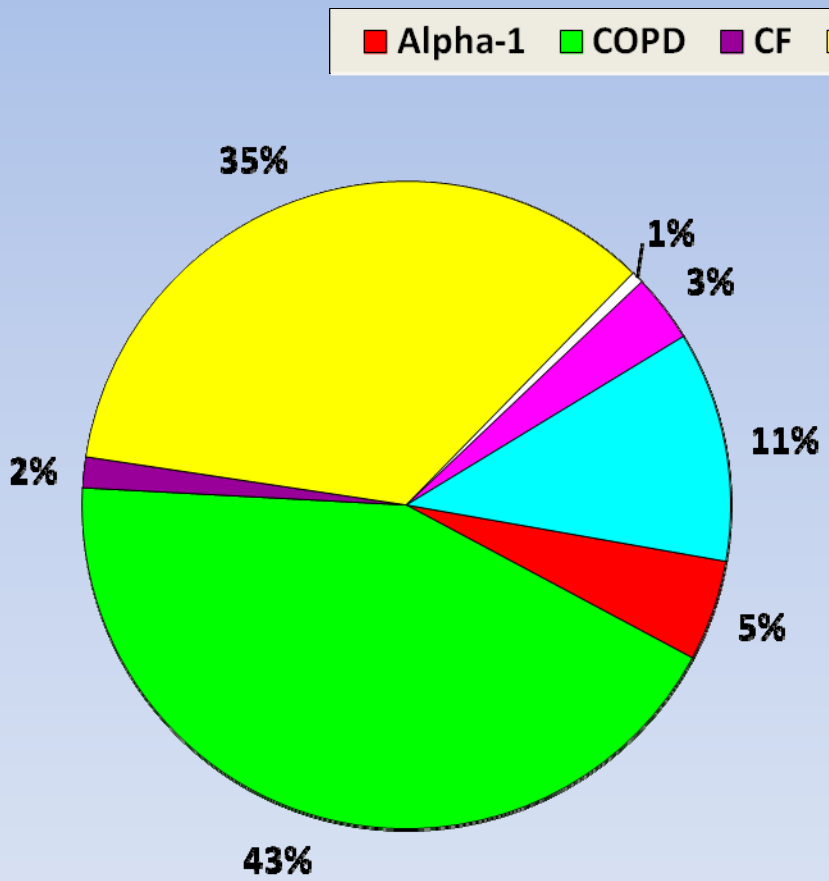
For some retransplants, diagnosis other than retransplant was reported, so the total number and percentage of retransplants may be greater.

Adult Lung Transplants
Indications for Single Lung Transplants
(Transplants: January 1995 – June 2013)



*Other includes:	
Pulmonary Fibrosis, Other:	4.4%
Bronchiectasis:	0.4%
Sarcoidosis:	1.8%
Connective Tissue Disease:	1.2%
OB (non-Retx):	0.7%
LAM:	0.9%
Congenital Heart Disease:	0.4%
Miscellaneous:	1.7%

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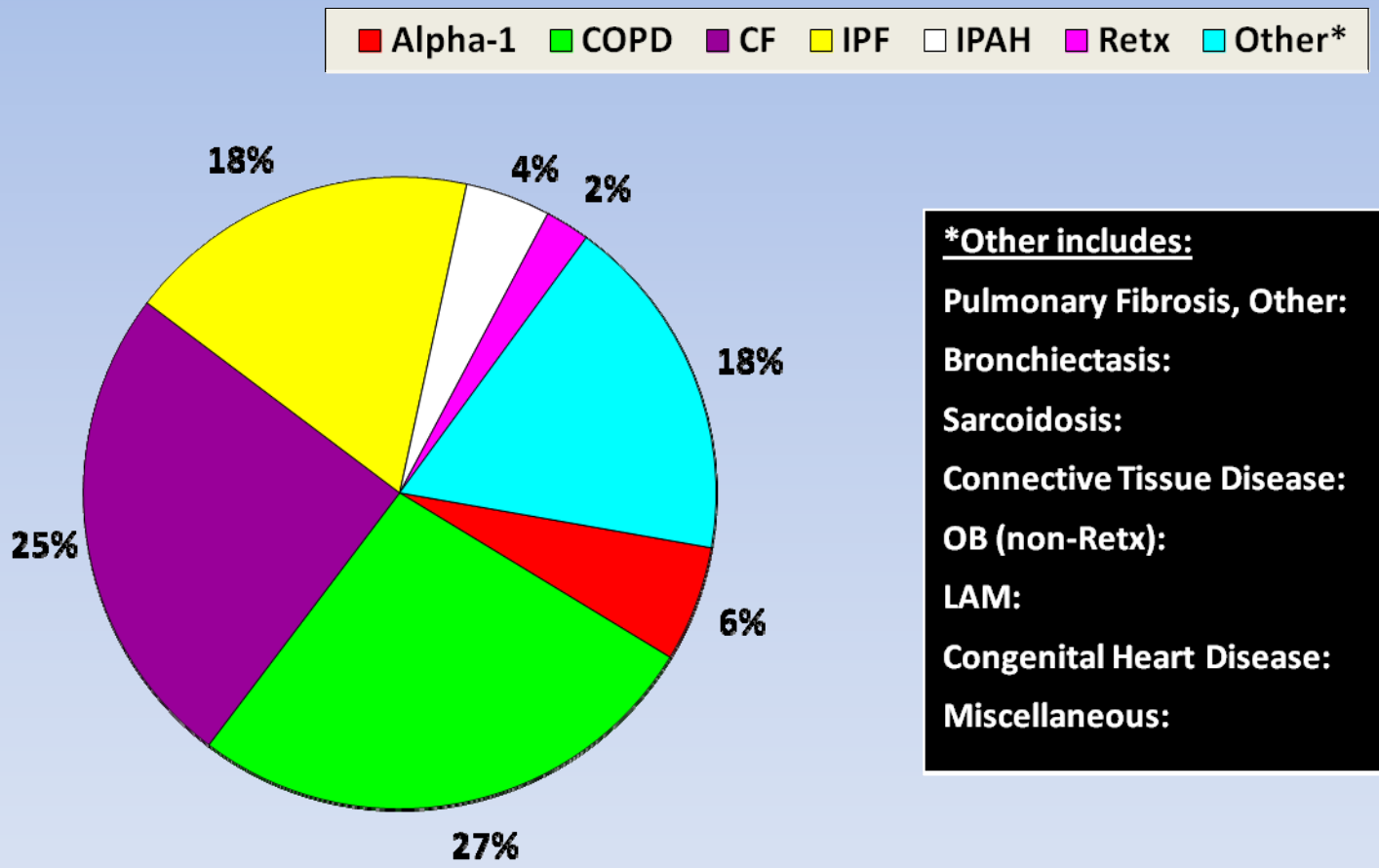
Adult Lung Transplants
Indications for Bilateral/Double Lung Transplants
(Transplants: January 1995 – June 2013)



*Other includes:	
Pulmonary Fibrosis, Other:	3.6%
Bronchiectasis:	4.0%
Sarcoidosis:	2.9%
Connective Tissue Disease:	1.5%
OB (non-Retx):	1.3%
LAM:	1.1%
Congenital Heart Disease:	1.1%
Miscellaneous:	2.0

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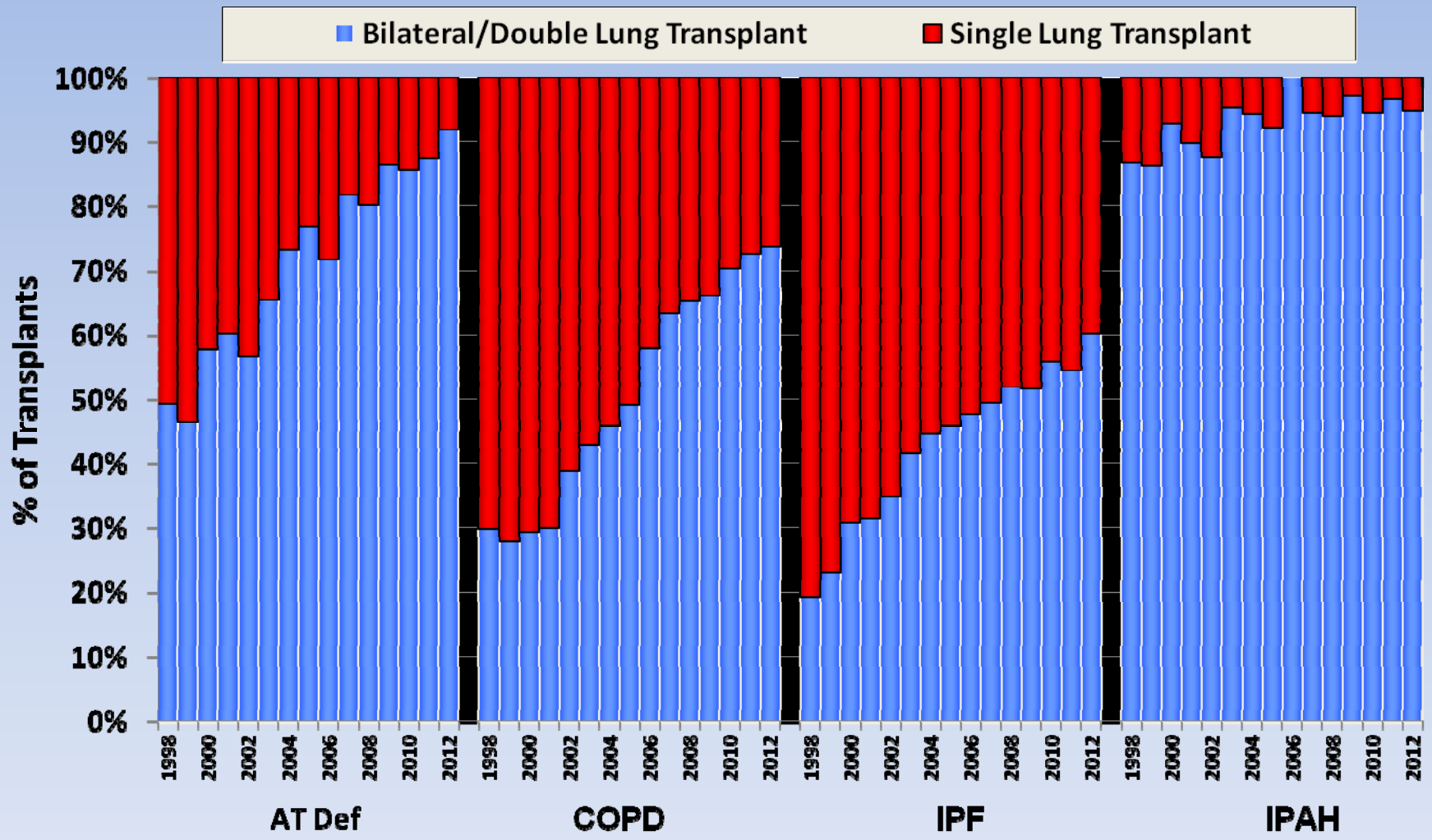
Adult Lung Transplants
Procedure Type within Indication, by Year



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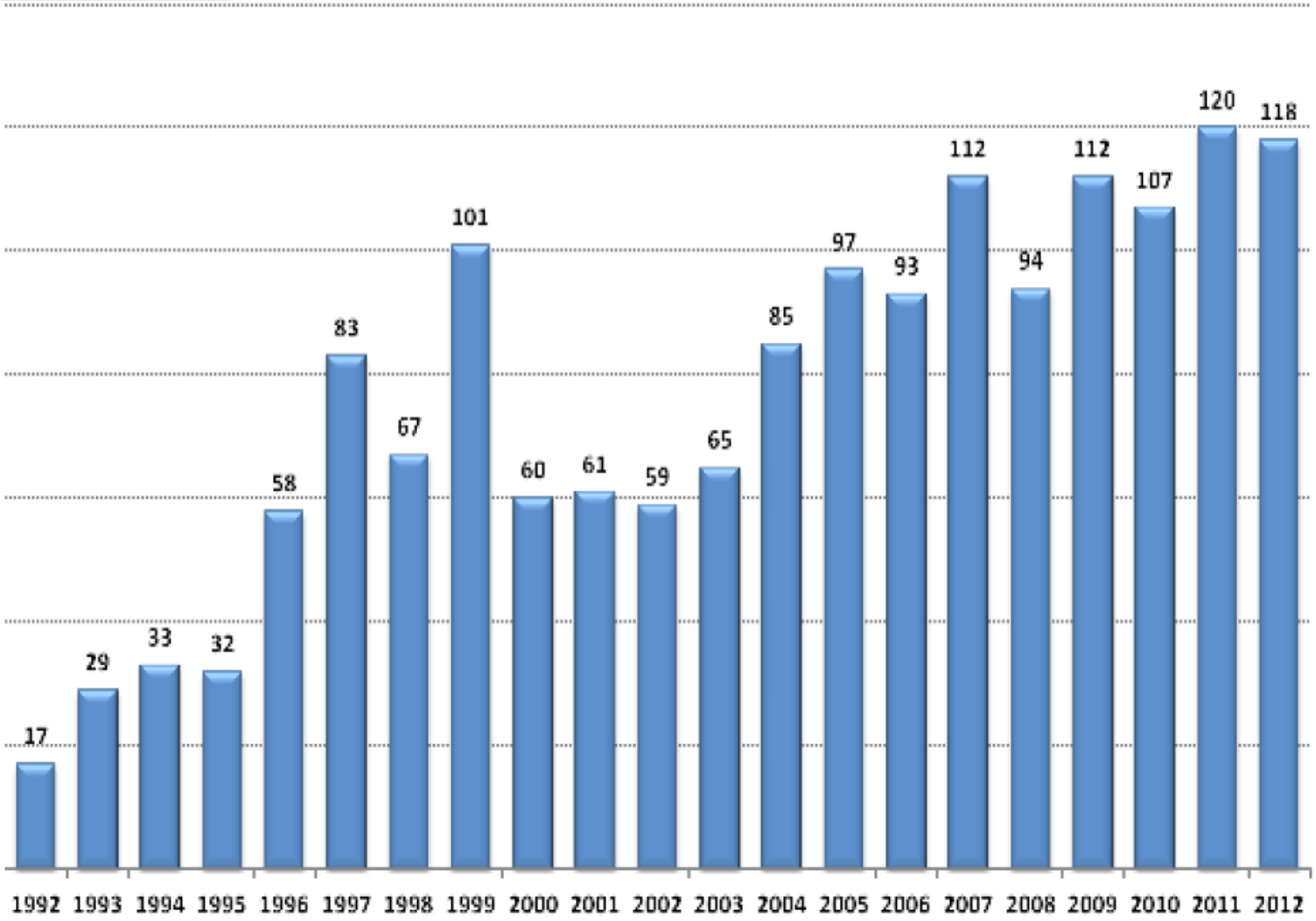
Trapianti di POLMONE – Anni 1992-2012*

Incluse tutte le combinazioni



Grazie dell'attenzione