# UPDATES IN LUNG TRANSPLANTATION

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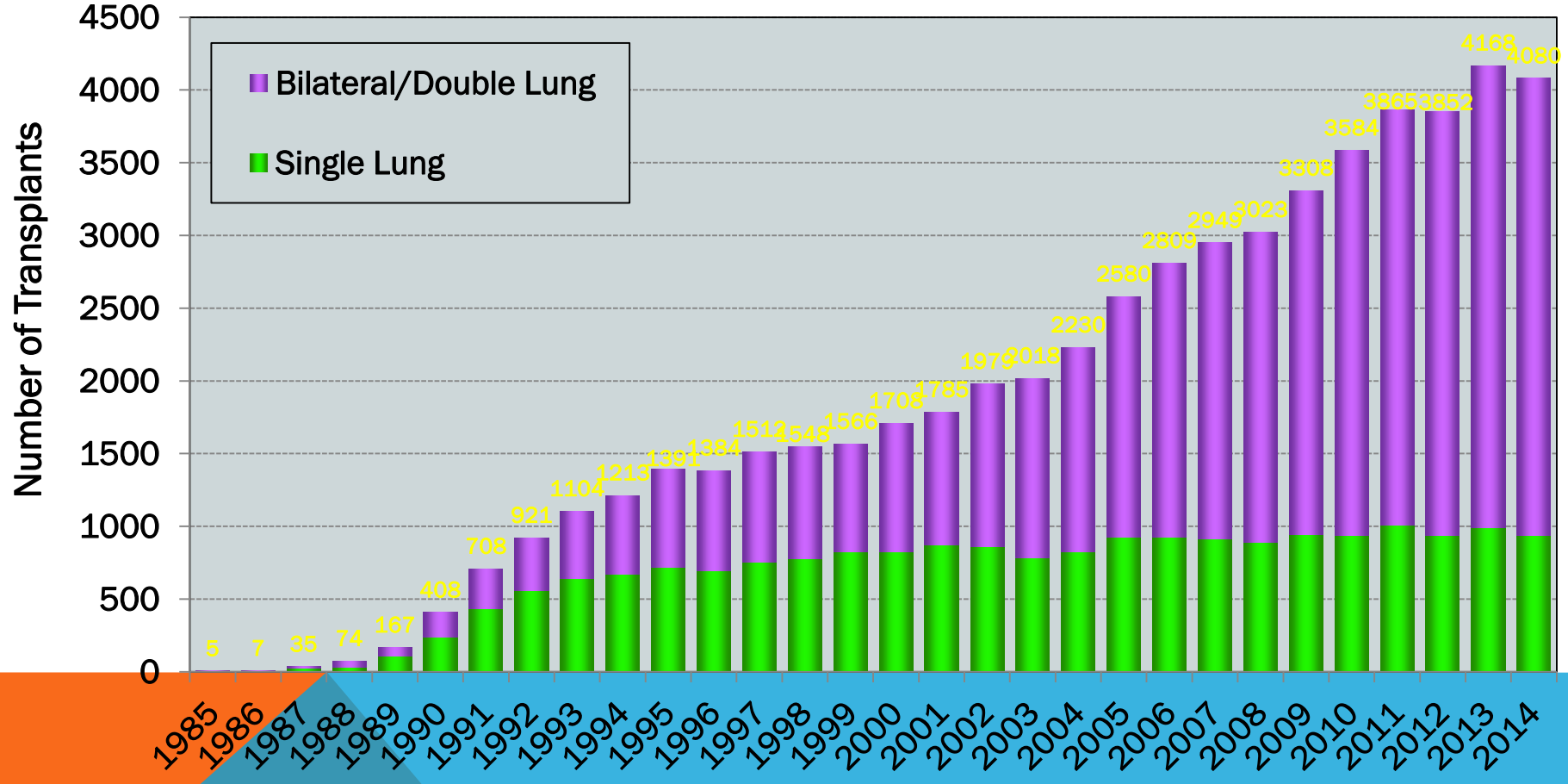
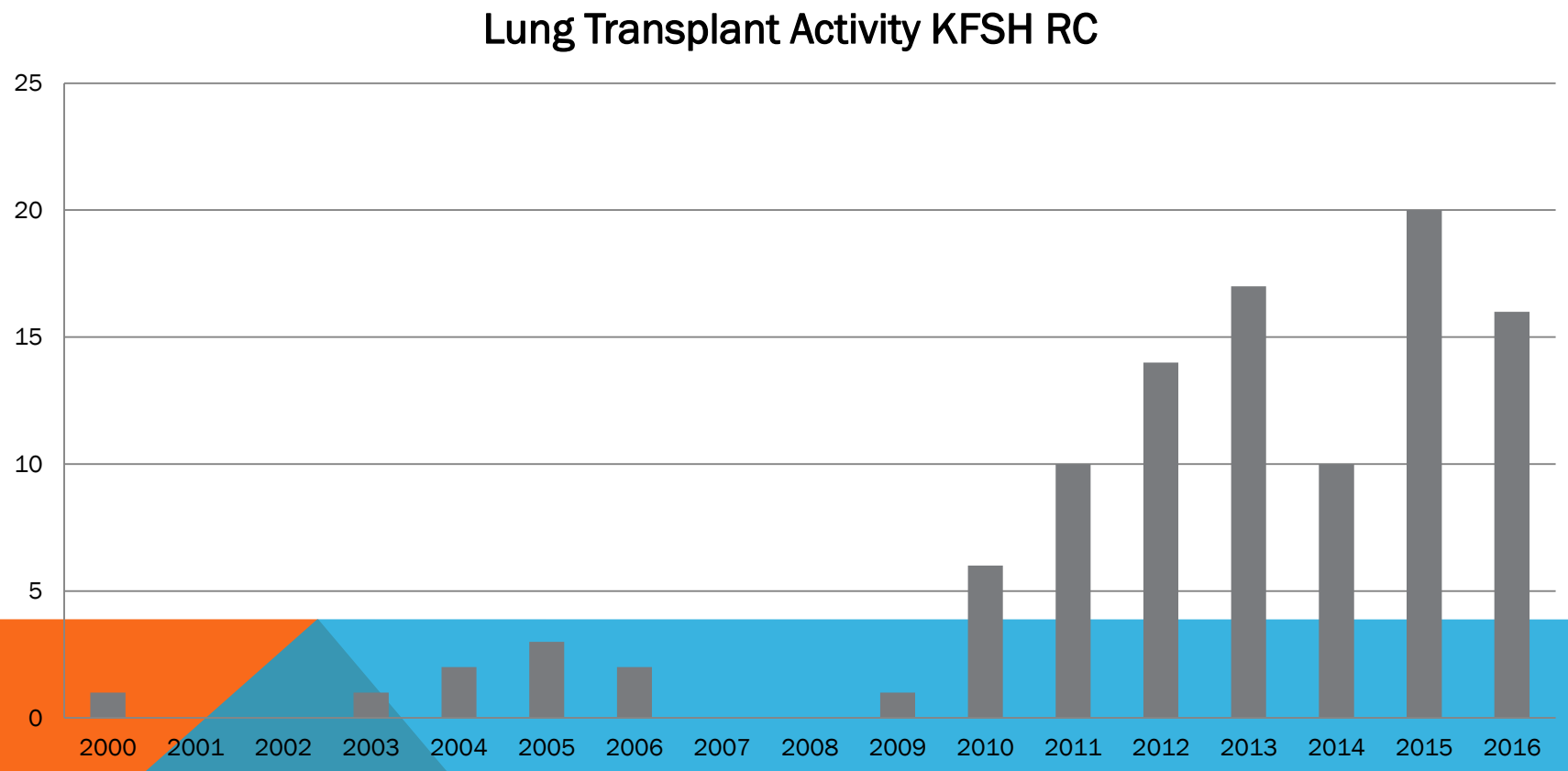
# ADULT AND PEDIATRIC LUNG TRANSPLANTS

## NUMBER OF TRANSPLANTS BY YEAR AND PROCEDURE TYPE



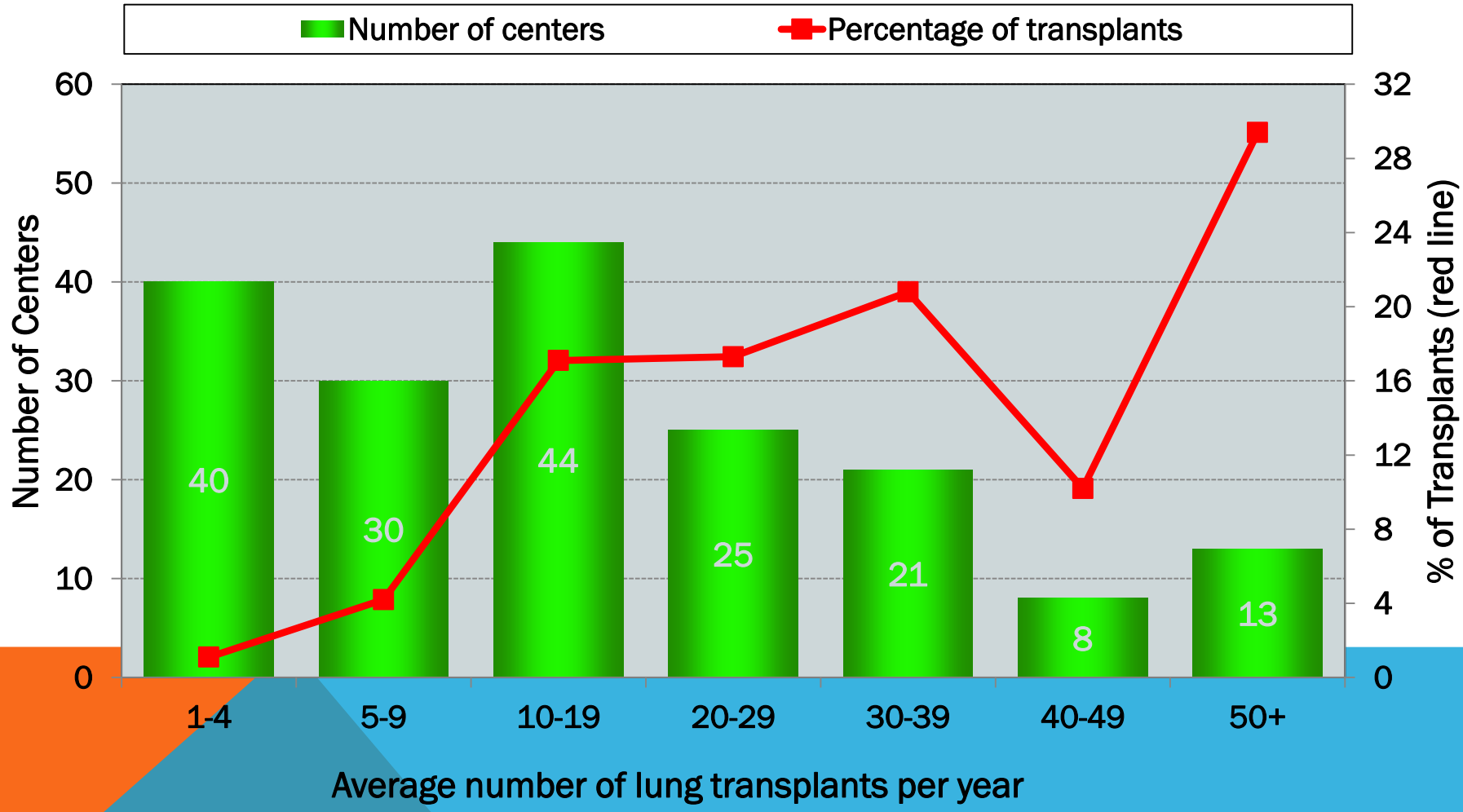

NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.

# LUNG TRANSPLANT PROGRAM IN SAUDI ARABIA



# Adult and Pediatric Lung Transplants

## Average Center Volume (Transplants: January 2004 – June 2015)



# INDICATIONS AND CONTRAINDICATIONS FOR LUNG TRANSPLANTATION

## Indications

- Untreatable end-stage pulmonary, parenchymal, and/or vascular disease
- Absence of other major medical illnesses
- Substantial limitation of daily activities
  - Projected life expectancy < 2 years
  - NYHA class III or IV functional level
  - Rehabilitation potential
  - Satisfactory psychosocial profile and emotional support system
  - Acceptable nutritional status

  Disease-specific mortality exceeding transplant specific mortality over 1 to 2 years

# SELECTION CRITERIA FOR LUNG TRANSPLANTATION

| | |
|---|---|
| **Obstructive airway disease** | **Class III NYHA $FEV_1$(≤ 20% predicted)** |
| **Emphsema (antitrypsin deficiency or from cigarette use** | **Pulm HTN or Cor Pulmonale despite O2, hypercapnia >50 during acute exacerbation, BODE index 7-10** |
| | **Class III or IV NYHA despite Max medical therapy** |
| **Pulmonary vascular disease** | **Mean right atrial pressure ≥ 15 mm Hg** |
| **Idiopathic pulmonary arterial hypertension** | **Cardiac index < 2 L/minute/$m^2$** |
| | **6 min walk < 350** |
| **Suppurative lung disease** | **Class III NYHA** |
| **Cystic fibrosis** | **$FEV_1$ < 30%, Rapidity of $FEV_1$ decline** |
| | **Weight loss, Hypoxia, Hypercapnia** |
| | **Repeated infections, Recurrent hemoptysis/pneumothorax** |
| **Restrictive lung disease** | **Class III NYHA** |
| **Idiopathic pulmonary fibrosis** | **Vital capacity or total lung capacity ≤ 65% predicted (this can be normal in combined emphysema/idiopathic lung disease)** |
| | **Hypoxia on exercise** |
| | **Low (≤ 30%) diffusing capacity for carbon monoxide** |

**CLINICS IN CHEST MEDICINE, June 1997**

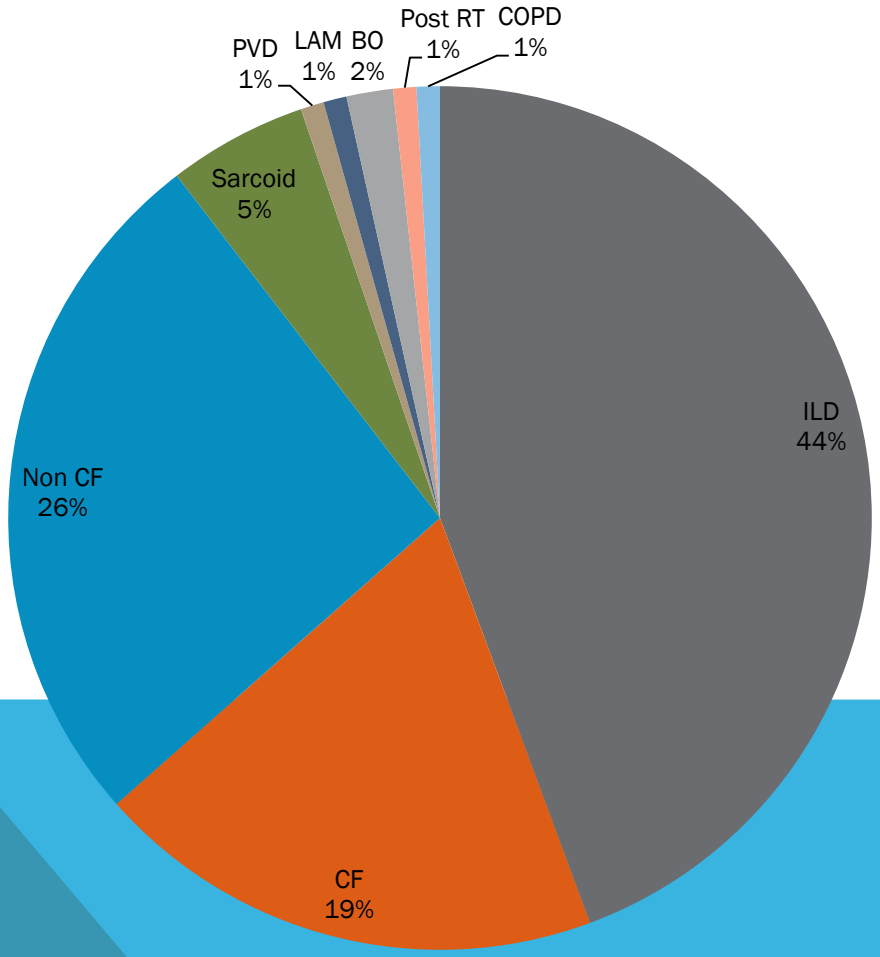
**J Heart lung Tx 2006**

# Adult Lung Transplants

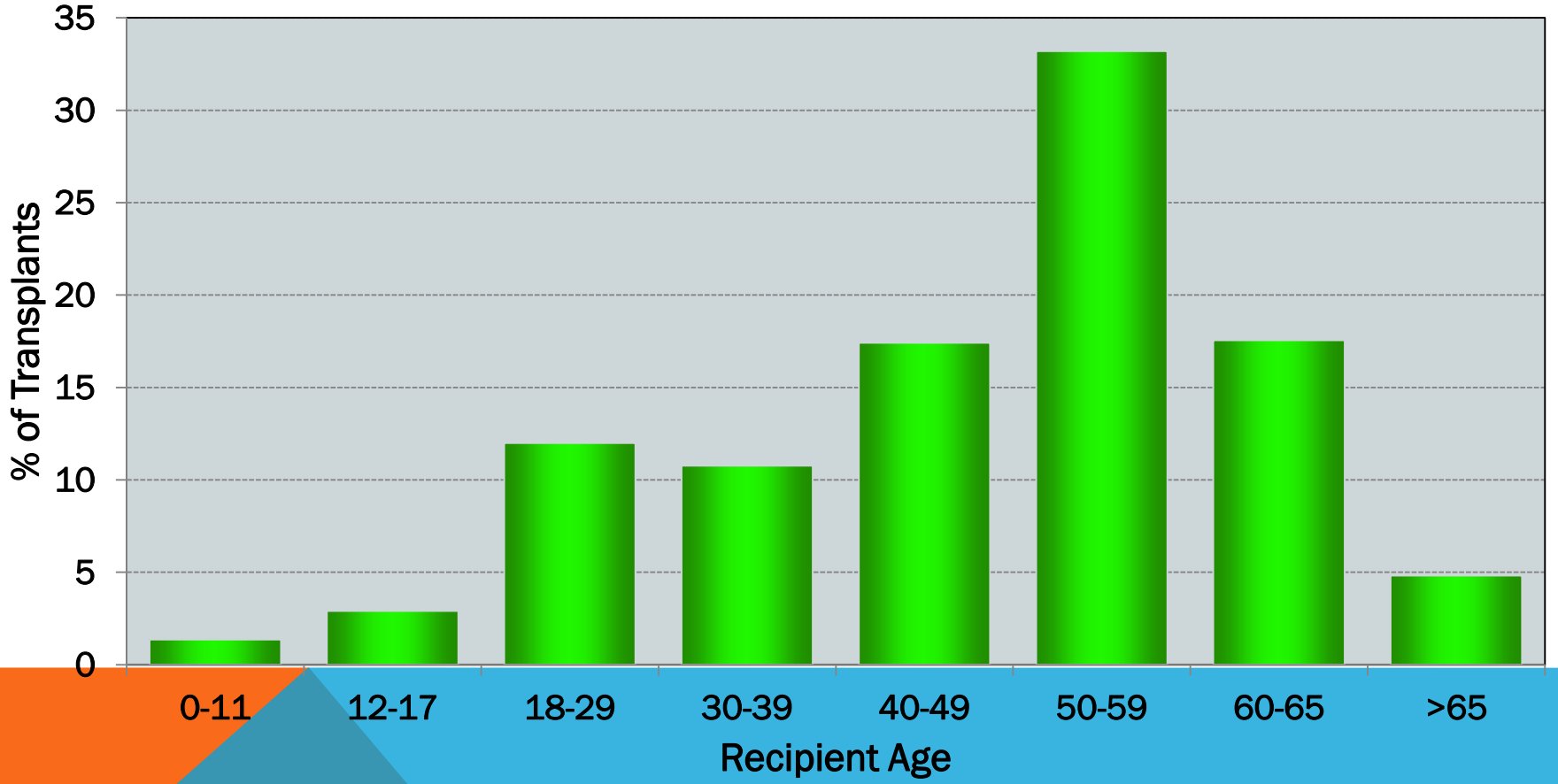
## Indications (Transplants: January 1995 – June 2015)

| Diagnosis | SLT (N=17,213) | BLT (N=32,789) | TOTAL (N=50,002) |
|---|---|---|---|
| COPD | 6,999 (40.7%) | 8,674 (26.5%) | 15,673 (31.3%) |
| IIP | 5,979 (34.7%) | 6,264 (19.1%) | 12,243 (24.5%) |
| CF | 209 (1.2%) | 7,686 (23.4%) | 7,895 (15.8%) |
| ILD-not IIP | 977 (5.7%) | 1,608 (4.9%) | 2,585 (5.2%) |
| A1ATD | 784 (4.6%) | 1,784 (5.4%) | 2,568 (5.1%) |
| Retransplant | 874 (5.1%) | 1,174 (3.6%) | 2,048 (4.1%) |
| IPAH | 87 (0.5%) | 1,348 (4.1%) | 1,435 (2.9%) |
| Non CF-bronchiectasis | 64 (0.4%) | 1,293 (3.9%) | 1,357 (2.7%) |
| Sarcoidosis | 307 (1.8%) | 941 (2.9%) | 1,248 (2.5%) |
| PH-not IPAH | 129 (0.7%) | 648 (2.0%) | 777 (1.6%) |
| LAM/tuberous sclerosis | 141 (0.8%) | 359 (1.1%) | 500 (1.0%) |
| OB | 75 (0.4%) | 354 (1.1%) | 429 (0.9%) |
| CTD | 122 (0.7%) | 240 (0.7%) | 362 (0.7%) |
| Cancer | 7 (0.0%) | 27 (0.1%) | 34 (0.1%) |
| Other | 459 (2.7%) | 389 (1.2%) | 848 (1.7%) |

# LUNG TRANSPLANT INDICATIONS KFSH RC 2010-2016



# AGE DISTRIBUTION OF LUNG TRANSPLANT RECIPIENTS (1/1985-6/2011)

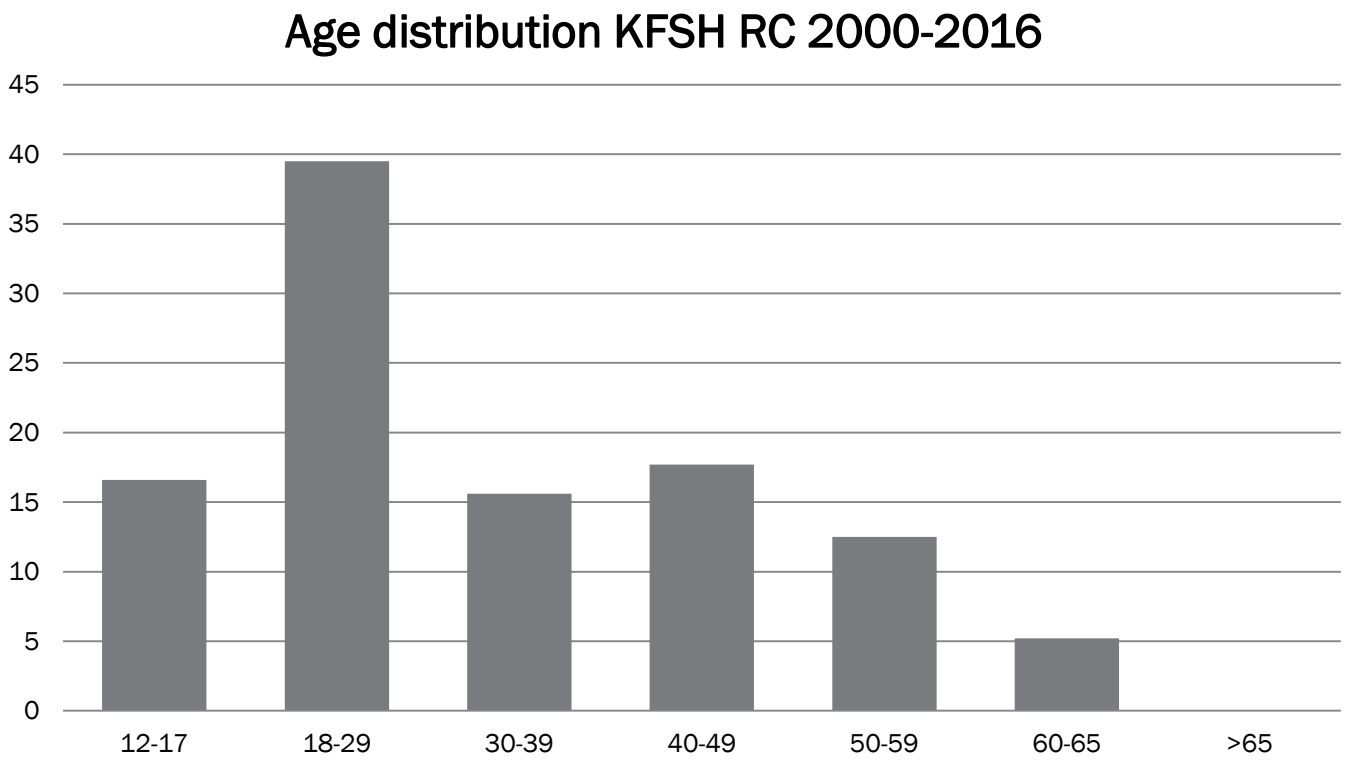



ISHLT

2012

J Heart Lung Transplant. 2012 Oct; 31(10): 1045-1095

# AGE DISTRIBUTION LUNG TRANSPLANT RECIPIENTS KFSH RC



# LUNG TRANSPLANTATION
# EARLY COMPLICATIONS

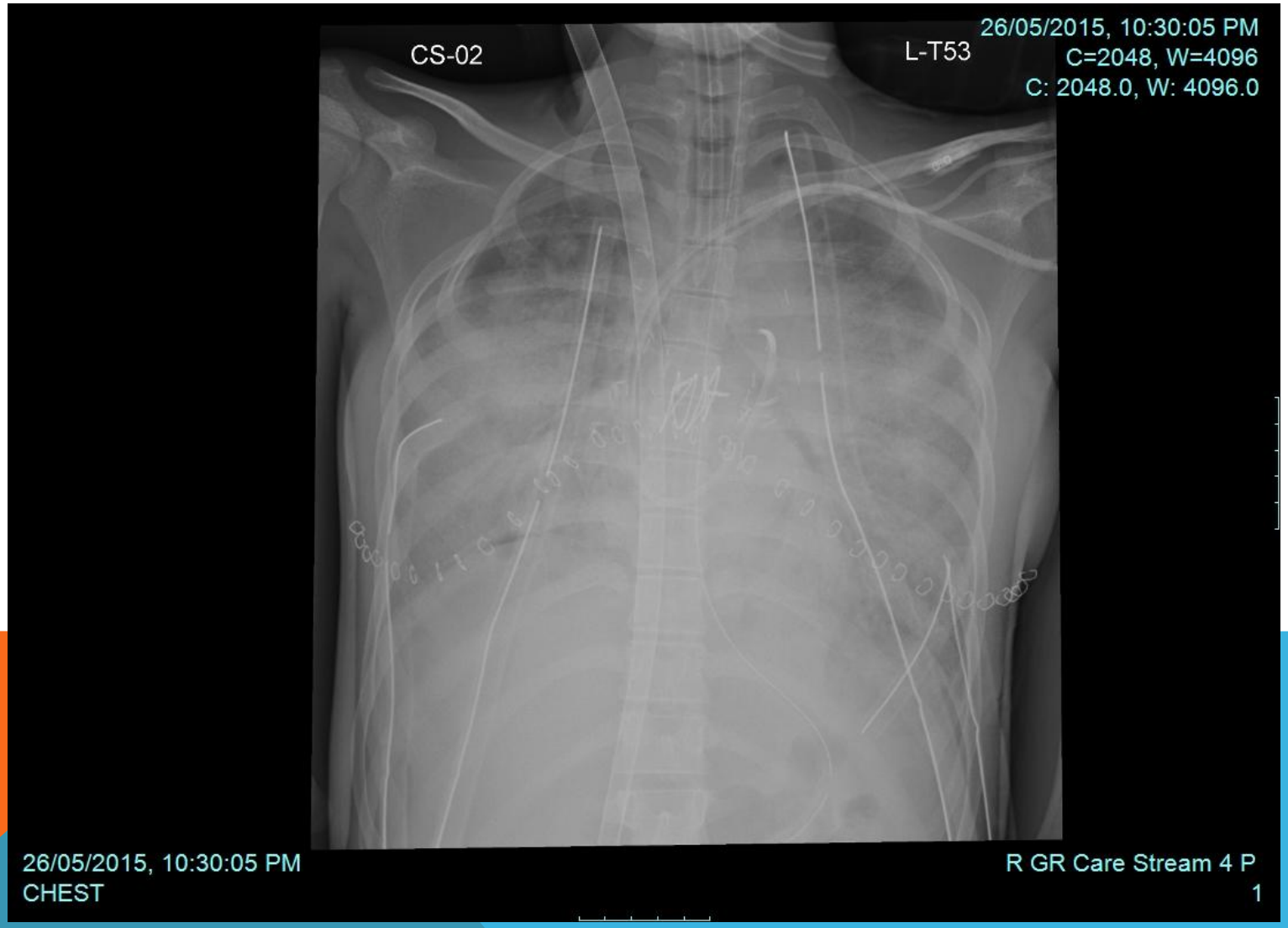
Early Graft Dysfunction

Infections

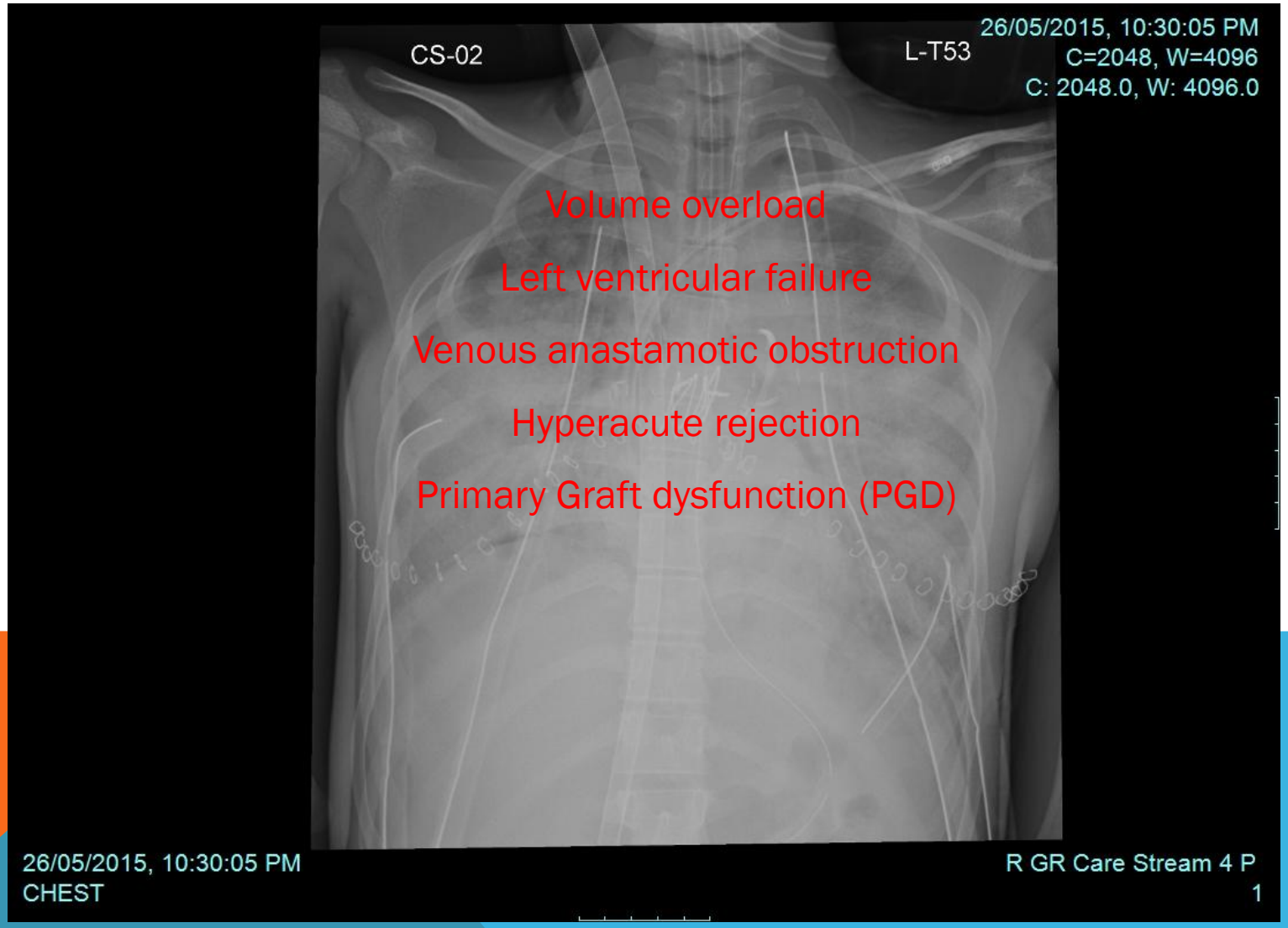
Anastamotic complications

Acute rejection

# EARLY GRAFT DYSFUNCTION



# EARLY GRAFT DYSFUNCTION



# LUNG TRANSPLANTATION
# PRIMARY GRAFT DYSFUNCTION

Primary graft dysfunction (PGD) is a form of acute lung injury (ALI) resulting from ischemia-reperfusion and other insults that accompany the lung transplantation process.

Increases risk of CLAD

SEMINARS IN RESPIRATORY AND CRITICAL CARE MEDICINE/VOLUME 31, NUMBER 2 2010

# LUNG TRANSPLANTATION
# PRIMARY GRAFT DYSFUNCTION

Primary Graft Dysfunction Grading Schema

| Grade | PaO2:FiO2 | Radiographic Infiltrates Consistent with edema |
|---|---|---|
| 0 | >300 | Absent |
| 1 | >300 | Present |
| 2 | 200–300 | Present |
| 3 | <200 | Present |

SEMINARS IN RESPIRATORY AND CRITICAL CARE MEDICINE/VOLUME 31, NUMBER 2 2010

# LUNG TRANSPLANTATION
# PRIMARY GRAFT DYSFUNCTION

Primary Graft dysfuntion (PGD)

Diffuse lung infilterates
Usually peaks by 3rd post op day
Severe in up to 15% cases
Mortality 60% in severe cases
Treatment is supportive
ECMO is one of the supportive treatment

NEJM 1998

# PRIMARY GRAFT DYSFUNCTION (PGD) AFTER LUNG TRANSPLANT


# ECMO

Extracorporeal membrane oxygenation

A form of extracorporeal life support

External artificial circulation carries venous blood from the patient to an oxygenator device. (gas exchange unit working as lungs)

The oxygen rich and CO2 removed blood is then returned to the patient's circulation.

# ECMO IN LUNG TRANSPLANTATION

ECMO as a bridge to lung transplant

ECMO as a bridge to recovery post lung transplant.

# ECMO IN LUNG TRANSPLANT PATIENTS

Respiratory failure with intact cardiac function

Respiratory failure + Compromised cardiac function (RHF)

The cardiac status will determine the type of ECMO to be initiated. Veno-venous (V-V) vs Veno-Arterial(V-A).

# V-V ECMO

Used with respiratory failure with intact cardiac function.

Access line(s). Collects blood from a central vein or two central veins

Return Line returns the oxygenated blood near the right atrium.

V-V ECMO improves oxygenation and removes carbon dioxide allowing level of ventilatory support to be reduced.

# V-V ECMO

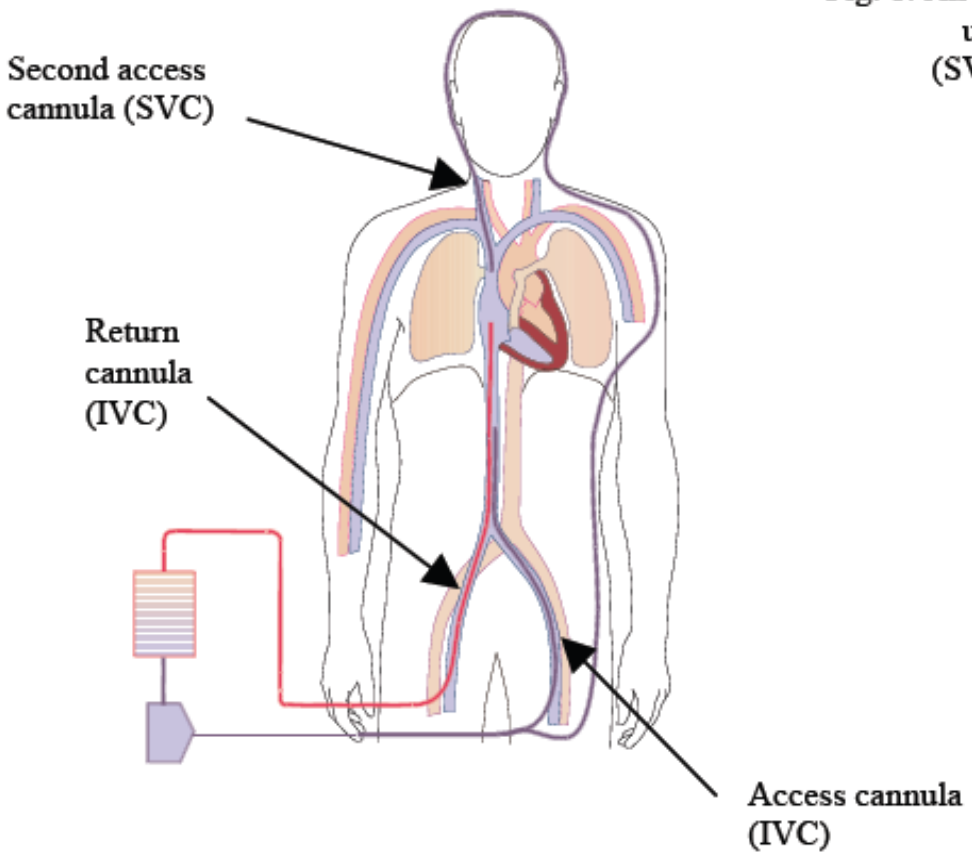
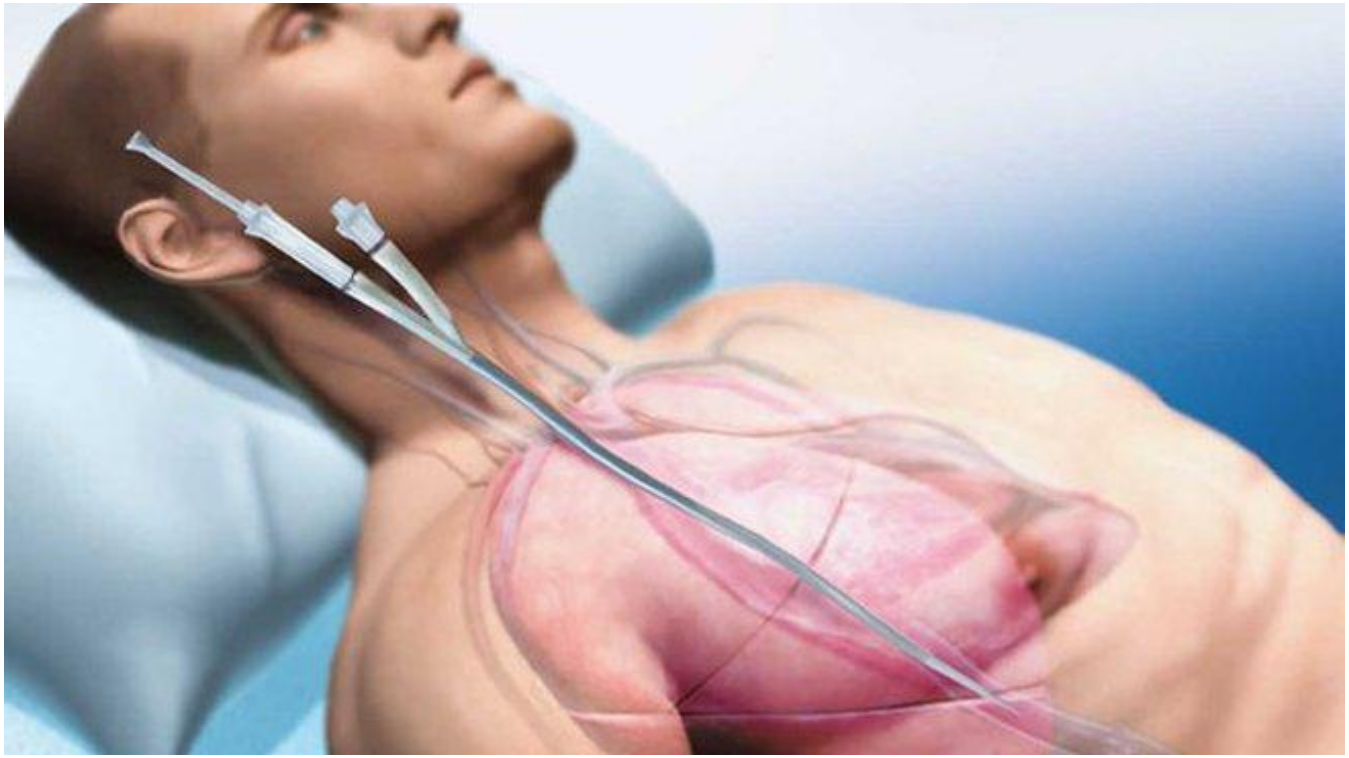


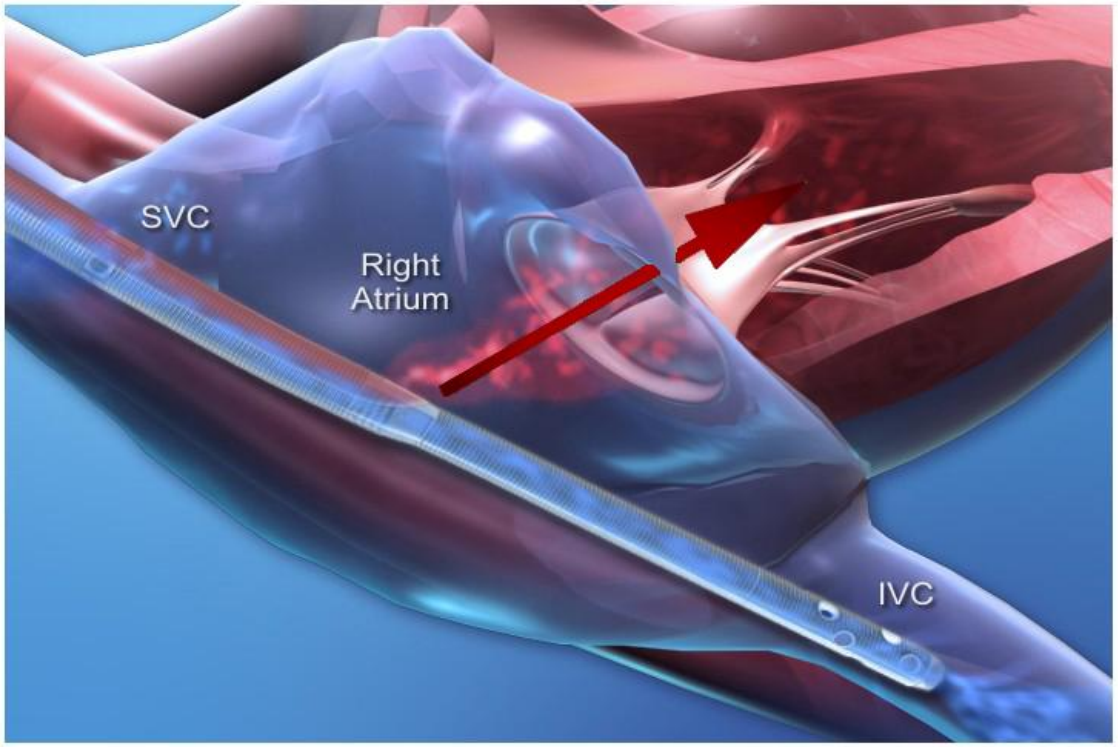

Fig. 1. An example of Veno – Venous ECMO using two access cannulae (SVC and IVC to right atrium)

# V-V ECMO WITH DOUBLE LUMEN (AVALON) CATHETER

# V-V ECMO WITH DOUBLE LUMEN (AVALON) CATHETER



# V-V ECMO WITH DOUBLE LUMEN (AVALON) CATHETER



# V-A ECMO

Used in compromised cardiac function +/- respiratory failure.

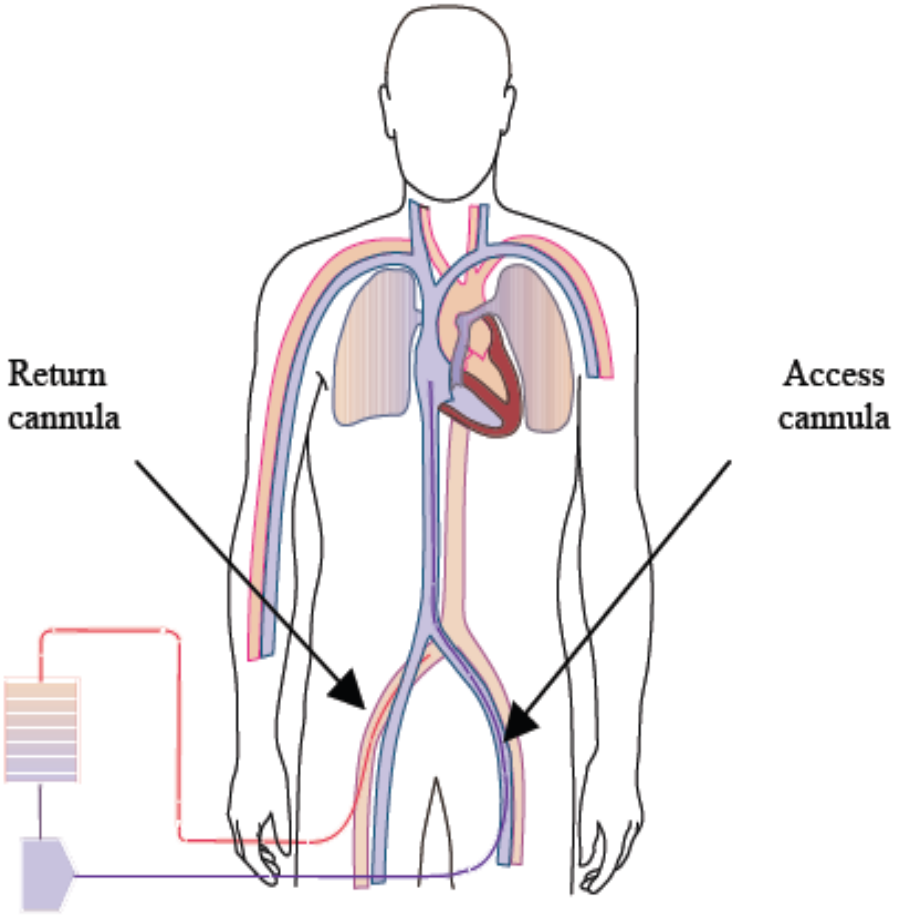
Access line collects blood from a central vein.

Return line returns oxygenated blood to a major artery.

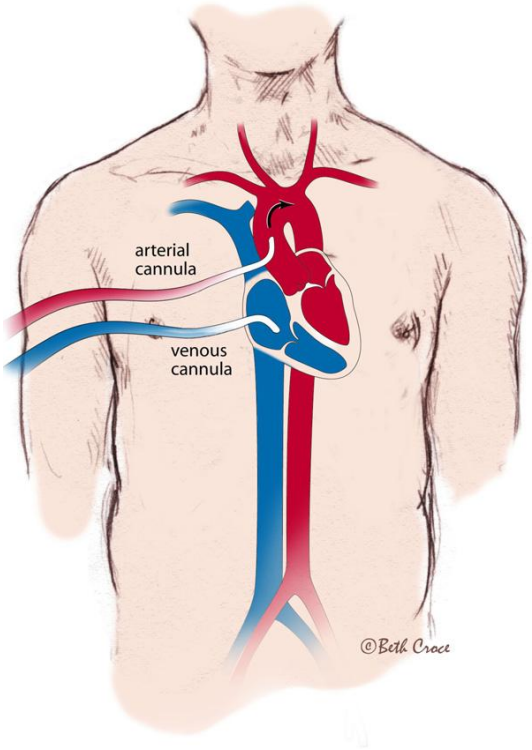
Central VA ECMO should be used if the lung function is poor (large shunt).

# V-A ECMO

Fig 2. Veno – Arterial ECMO



# CENTRAL VA ECMO



# ECMO PRE LUNG TX

1. Should lung transplantation be performed for patients on mechanical respiratory support? The US experience

(J Thorac Cardiovasc Surg 2010;139:765-73)

2. Extracorporeal membrane oxygenation as a bridge to lung transplantation and recovery.

(J Thorac Cardiovasc Surg 2012;1-6)

3. Efficacy of extracorporeal membrane oxygenation as a bridge to lung transplantation

(J Thorac Cardiovasc Surg 2013;145:1065-71)

4. Extracorporeal Membrane Oxygenation in Awake Patients as Bridge to Lung Transplantation

Am J Respir Crit Care Med Vol 185, Iss. 7, pp 763–768, Apr 1, 2012

# EXTRACORPOREAL MEMBRANE OXYGENATION AS A BRIDGE TO LUNG TRANSPLANTATION AND RECOVERY

Survival

1 mo (N = 10, at risk) 100%

6 mo (N = 7, at risk) 100%

1 y (N = 6, at risk) 100%

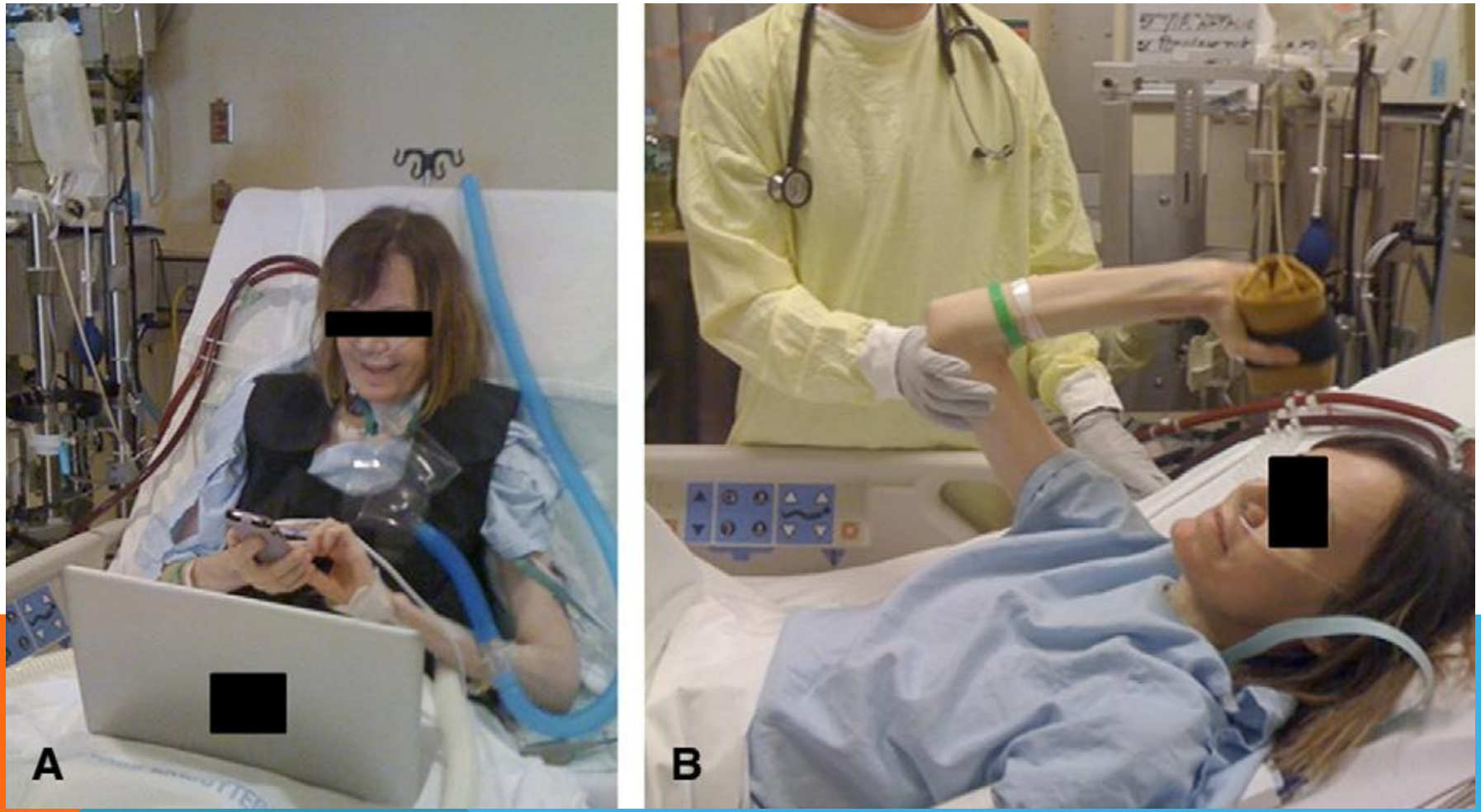
2 y (N = 3, at risk) 100%

Overall survival in subgroup that underwent

Transplantation =100%

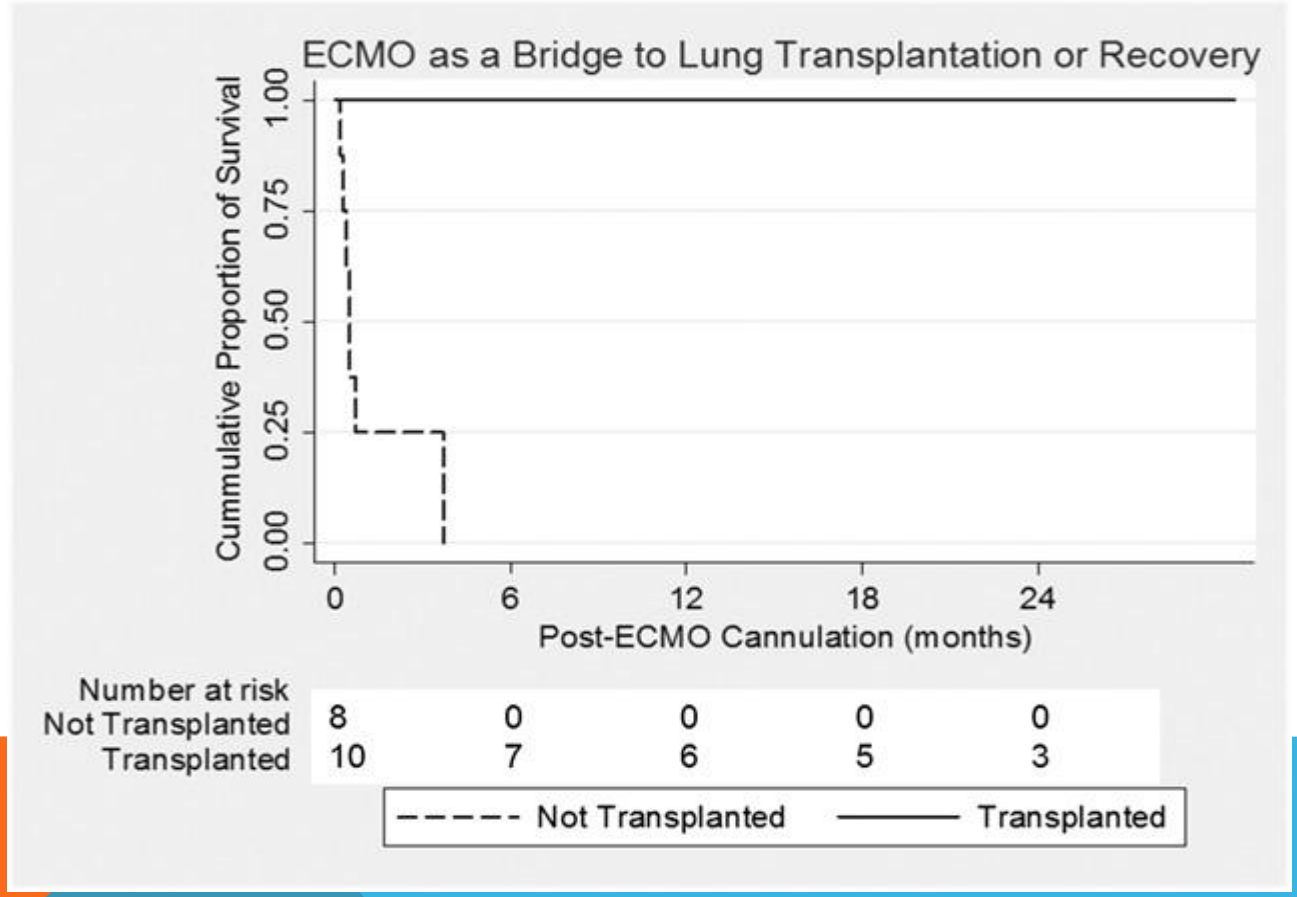
The Journal of Thoracic and Cardiovascular Surgery - 2012

# ECMO AS A BRIDGE TO LUNG TRANSPLANTATION AND RECOVERY




The Journal of Thoracic and Cardiovascular Surgery -

# EXTRACORPOREAL MEMBRANE OXYGENATION AS A BRIDGE TO LUNG TRANSPLANTATION AND RECOVERY




The Journal of Thoracic and Cardiovascular Surgery -

# ECMO AS A BRIDGE TO LUNG TRANSPLANT

| Study | Number of Pts on ECMO | Number succesfully bridged | Survival to hospital discharge | One year survival | Median time on ECMO |
|---|---|---|---|---|---|
| Columbia 2012 | 18 | 13 (72%)<br>* 3 recovered to baseline | 100% | 100% (n=6) | 6(3.5-31) |
| Pittsburg 2013 | 31 | 24(77%) | 88%<br>* at 3 months | 74% | 7 (1-46) |
| Hannover | 26 | 20 (76%) | 80% | 80% * 6months | 9 (1-71) |

# ECMO POST LUNG TRANSPLANT

PGD incidence 15-60%

1/3rd of all deaths in first 90 days post Tx due to PGD.

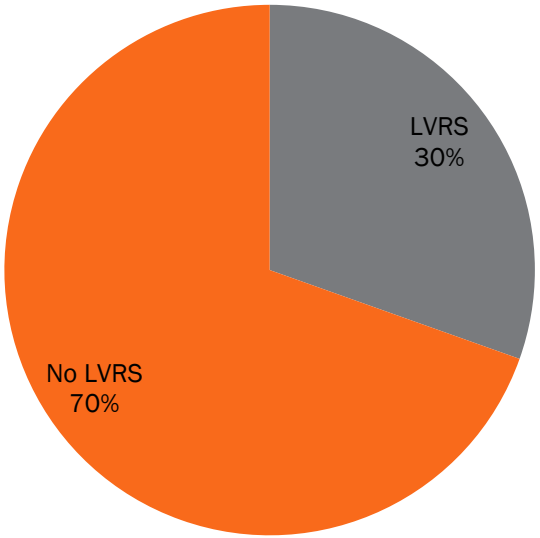
Treatment is supportive

ECMO is one of the supportive treatments for PGD

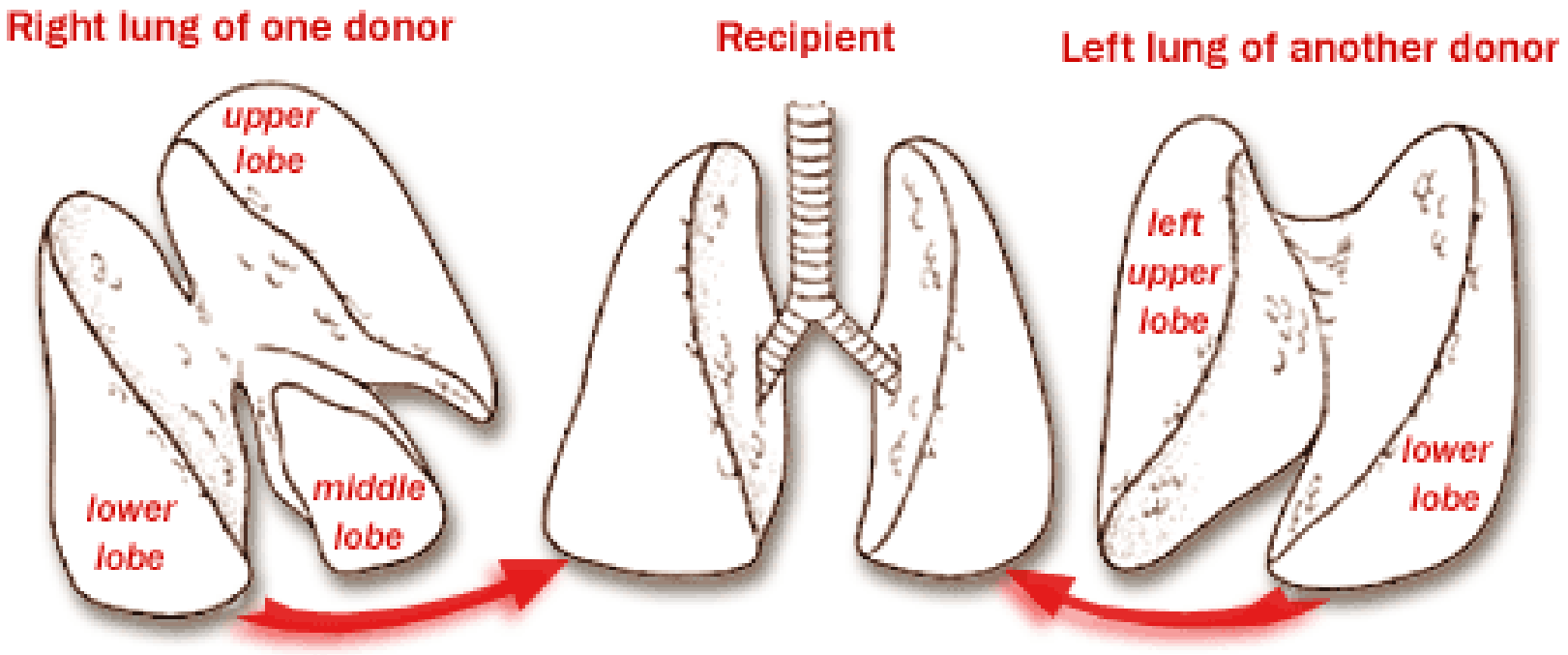
ECMO program initiated in KFSH RC surgical ICU in 2015 both as a bridge to recovery and as a bridge to lung transplant

# CHALLENGE IN DONOR-RECIPIENT SIZE MISMATCH KFSH RC

Donor Recipient size mismatch 2010-2015



# EXTREME DONOR-RECIPIENT SIZE MISMACH



# CHALLENGE IN DONOR-RECIPIENT SIZE MISMATCH KFSH RC

Bilateral lobar transplant was performed for the first time in KFSH RC in 2015.

Two recipients received successful bilateral lower lobe transplant from two donors

# LUNG TRANSPLANTATION
# BACTERIAL INFECTIONS

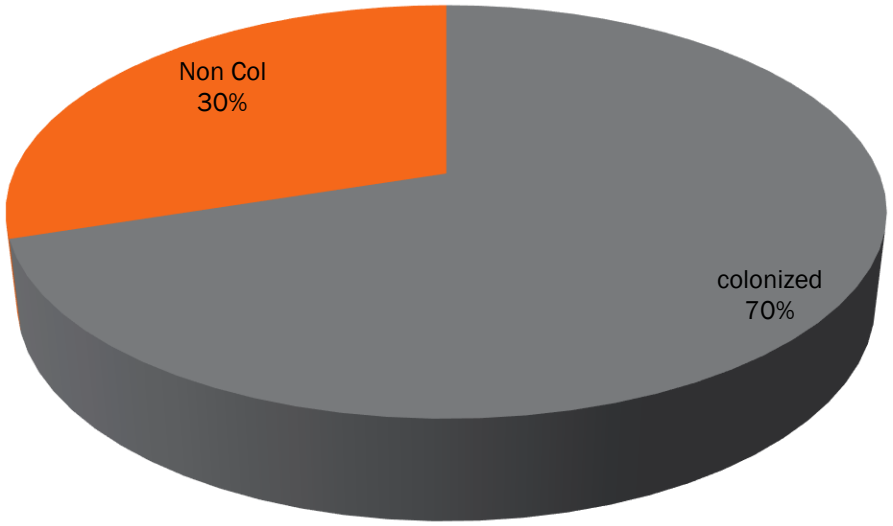
Early post transplant period

Transmission from donor

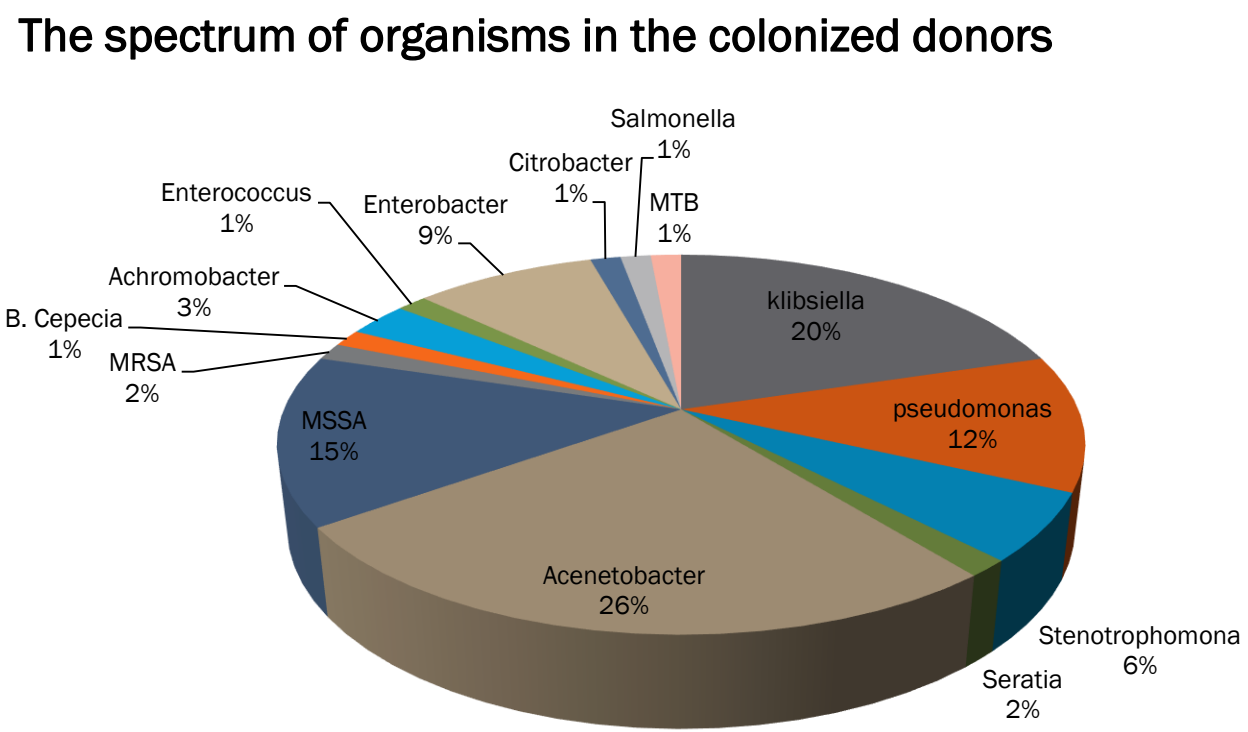
Recipient colonization

# DONOR ISSUES KFSH 2010-2015

Colonized vs noncolonized donors 2010-2015



# DONOR ISSUES KFSH 2010-2015




Note some donors with multiple organisms

# LUNG TRANSPLANTATION
# ACUTE REJECTION

Majority episodes occur in first 90 days but can happen at any time.

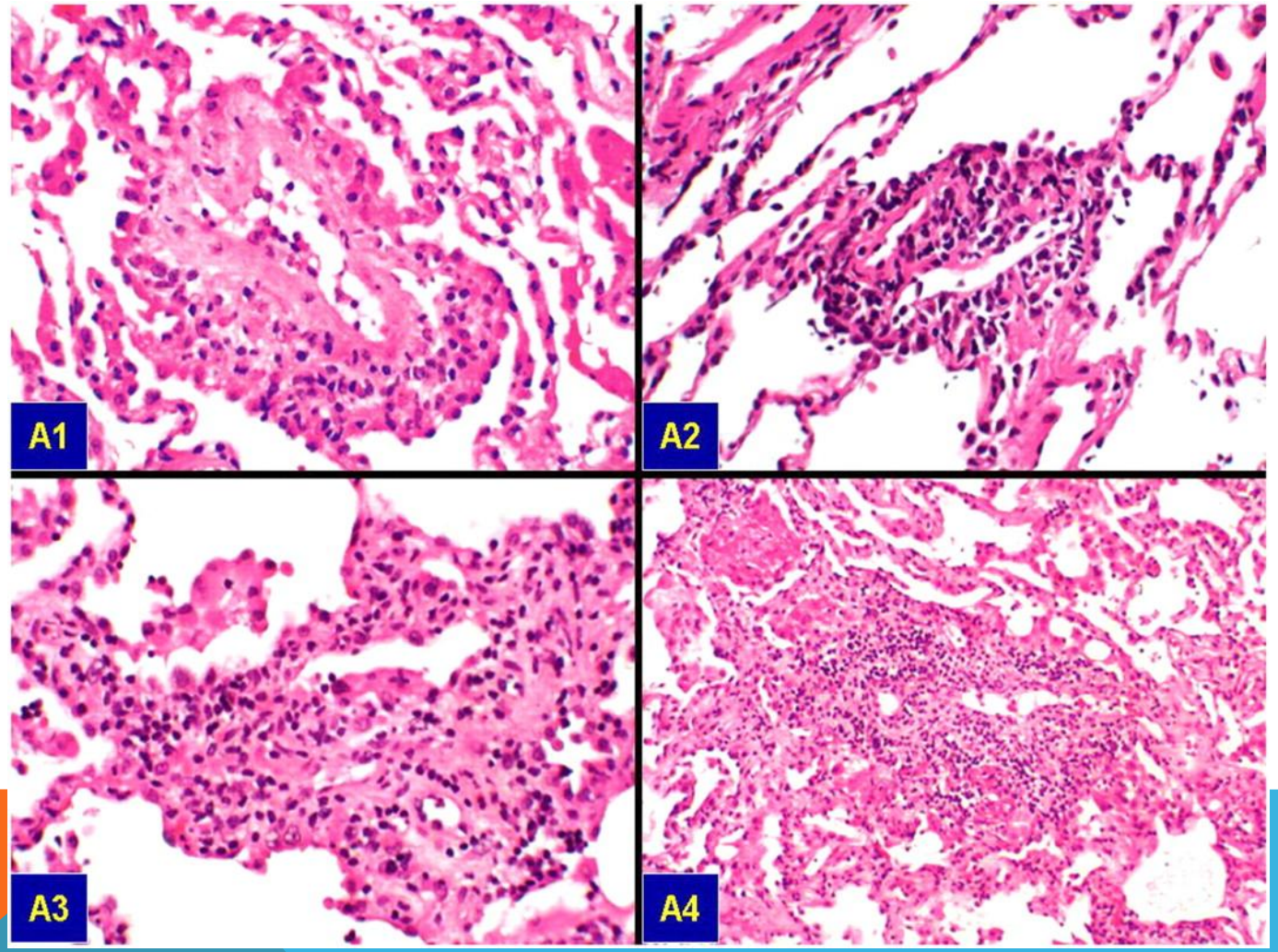
Can happen as early as 3 days post op

Suspect rejection if >10% decline in FEV1, hypoxemia, fever, cough, dyspnea

Radiologic findings are rare after 1st month

Diagnosis requires biopsy.

**Histopathology of acute lung allograft rejection (hematoxylin and eosin stain; original magnification × 40).**



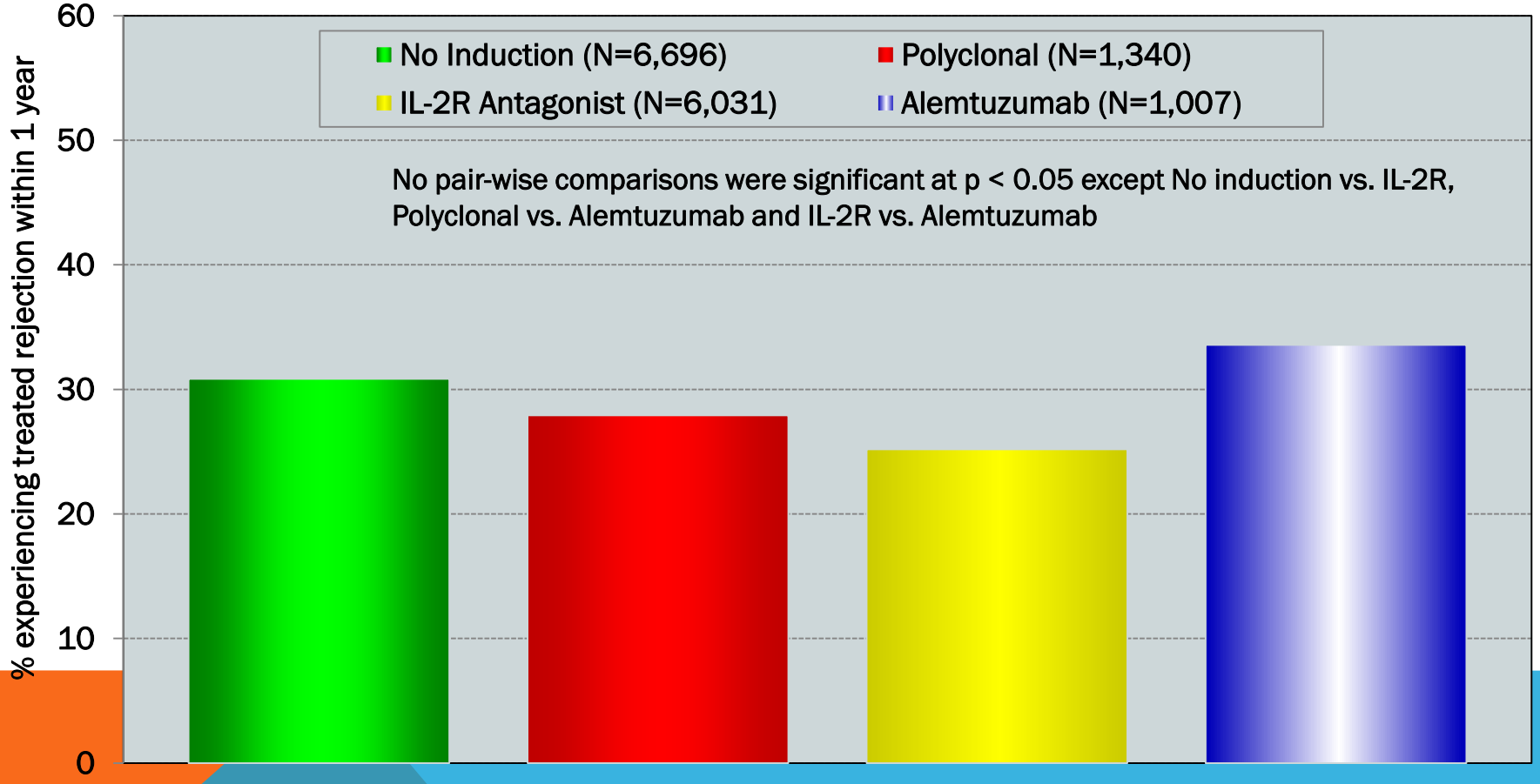

**Ahmad S et al. Chest 2011;139:402-411**

©2011 by American College of Chest Physicians

CHEST

# Adult Lung Transplants

## Percentage Experiencing *Treated* Rejection between Discharge and 1-Year Follow-Up by Type of Induction (Follow-ups: July 2004 – June 2015)




Analysis is limited to patients who were alive at the time of the follow-up.

Treated rejection = Recipient was reported to (1) have at least one acute rejection episode that was treated with an anti-rejection agent; or (2) have been hospitalized for rejection.

# CLINICAL EX VIVO LUNG PERFUSION

Organ availability continues to be a major hurdle for lung transplantation.

Only 15% to 25% of lungs from donors of at least one other organ are transplanted.

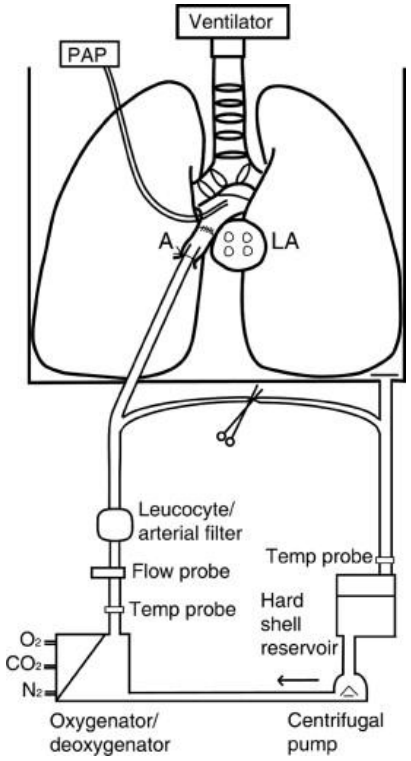
“Marginal lungs” have been successfully transplanted.

Ex vivo lung perfusion (EVLP) has been suggested as a novel method to differentiate between “good” and “bad” grafts among these marginal lungs.

J heart lung Transplant 2012

# CLINICAL EX VIVO LUNG PERFUSION VIVOLINE

# CLINICAL EX VIVO LUNG PERFUSION



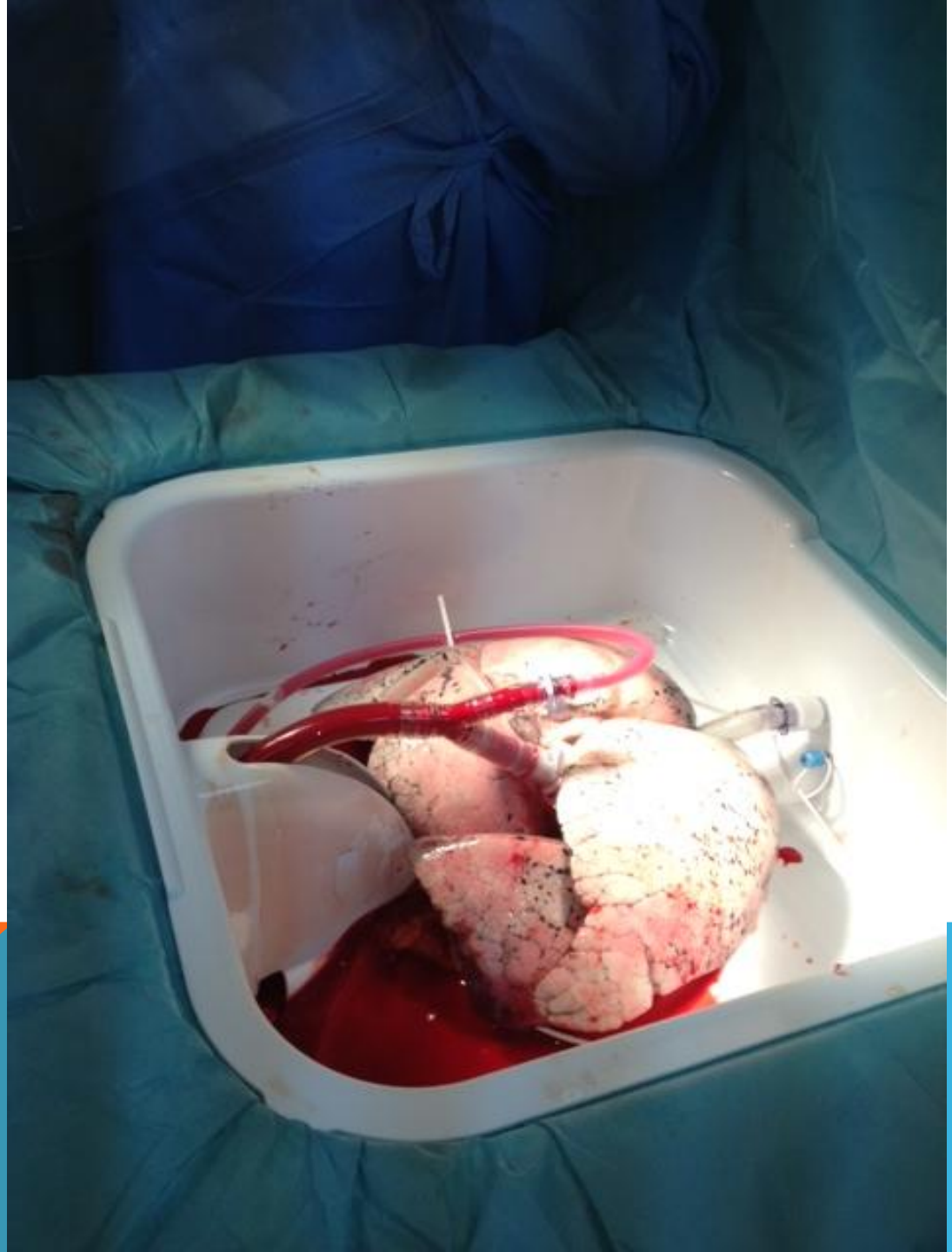
# CLINICAL EX VIVO LUNG PERFUSION

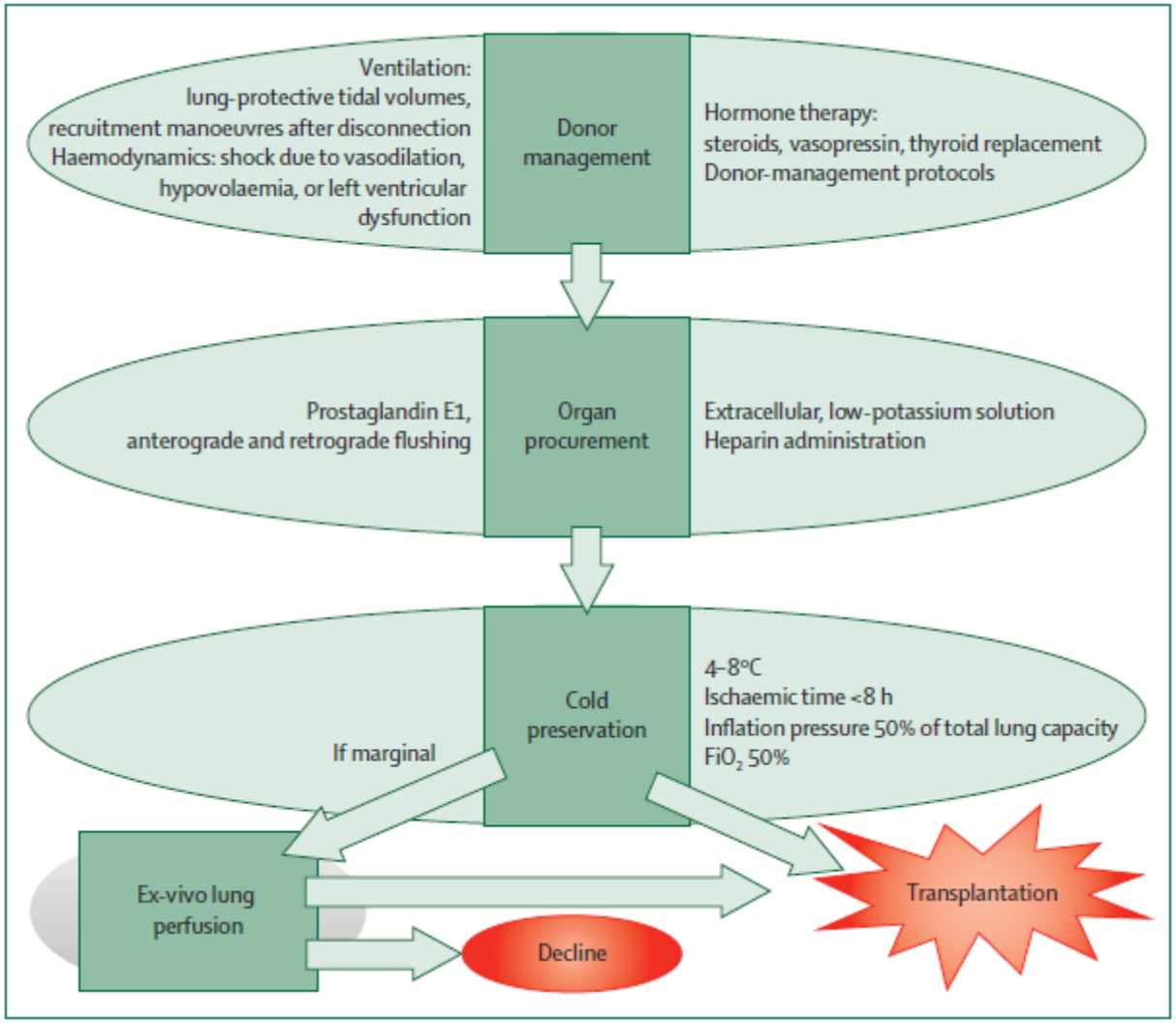
The first successful conditioning of marginal lungs performed in December 2013.

Pre conditioning P/F ratio <200 mm Hg.

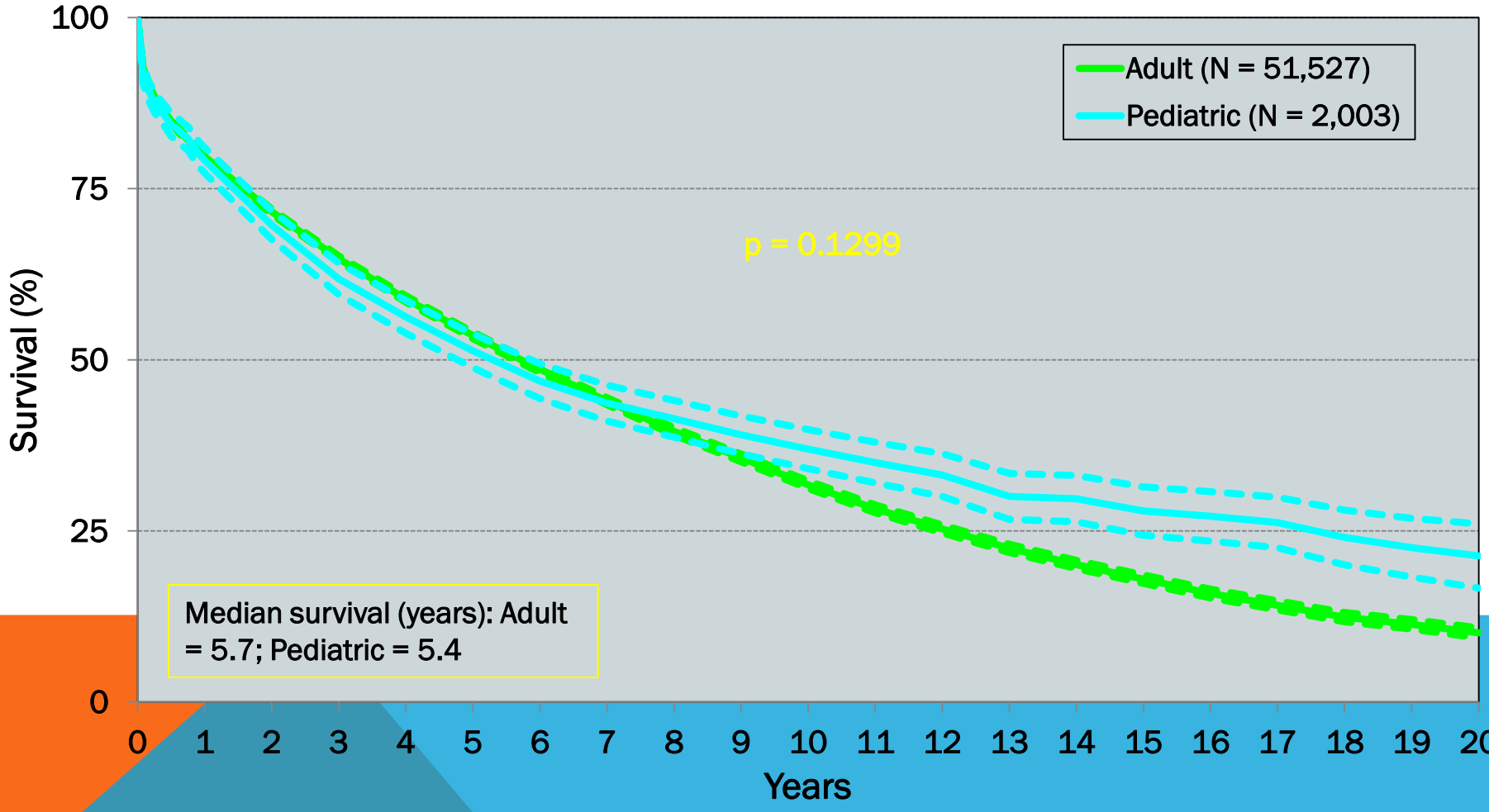
(Need >300)


12 46



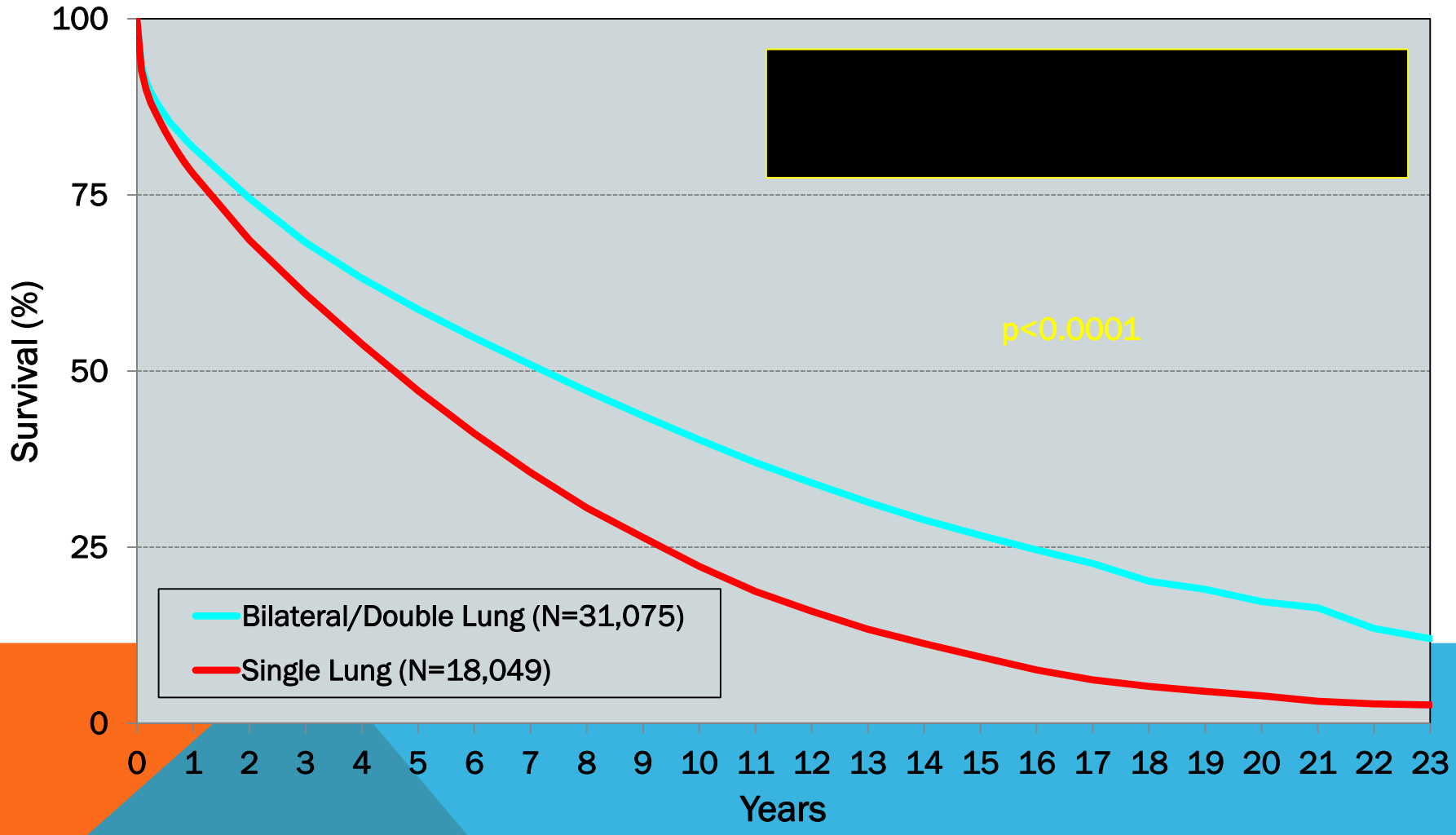

Ventilation:
lung-protective tidal volumes,
recruitment manoeuvres after disconnection
Haemodynamics: shock due to vasodilation,
hypovolaemia, or left ventricular
dysfunction
Donor management
Hormone therapy:
steroids, vasopressin, thyroid replacement
Donor-management protocols
Prostaglandin E1,
anterograde and retrograde flushing
Organ procurement
Extracellular, low-potassium solution
Heparin administration
Cold preservation
4–8°C
Ischaemic time <8 h
Inflation pressure 50% of total lung capacity
$FiO_2$ 50%
If marginal
Ex-vivo lung perfusion
Decline
Transplantation

# Adult and Pediatric Lung Transplants
## Kaplan-Meier Survival by Age Group
(Transplants: January 1990 – June 2014)

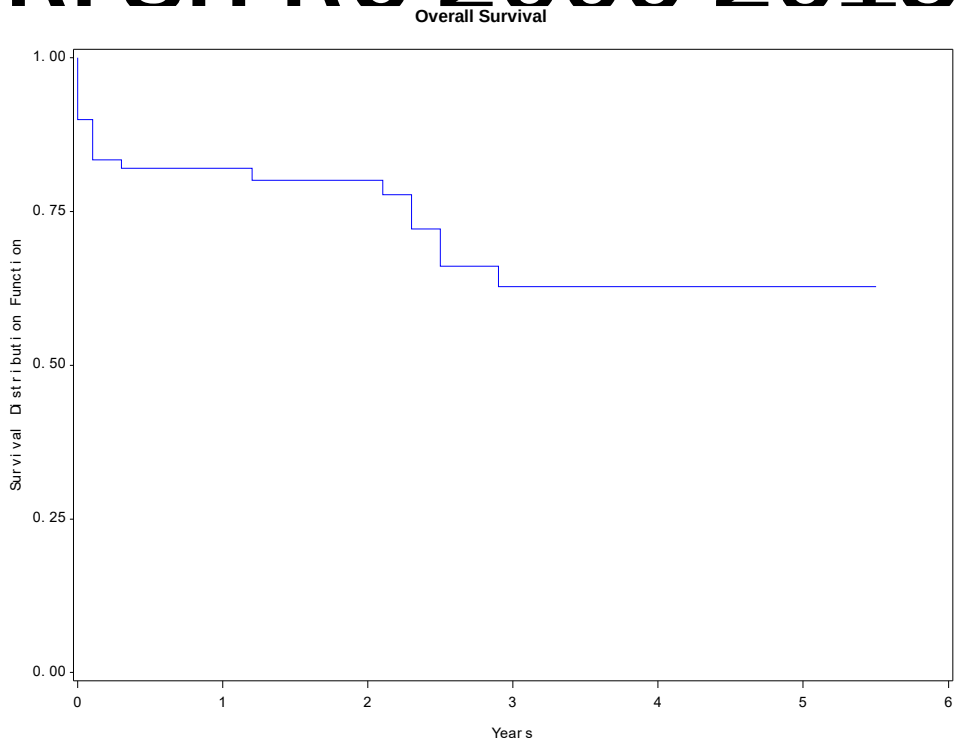


# Adult Lung Transplants

## Kaplan-Meier Survival by Procedure Type for Primary Transplant Recipients (Transplants: January 1990 – June 2014)



# LUNG TRANSPLANT SURVIVAL KFSH RC 2000-2015




Organ
Donor