Lung Transplantation in PAH

Clemens Aigner

Professor of Thoracic Surgery

Head Dept. of Thoracic Surgery

MEDICAL UNIVERSITY OF VIENNA

Vienna Healthcare Group
University Hospital Vienna

Todays talk will cover

1. Overview
2. Referral and listing
3. ECLS bridging of PAH patients
4. Type of Tx procedure
5. Postoperative challenges and outcomes

James D. Hardy 1963

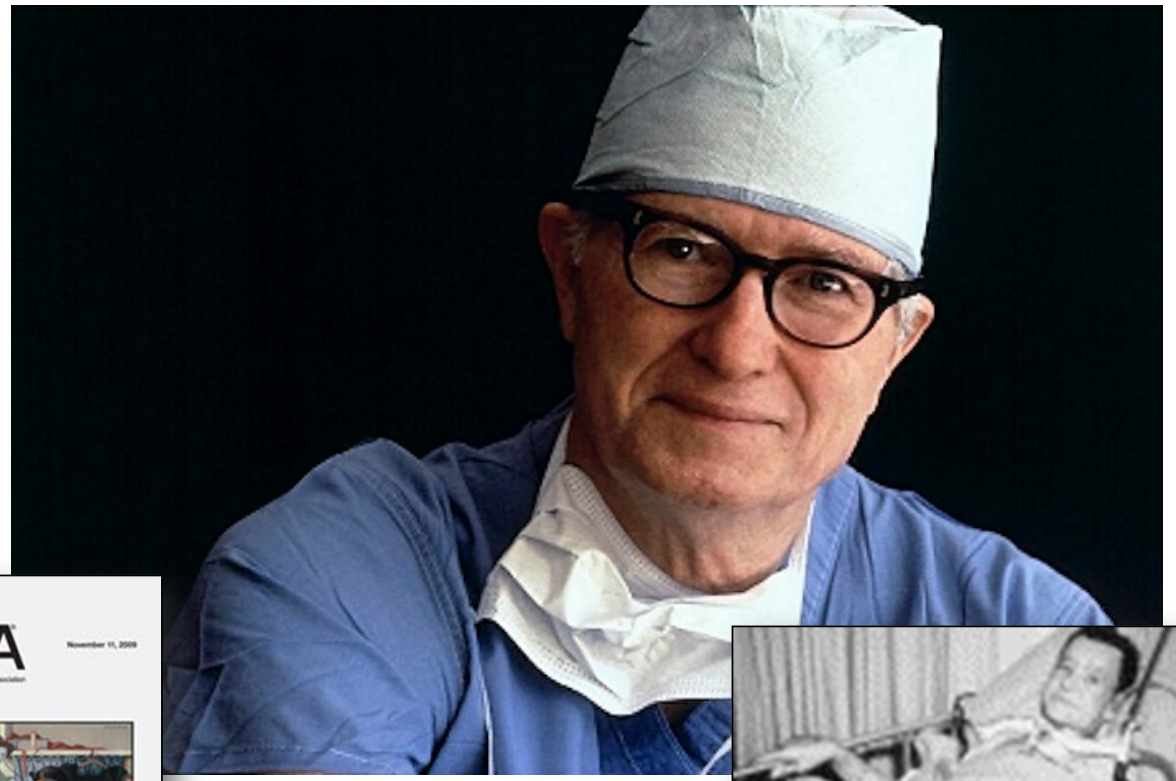
Special Contribution

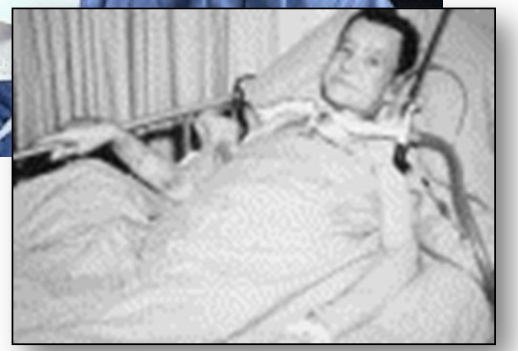
This patient, satisfying stringent preset technical and moral criteria for the procedure, is believed to be the first recipient of a successful lung transplant. Although the patient died of renal failure on the 18th postoperative day, the lung was demonstrated to have functioned and immunologic rejection did not occur.

Lung Homotransplantation in Man

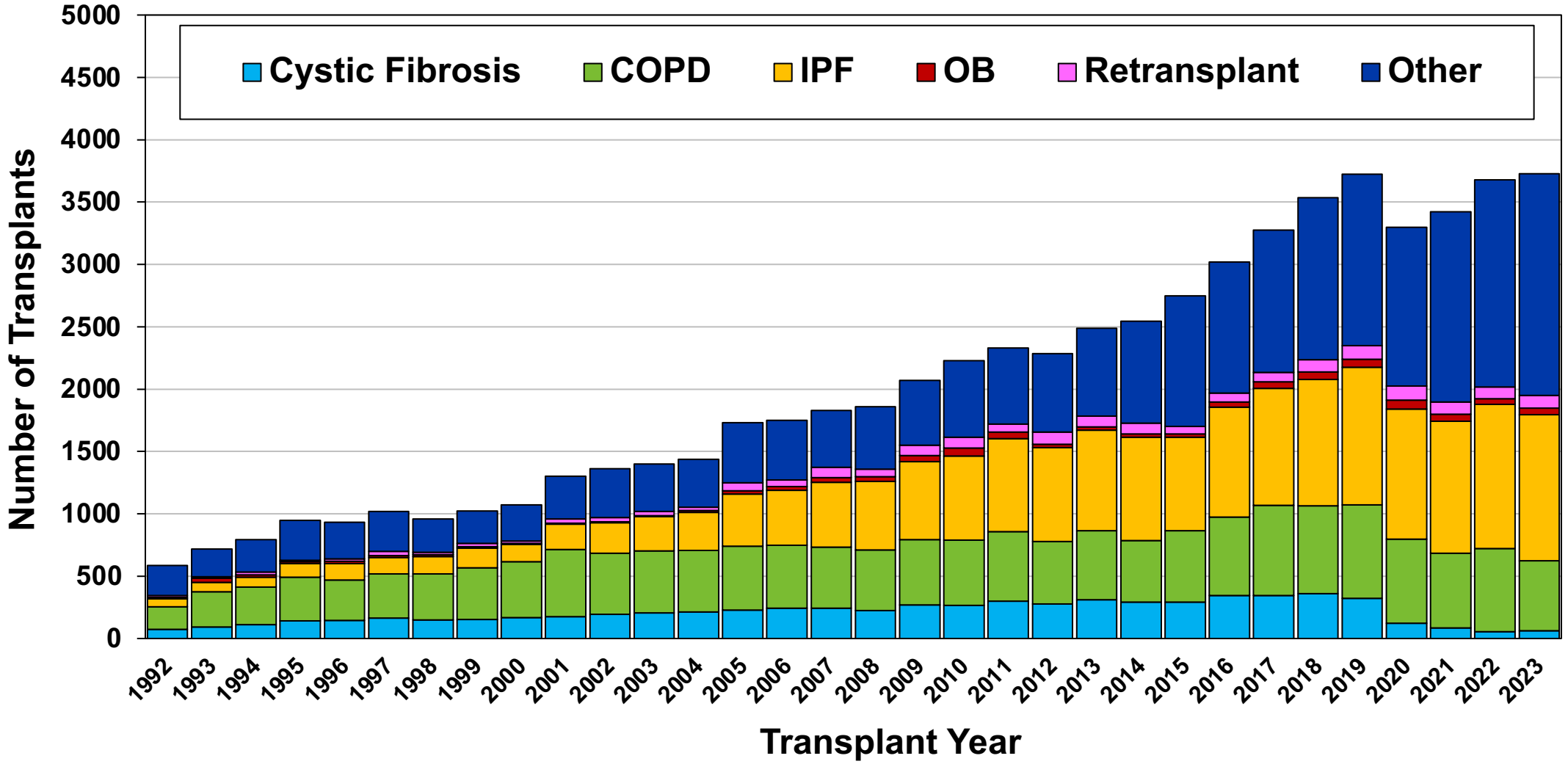
Report of the Initial Case

James D. Hardy, MD, Watts R. Webb, MD, Martin L. Dalton, Jr., MD, and George R. Walker, Jr., MD, Jackson, Miss





Annual Number of Adult Lung Transplants by Diagnosis, 1992-2023



LTx for PAH is rare … ISHLT registry data (1992-2018)

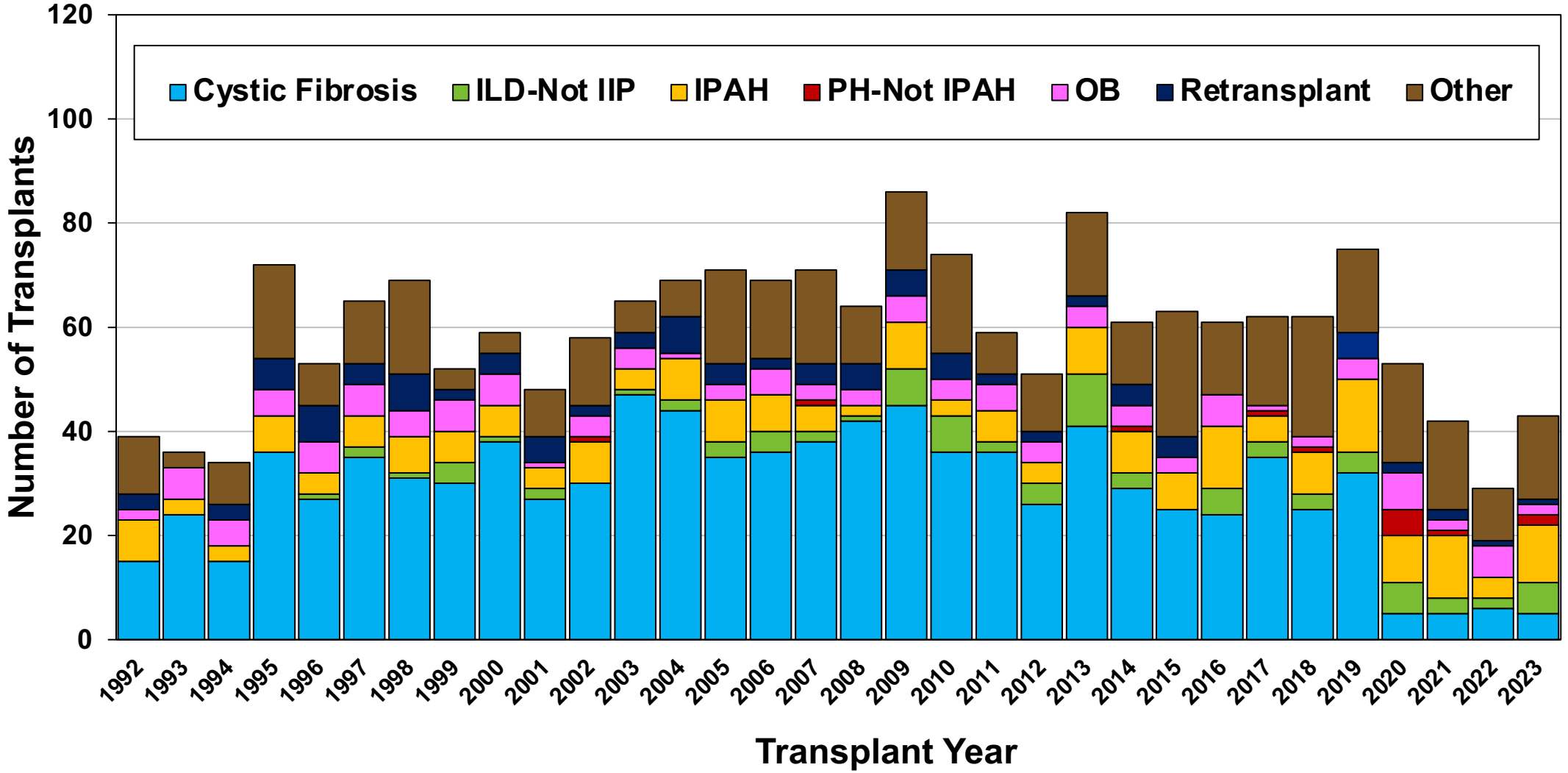
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION 2022

JHLT. 2022 Oct; 41(10): 1335-1375

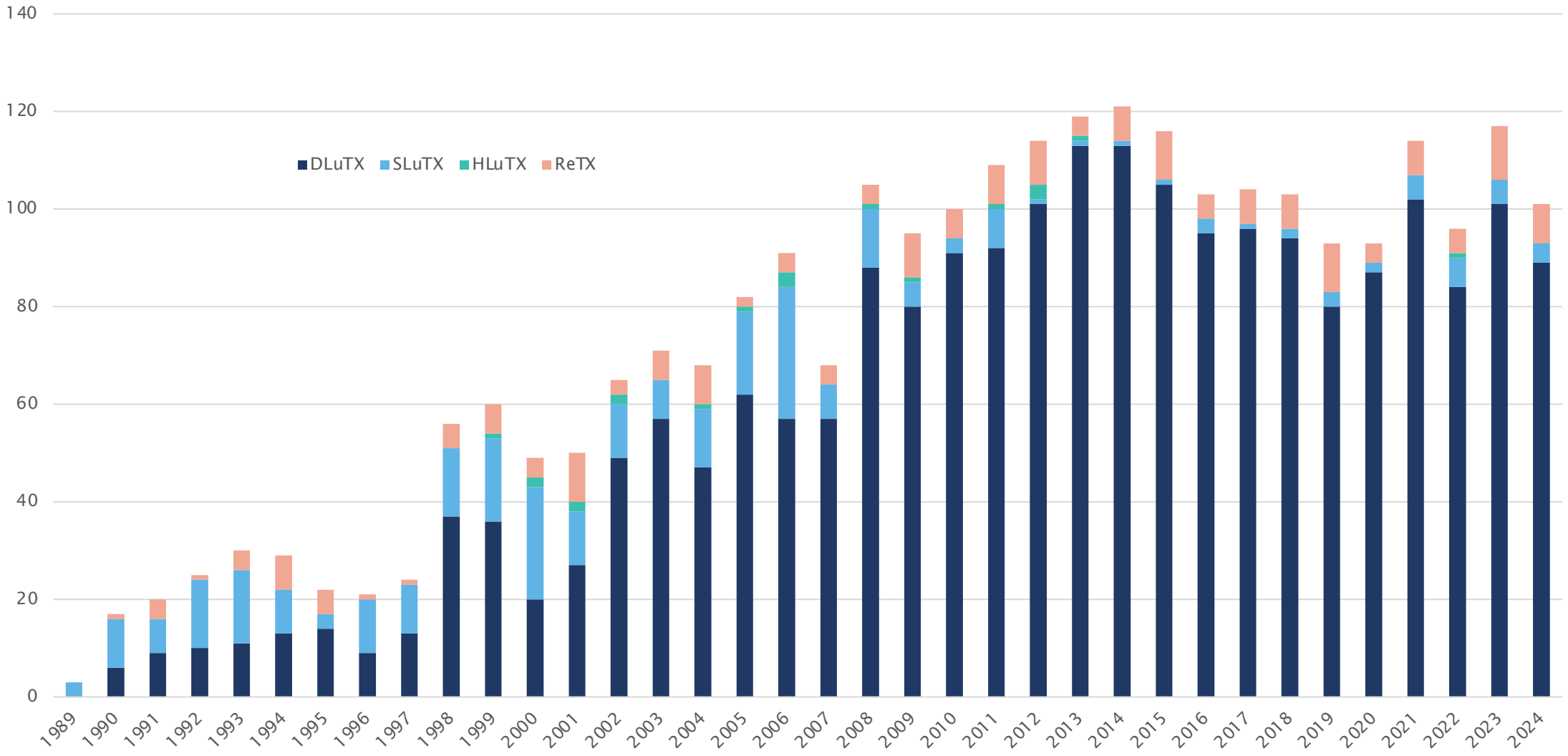
	Jan 1992-Dec 2000 (N = 11,796)	Jan 2001-Dec 2009 (N = 21,806)	Jan 2010-Jun 2018 (N = 33,891)	P-value
Diagnosis				<0.0001
- COPD	4162 (37.3%)	7102 (33.1%)	8917 (26.5%)	
- A1ATD	1169 (10.5%)	1131 (5.3%)	1054 (3.1%)	
- CF	1717 (15.4%)	3470 (16.2%)	4771 (14.2%)	
- IPAH	578 (5.2%)	563 (2.6%)	945 (2.8%)	
- IPF	1677 (15.0%)	4899 (22.8%)	9755 (29.0%)	
- Retransplant	394 (3.5%)	921 (4.3%)	1364 (4.1%)	
- Other	1471 (13.2%)	3392 (15.8%)	6822 (20.3%)	

→ Evidence mostly limited to single-center retrospective analysis

Annual Number of Pediatric Lung Transplants by Diagnosis, 1992-2023

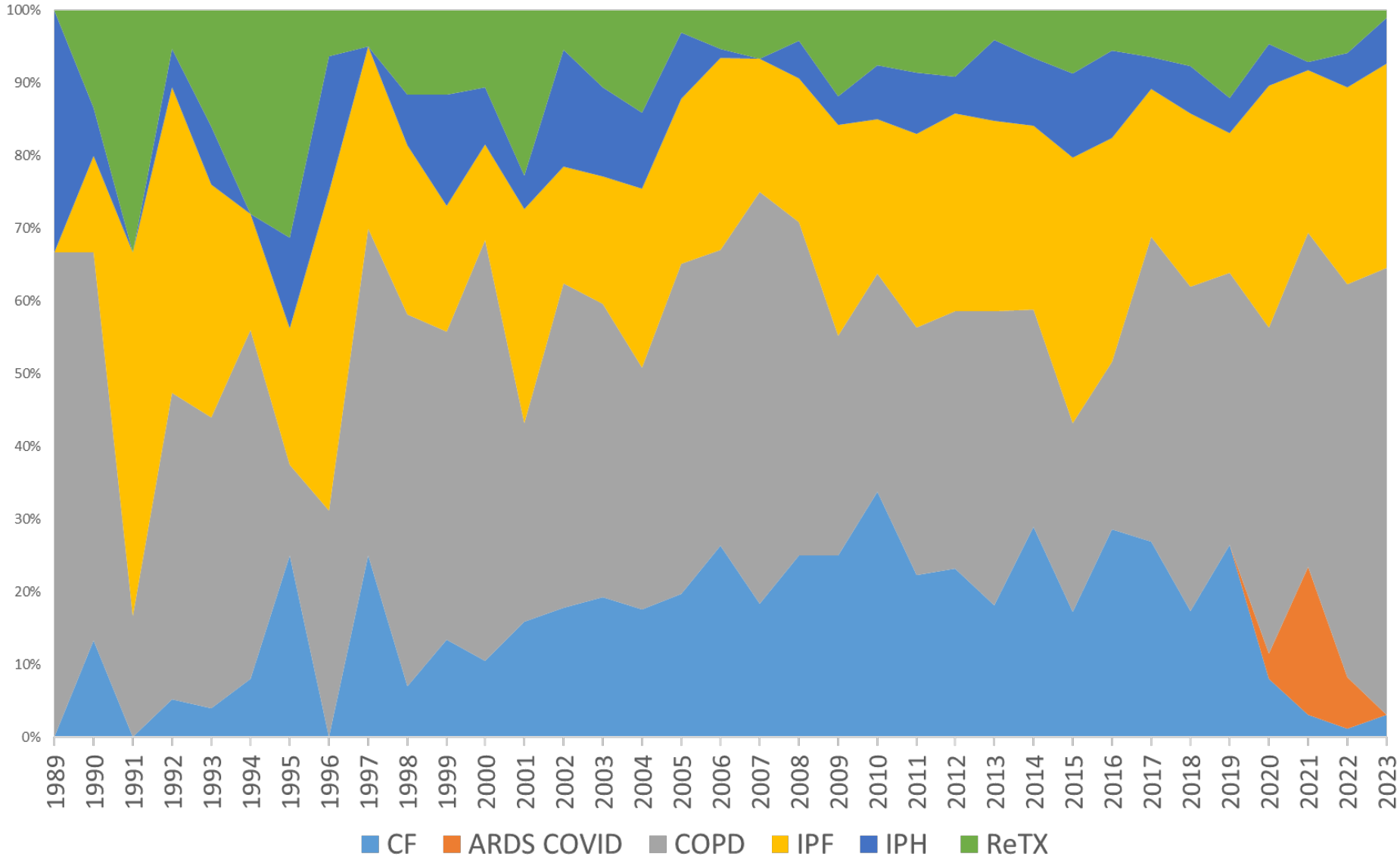


Vienna Lung Transplant Program



Clemens Aigner
Dept. of Thoracic Surgery

Indications for lung transplantation in Vienna

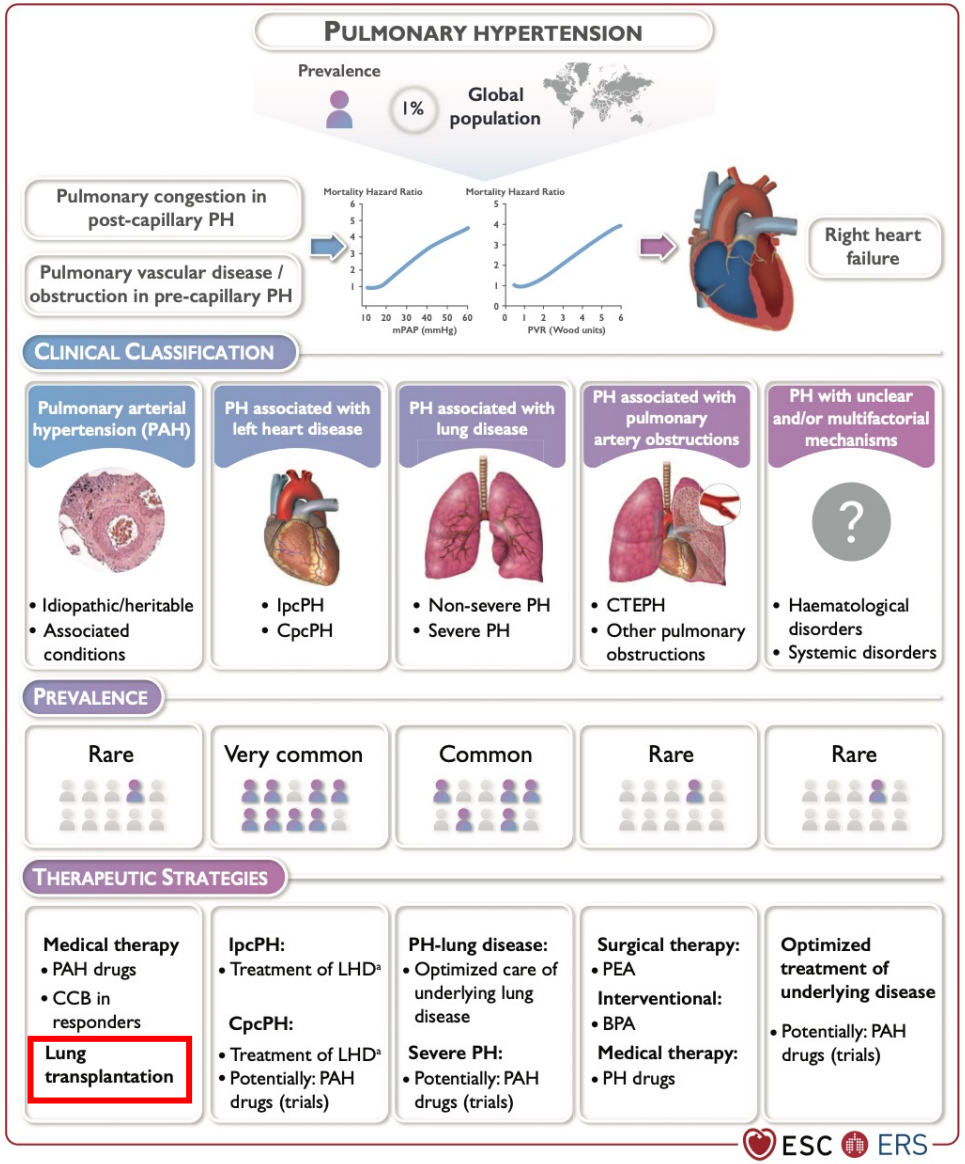


Clemens Aigner
Dept. of Thoracic Surgery

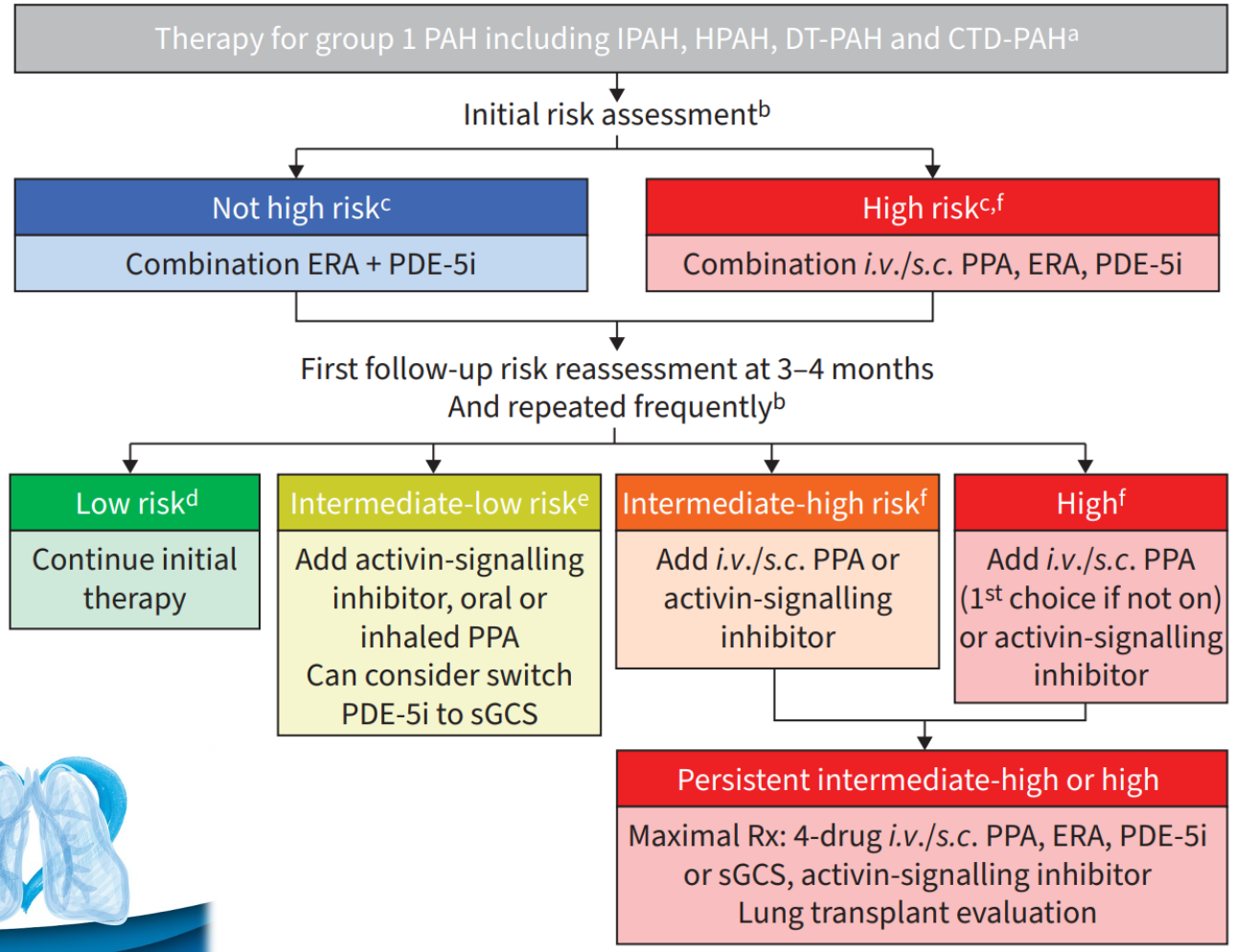
Referral and listing

Building a safety net… Time is the key

Discussion → **Referral** → **Listing**



European Heart Journal (2022) 43, 3618–3731



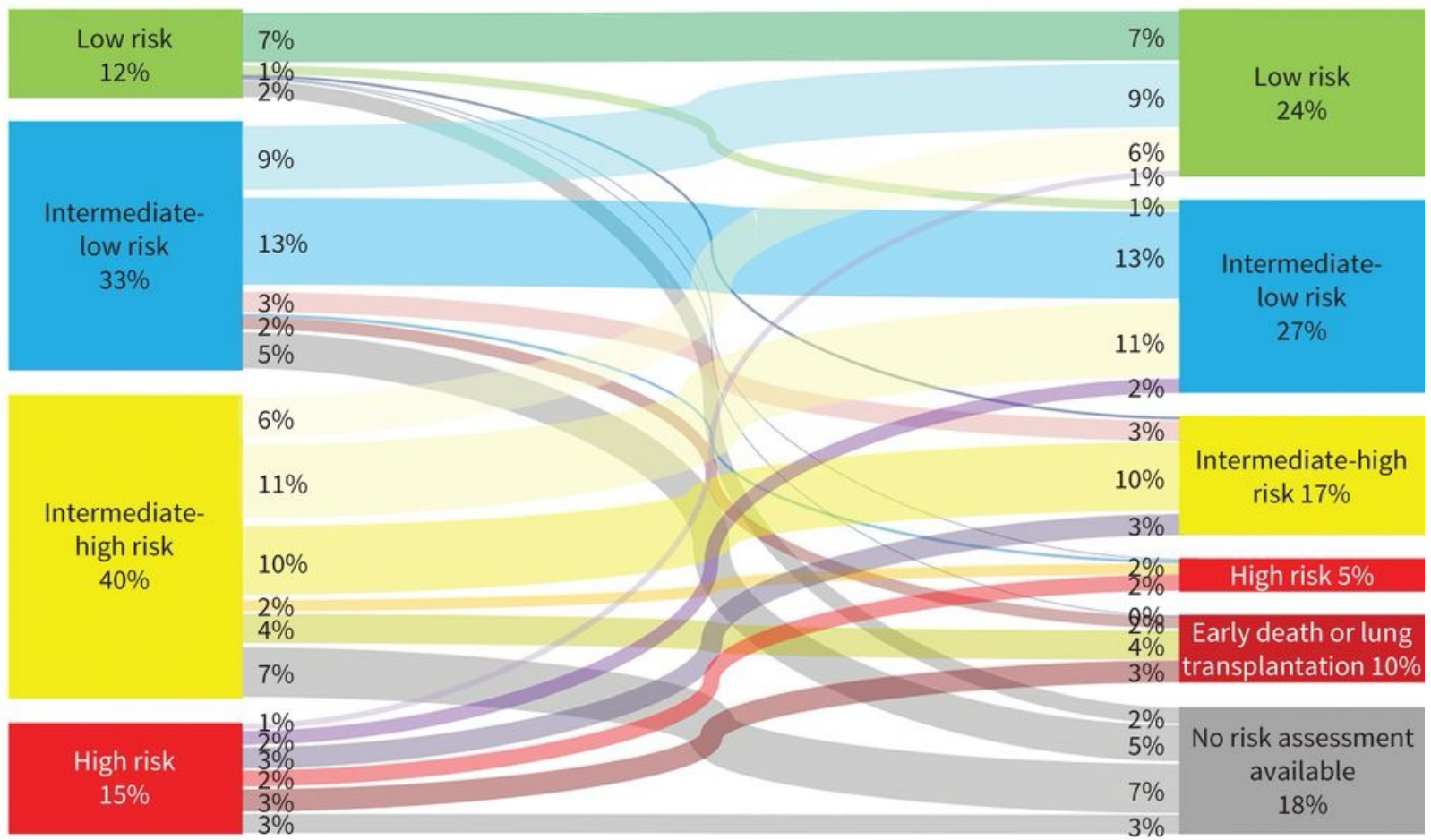
Treatment algorithm key points

a. The treatment algorithm is intended for patients with confirmed group 1 PAH (phenotypically clear-cut, including **mPAP ≥25 mmHg and PVR >3 Wood Units** and no significant response on acute vasoreactivity testing). See text for treatment in PAH with complex phenotypes.
b. ***Risk assessment*** should be performed at baseline, within 3–4 months and periodically thereafter, and using FC, 6MWD and natriuretic peptides as a part of a validated risk calculator. Haemodynamics, RV imaging and other measures should be used to supplement risk assessment.
c. ***Initial triple therapy*** with an *i.v./s.c.* PPA is recommended in high-risk patients and may be considered in non-high risk with severe haemodynamics and/or poor RV function.
d. Most ***low-risk patients*** at follow-up should continue initial therapy.
e. Clinical trials with oral and inhaled treprostinil included ***only patients on monotherapy***, while studies of selexipag and sotarcept included patients on combination therapy.
f. ***Transplant referral*** should be considered for select high-risk patients at diagnosis, and for intermediate-high and high-risk patients at first or subsequent follow-up.

7th WORLD SYMPOSIUM ON PULMONARY HYPERTENSION

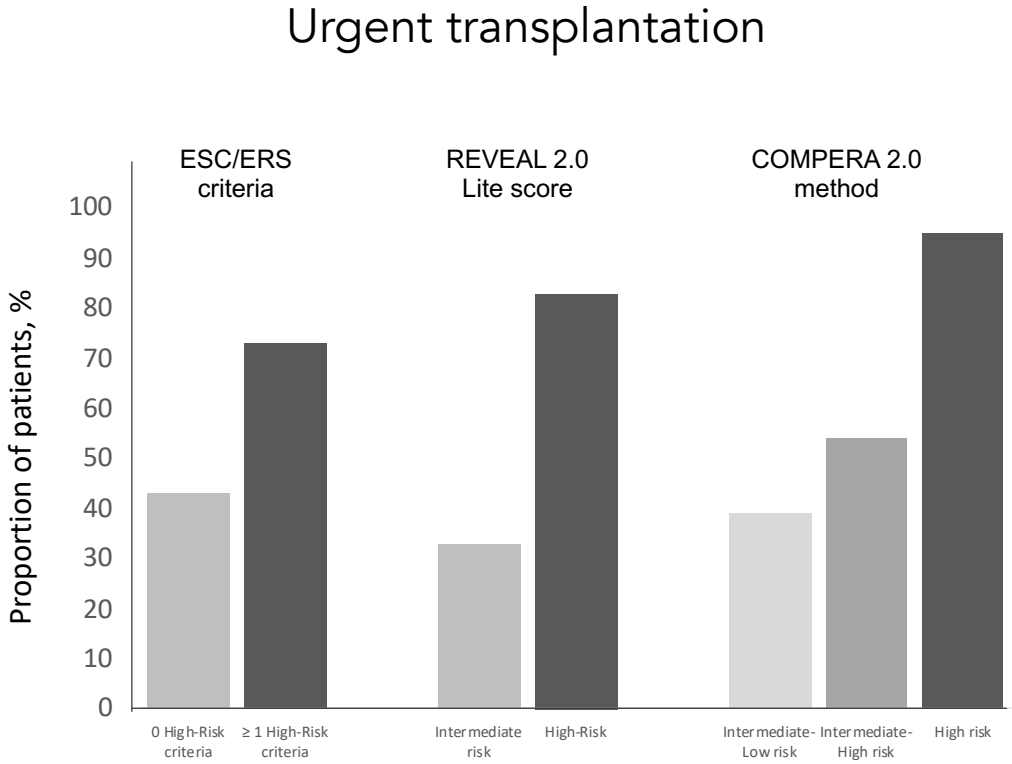
Eur Respir J. 2024 Sep 2:2401222.

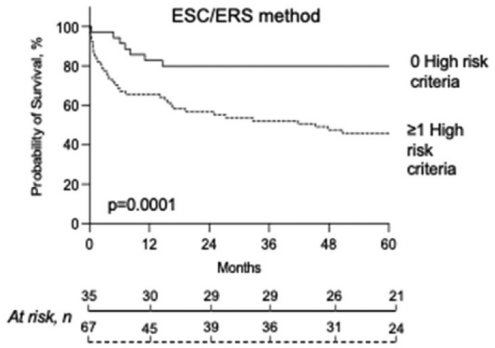
Changes in risk status

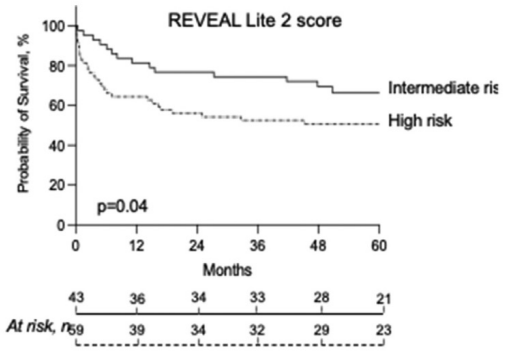


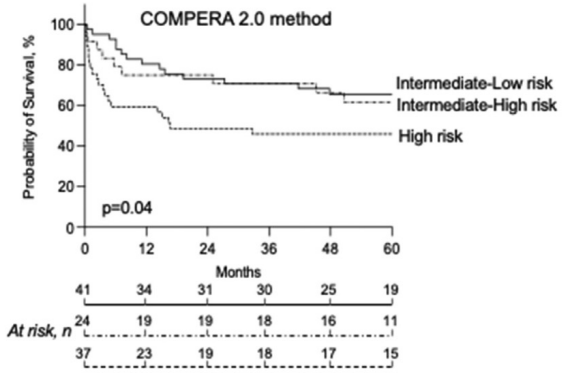
Athénaïs B et al. Eur Respir J 2022;59:2102419

Impact of risk status at time of listing on outcomes









Vicaire H et al, J Heart Lung Transplant 2022

The reality of referral for PAH patients – PHAR

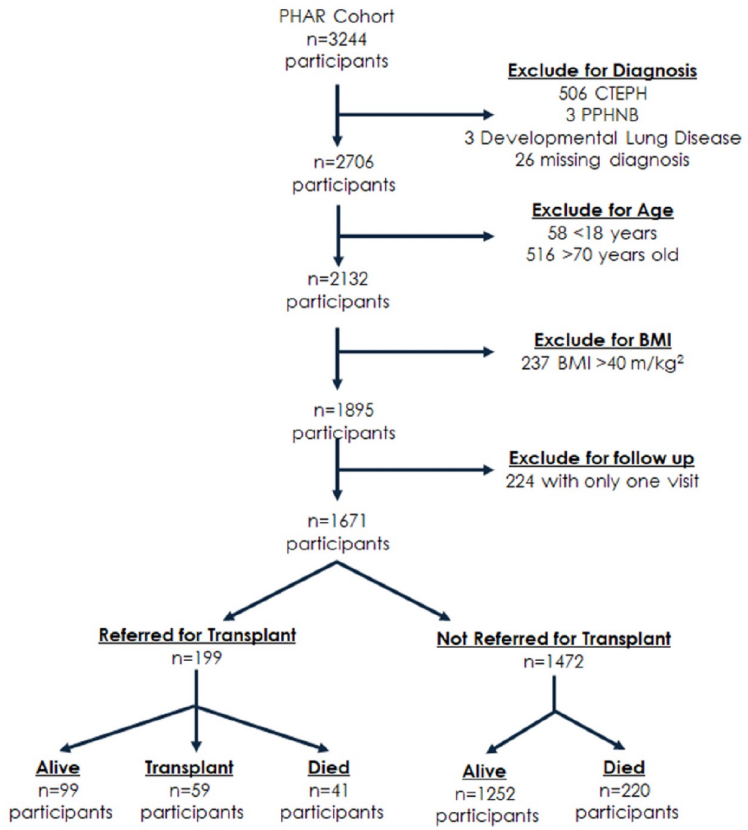


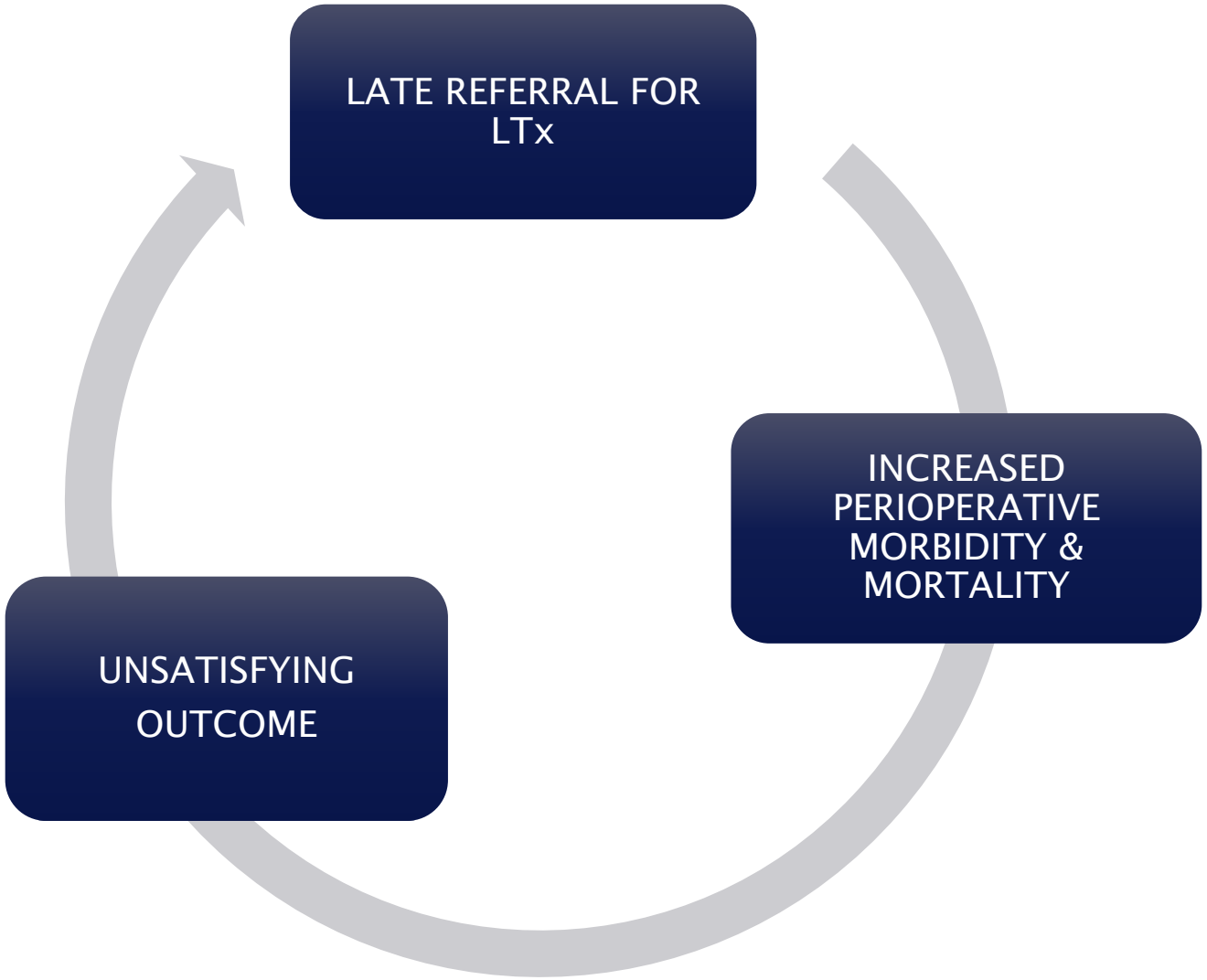
Table 6 Stepwise Backwards Elimination for Referral for Transplantation

Predictor of time to referral for lung transplantation	HR for referral for transplantation (95% CI)	*p*-value
Variables associated with referral for transplant using stepwise backwards elimination		
Age (10 year increase)	0.70 (0.59, 0.84)	$p < 0.001$
Diagnosis of Pulmonary Veno-Occlusive Disease	26.69 (12.78, 55.77)	$p < 0.001$
Body Mass Index (1 kg/m^2 increase)	0.95 (0.91, 0.98)	$p < 0.003$
REVEAL Lite 2 (1 point Risk Shift)	1.28 (1.15, 1.43)	$p < 0.001$
Parenteral Prostacyclin Use	2.55 (1.52, 4.25)	$p < 0.001$

Rates of referral for lung transplantation in patients with PAH remain unacceptably low and occur too late. Increased awareness of the benefit of early referral is necessary, even at expert centers.

Kolaitis NA et al, J Heart Lung Transplant 2025

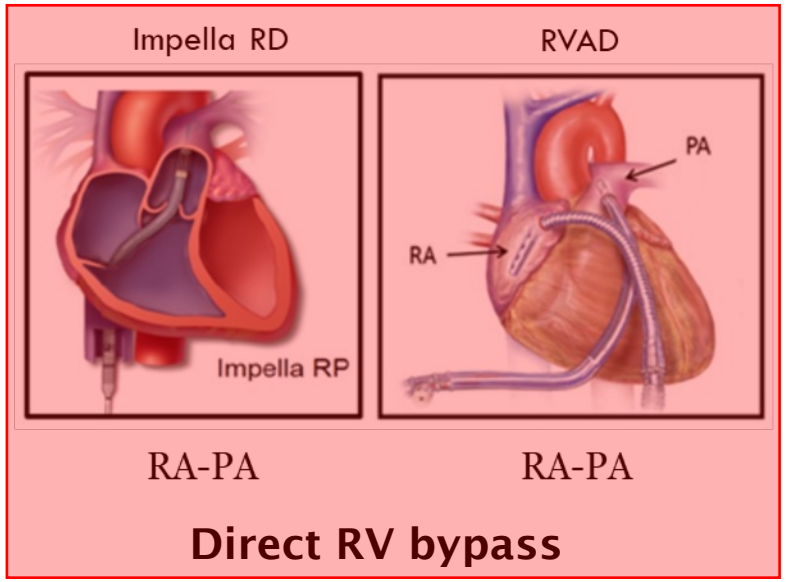
The reality of referral of PAH patients

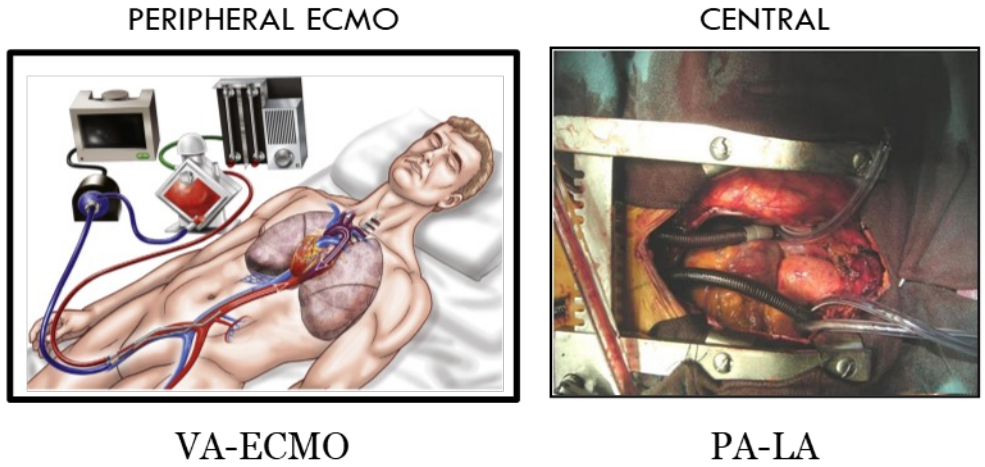


ECLS Bridging

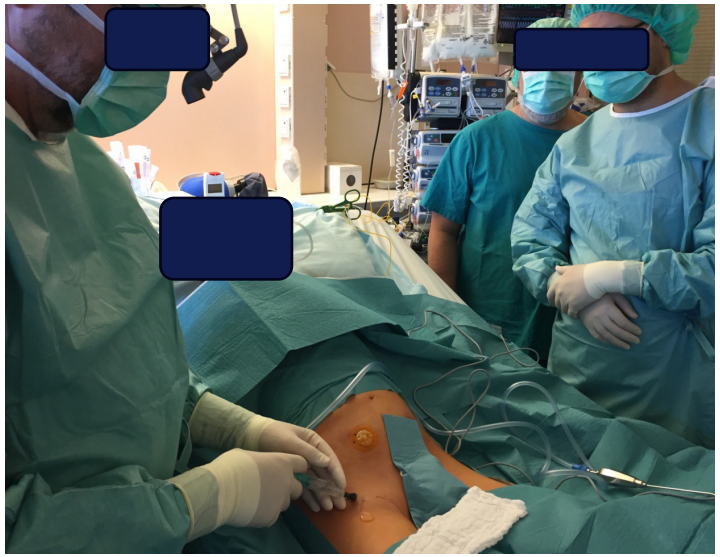
Principles of ECLS bridging

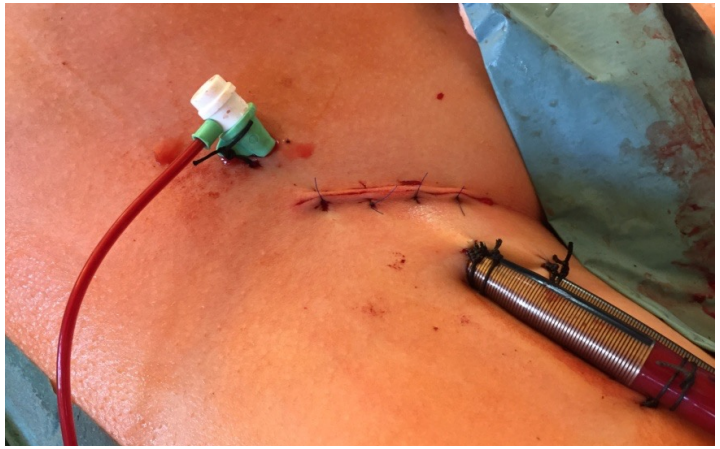
1. Provide hemodynamic stability
2. Relieve the right heart
3. Improve splanchnic circulation → protect kidney and liver function





fem/fem VA ECMO



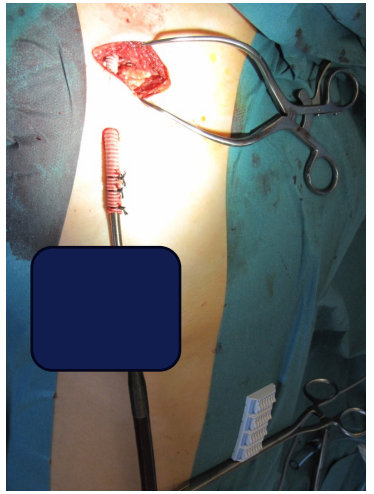


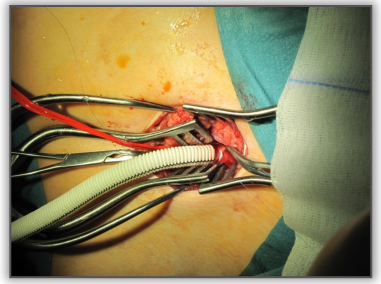
- Relatively easy to insert
- Implantation in the ICU
- In local anesthesia

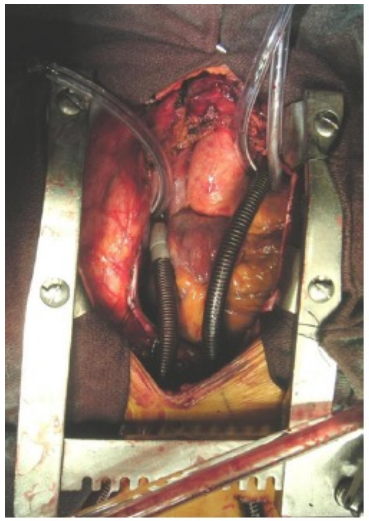
- North/South syndrome
- Difficult mobilization
- Flow limited to femoral vessel size (usually 3.5L/min)

Alternatives to fem/fem VA ECMO

1. Subclavian cannulation
2. Central cannulation
3. PA/LA Novalung

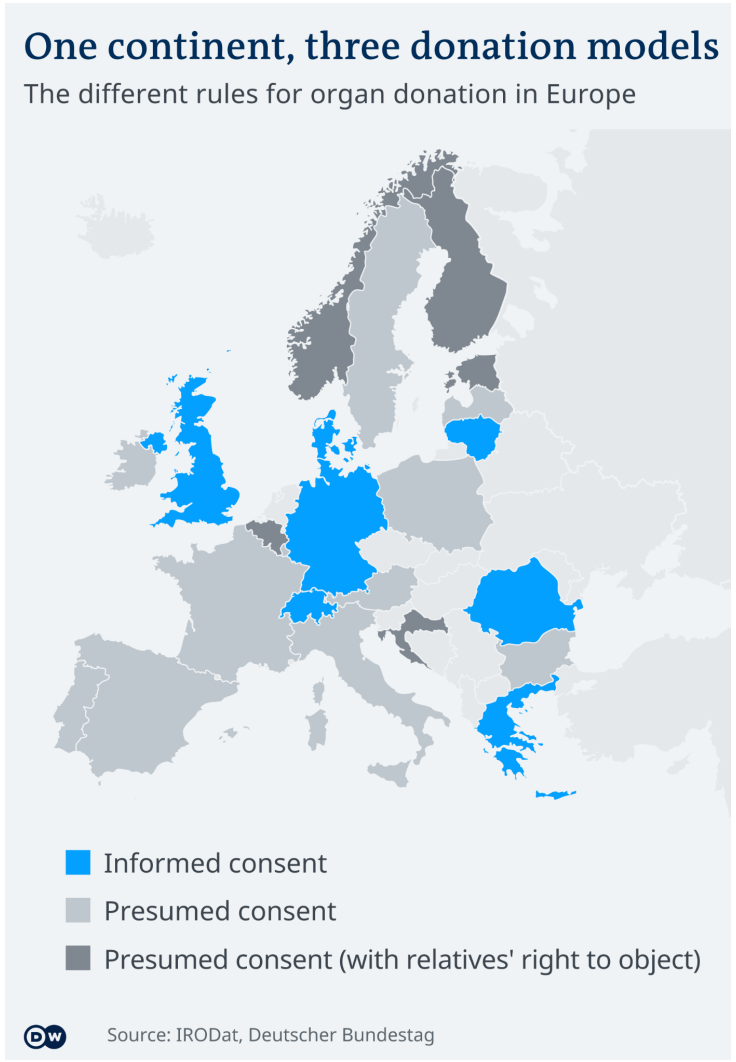


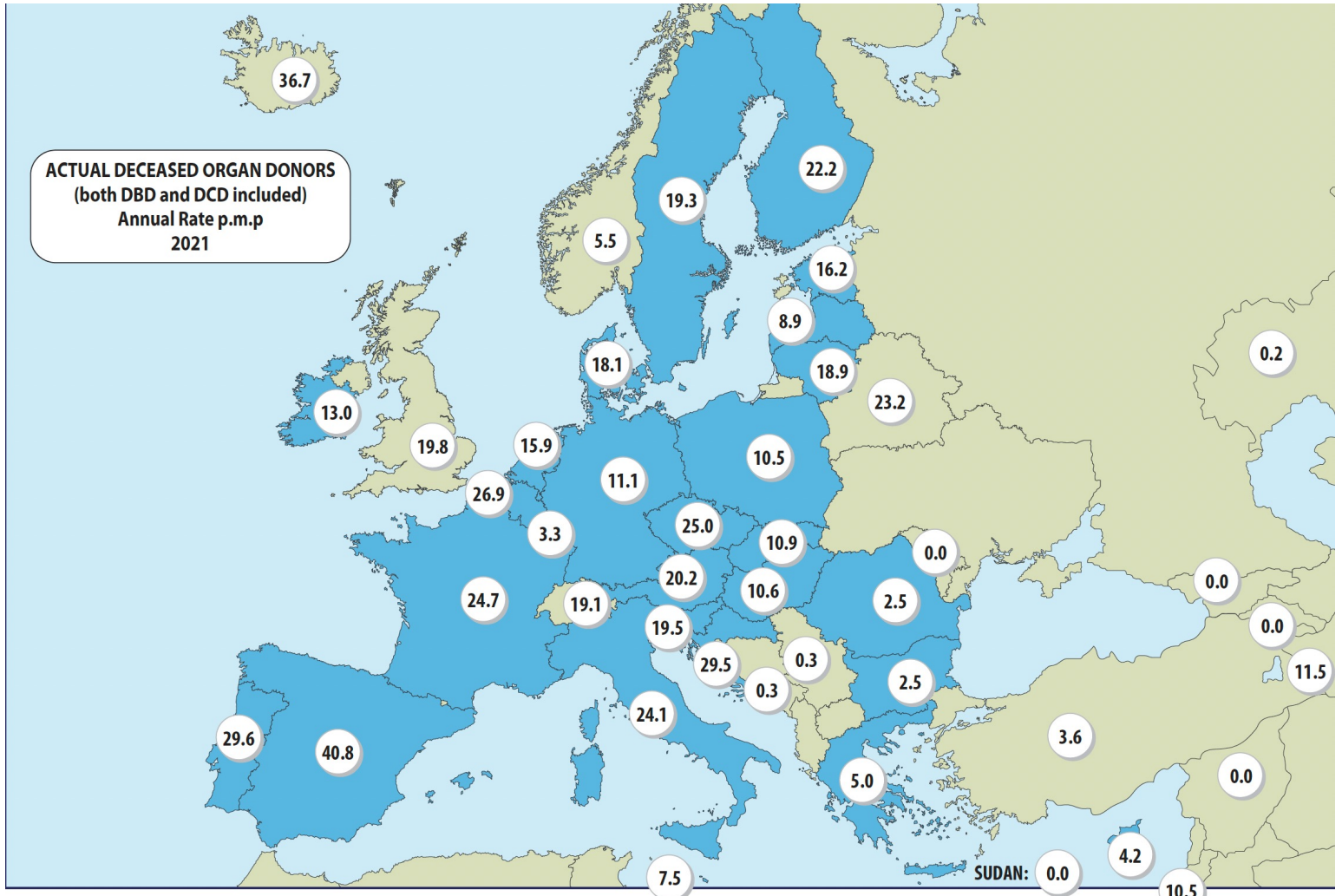




Ambulation on ECMO

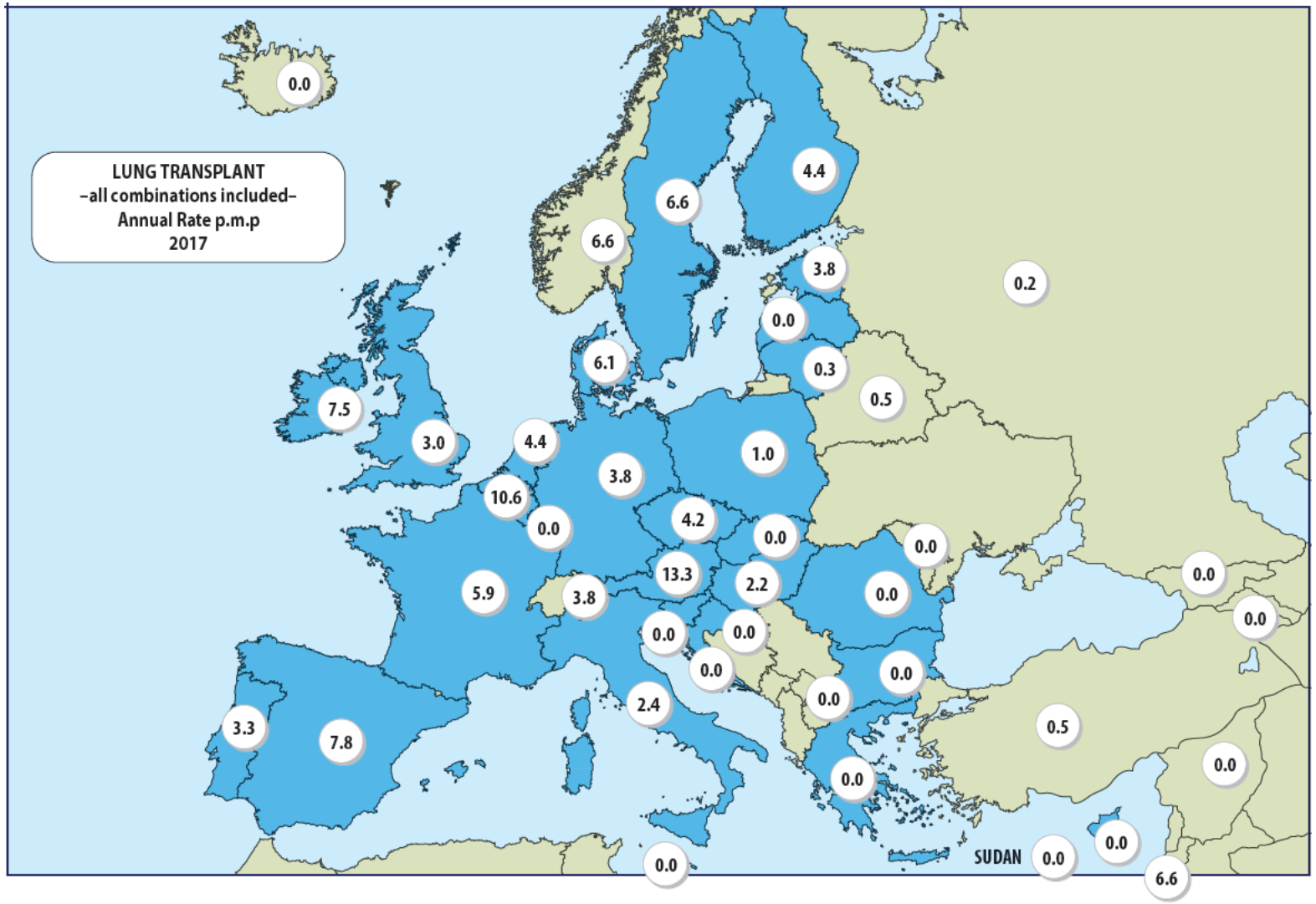
Organ Donation in Europe



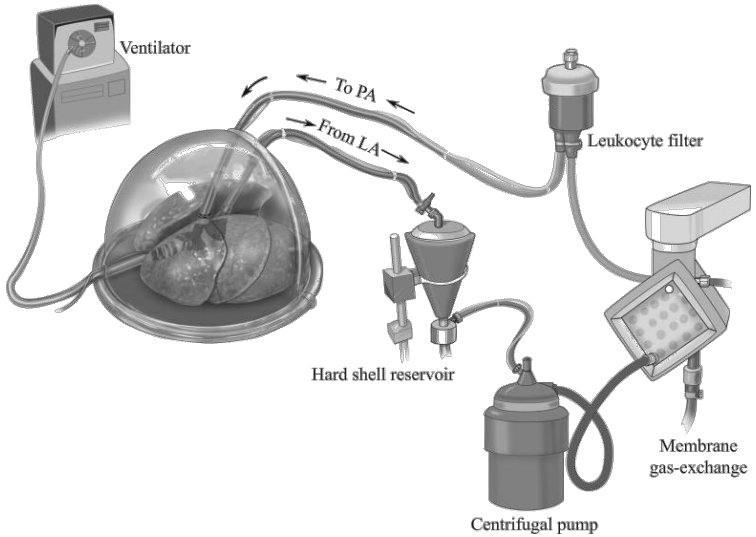


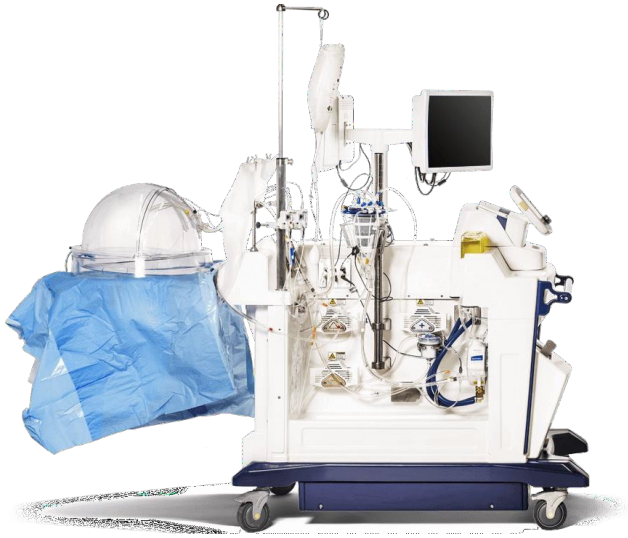
Cuncil of Europe Transplant Newsletter 2021

Lung transplantation in Europe



EVLP and 10° storage





Images: Manual System: Ex Vivo Lung Perfusion Cypel, Marcelo et al., Operative Techniques in Thoracic and Cardiovascular Surgery | Xvivo XPS, Göteborg | Transmedics OCS lungs, Andover | Traferox 10° Box, Toronto | Tevosol/Bridge for Life EVOSS, Alberta | XOR Labs, Toronto

Take home message referral, listing and pretransplant phase

Don´t wait too long….

Referral:

- Intermediate high risk/REVEAL 8; RV dysfunction despite optimized PH therapy
- Frequent hospitalization or syncope, recurrent hemoptysis, secondary liver or kidney dysfunction
- Need for iv or sc prostacyclin therapy
- Worsening risk scores
- Known or suspected high riak variants (PVOD, scleroderma, PA aneurysm)
- Allow sufficient time to complete evaluation and avoid emergency bridging

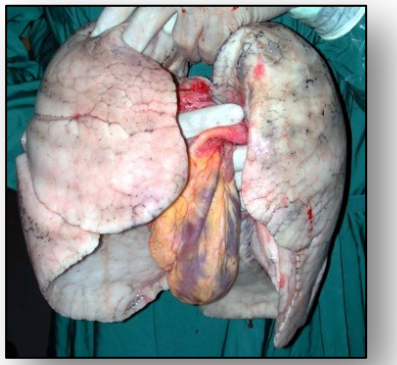
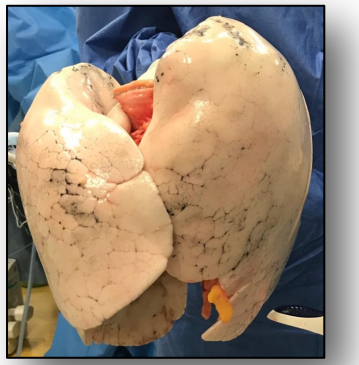
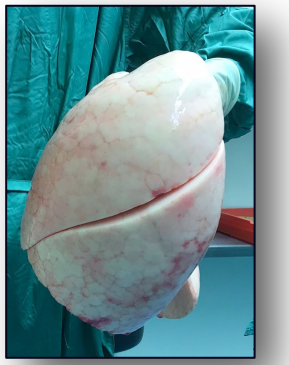
Listing

- High risk, REVEAL >10 on appropriate therapy
- Progressive hypoxemia, progressive liver or kidney dysfunction
- Life threatening hemoptysis

Bridging options available

- VA ECMO, PA/LA Novalung, potentially awake ECMO

Which transplant procedure?

Which transplant procedure?

In the early days of Tx for PAH the heart was considered too damaged → Heart/Lung Tx

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

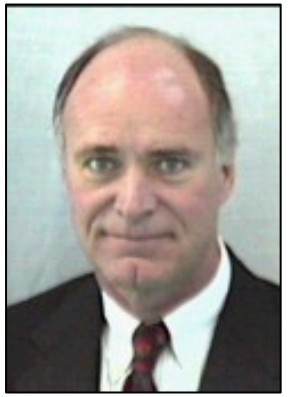
Volume 306:557-564 March 11, 1982 Number 10

Heart-lung transplantation: successful therapy for patients with pulmonary vascular disease

BA Reitz, JL Wallwork, SA Hunt, JL Pennock, ME Billingham, PE Oyer, EB Stinson, and NE Shumway

We report our initial experience with three patients who received heart-lung transplants. The primary immunosuppressive agent used was cyclosporin A, although conventional drugs were also administered. In the first patient, a 45-year-old woman with primary pulmonary hypertension, acute rejection of the transplant was diagnosed 10 and 25 days after surgery but was treated successfully; this patient still had normal exercise tolerance 10 months late. The second patient, a 30-year-old man, underwent transplantation for Eisenmenger's syndrome due to atrial and ventricular septal defects. His graft was not rejected, and his condition was markedly improved eight months after surgery. The third patient, a 29-year-old woman with transposition of the great vessels and associated defects, died four days postoperatively of renal, hepatic, and pulmonary complications. We attribute our success to experience with heart-lung transplantation in primates, to the use of cyclosporin A, and to the anatomic and physiologic advantages of combined heart-lung replacement. We hope that such transplants may ultimately provide an improved outlook for selected terminally ill patients with pulmonary vascular disease and certain other intractable cardiopulmonary disorders.

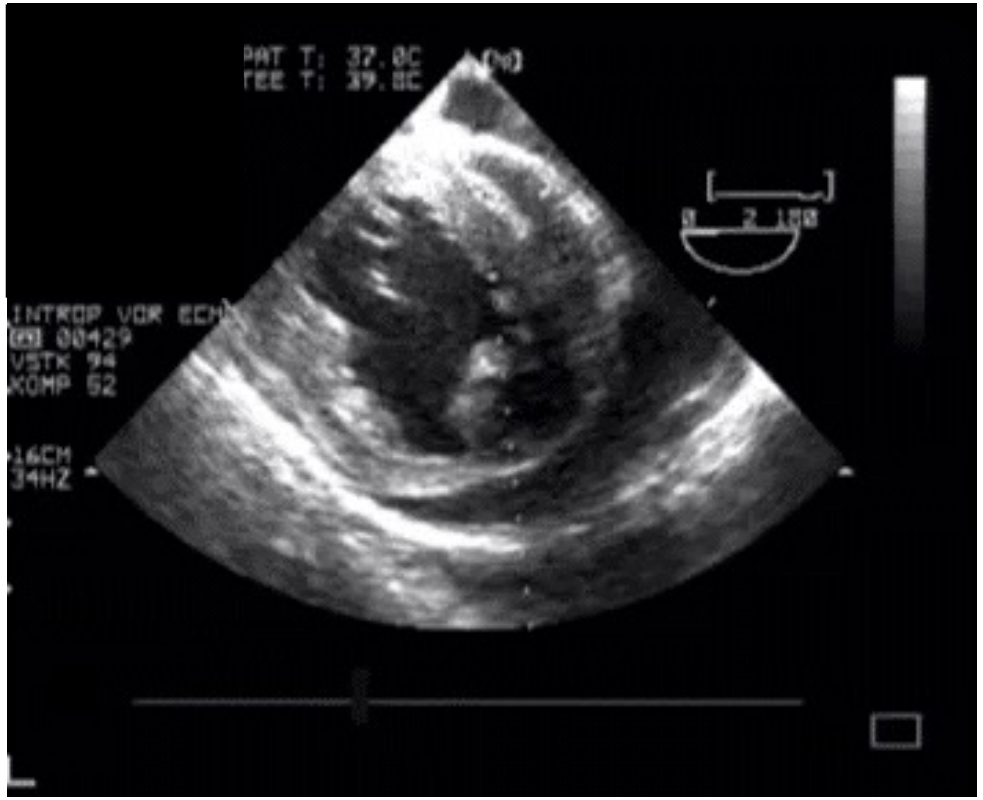
Norman Shumway
Stanford 1981



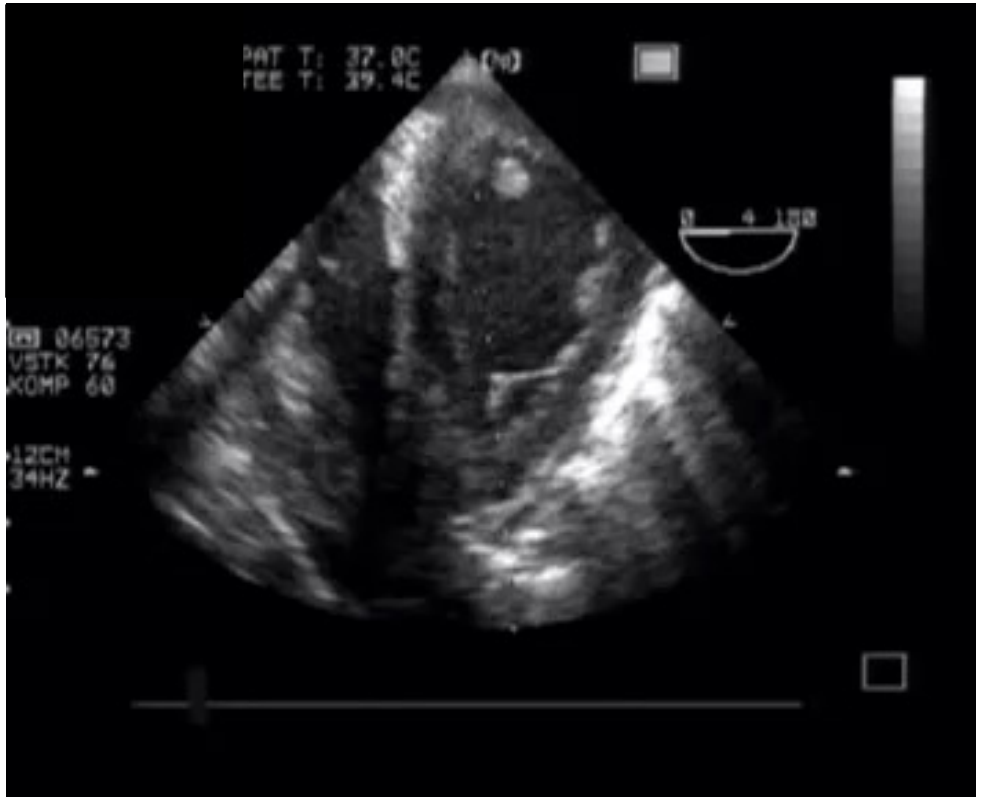
Bruce A. Reitz
Stanford 1981

Reverse cardiac remodelling

Pre-Tx



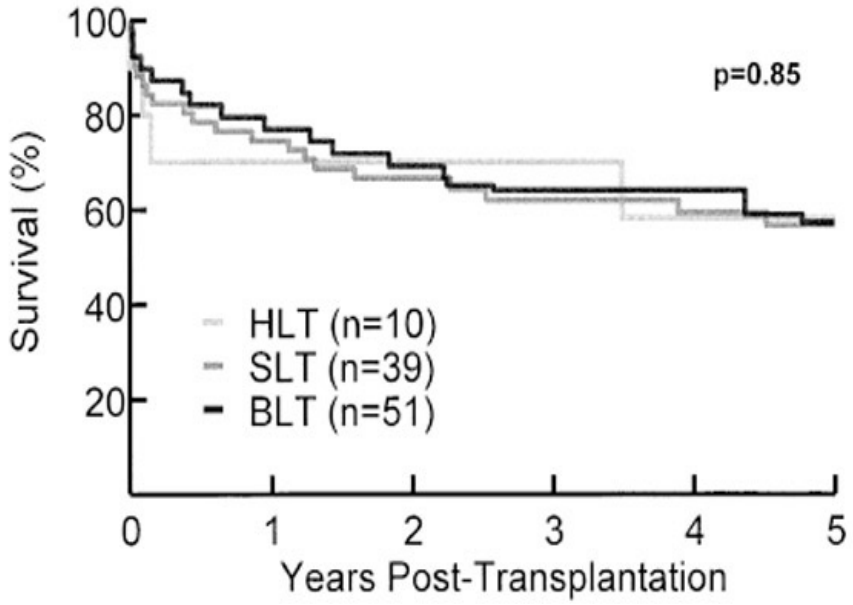
Post-Tx



Kasimir, Mereles, Aigner et al. J Heart Lung Transplant. 2008 Jan;27(1):66-71

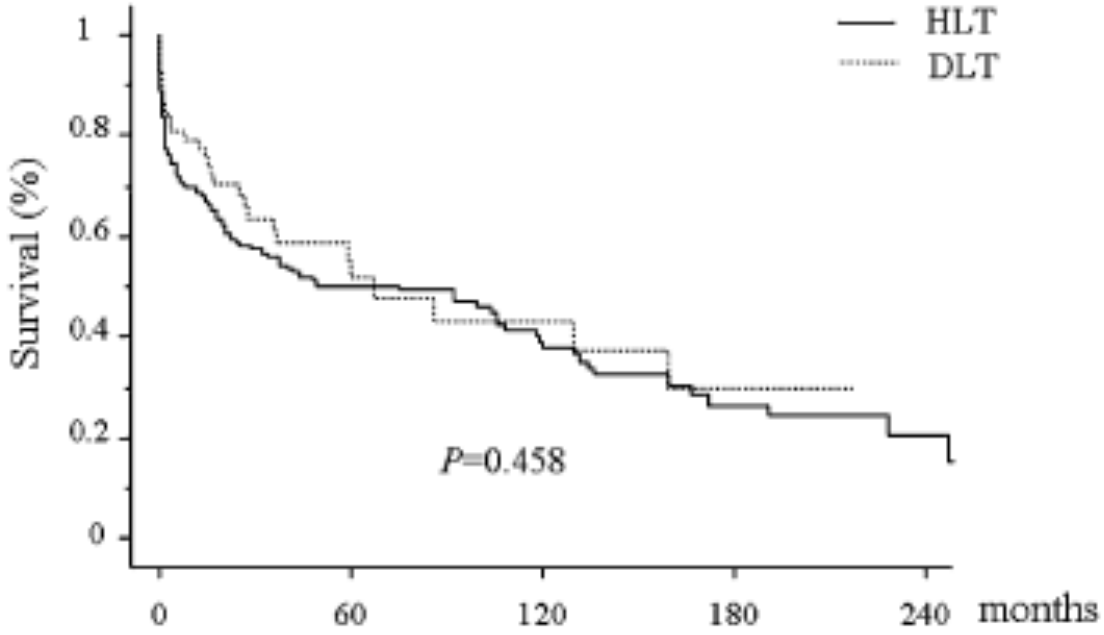
Survival after Tx for PAH: lung Tx vs heart/lung Tx

St. Louis



Mendeloff EN et al. Ann Thorac Surg 2002;73: 209-19.

Paris

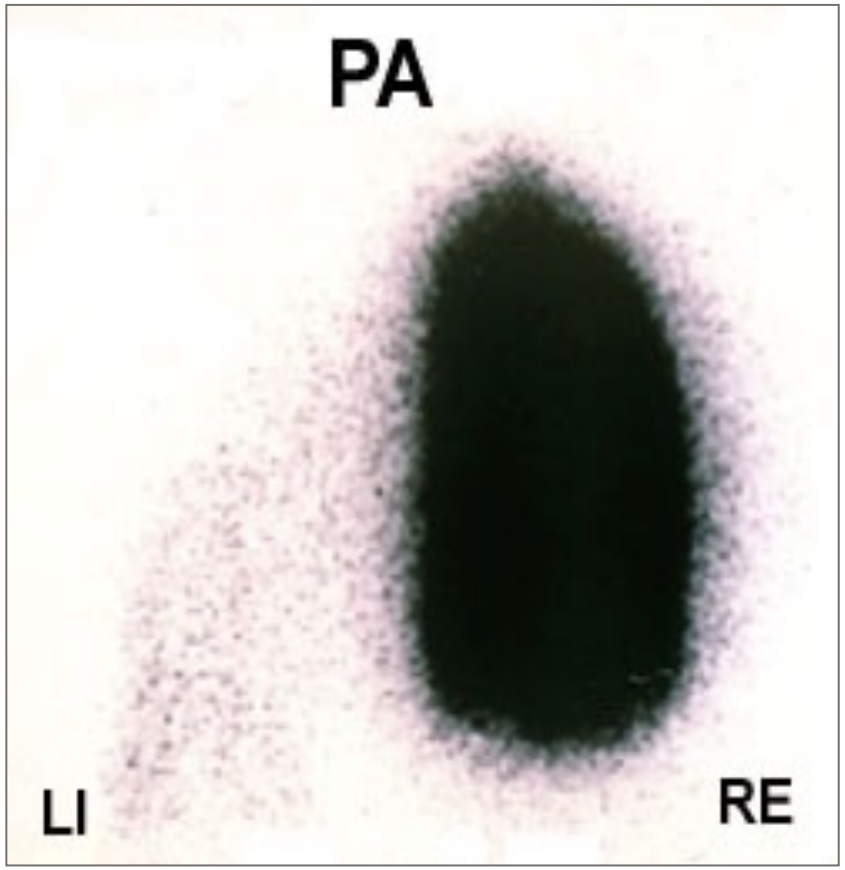


Fadel E. et al. Eur J Cardiothorac Surg. 2010; 38:277-84.

→ Double lung transplantation has become the standard of care for PAH

What about single lung Tx for PAH?

NOT RECOMMENDED!!!



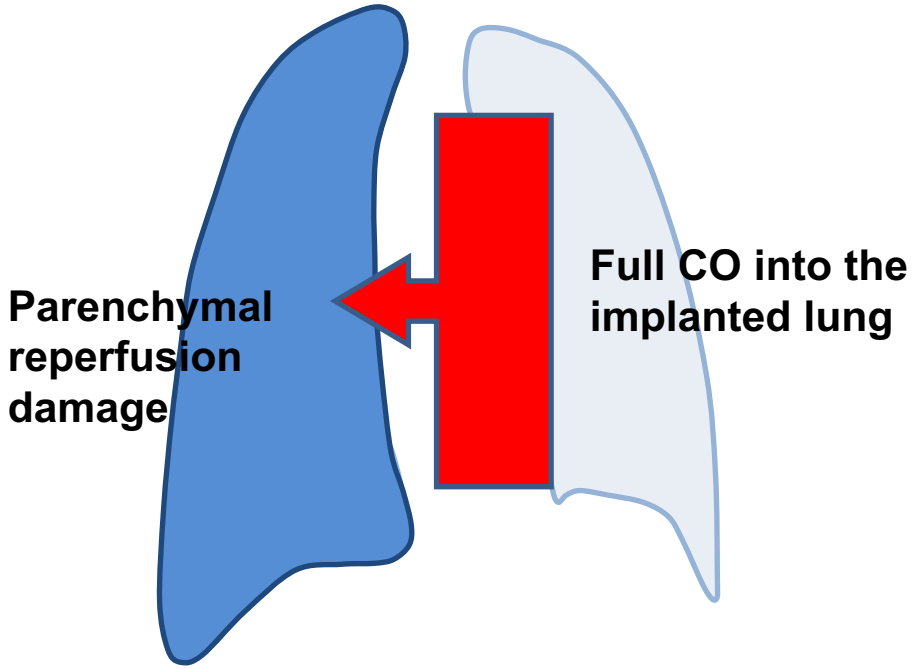
Postoperative period:

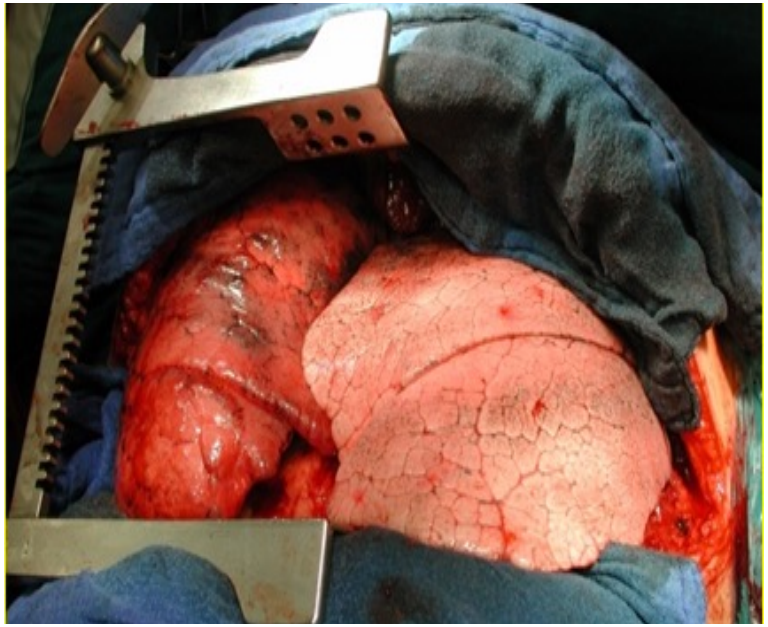
1. *Volume overflow of single-lung graft*
2. *Hemodynamic instability*
3. *Primary graft dysfunction*

Later problems:

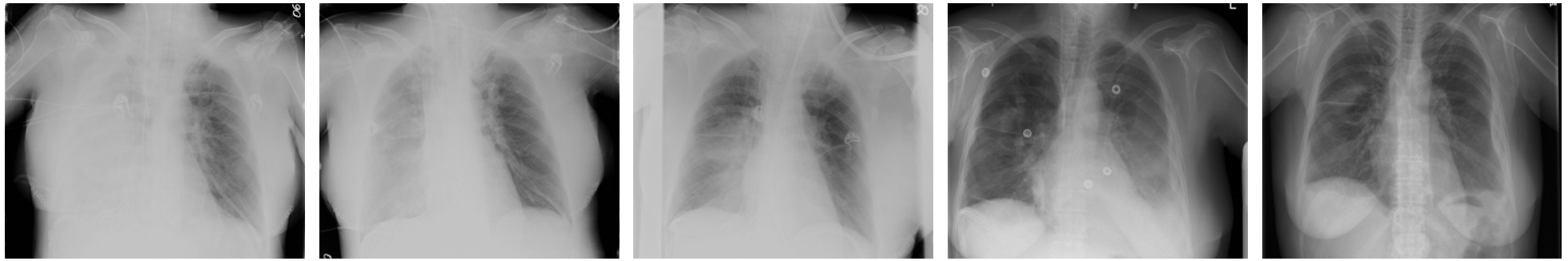
V/Q mismatch with early CLAD

Bilateral Lung Transplantation on ECMO is standard



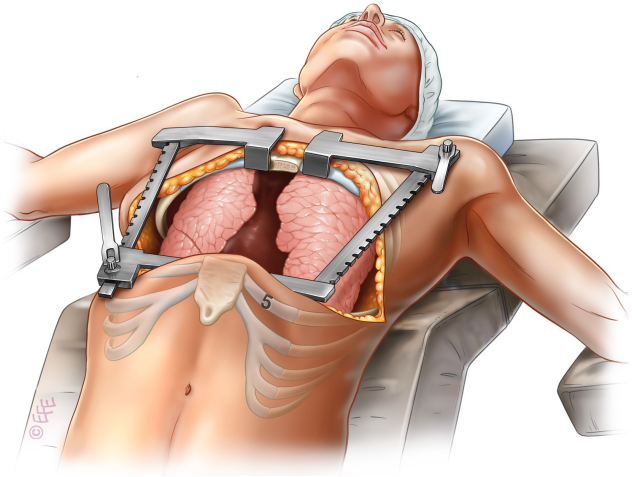


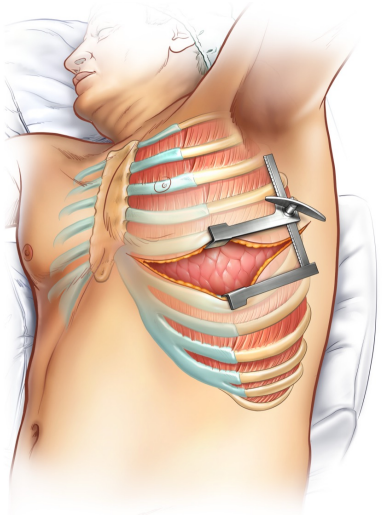
POD 1 POD 2 POD 6 POD 18 POD 30

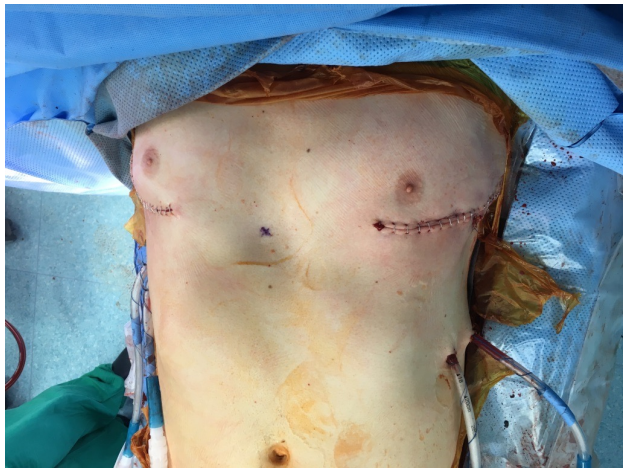


Surgical Access

- Clamshell Incision
- Anterolateral Thoracotomy
- Central cannulation (Aorta, right atrium)



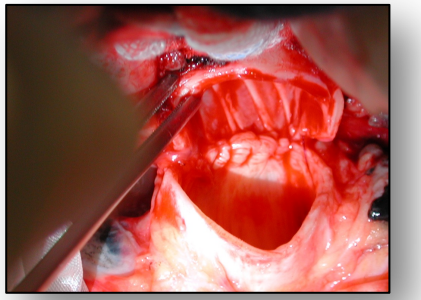


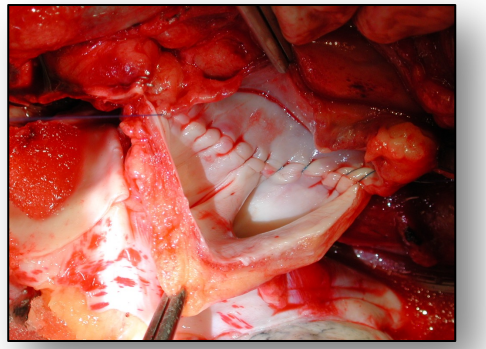


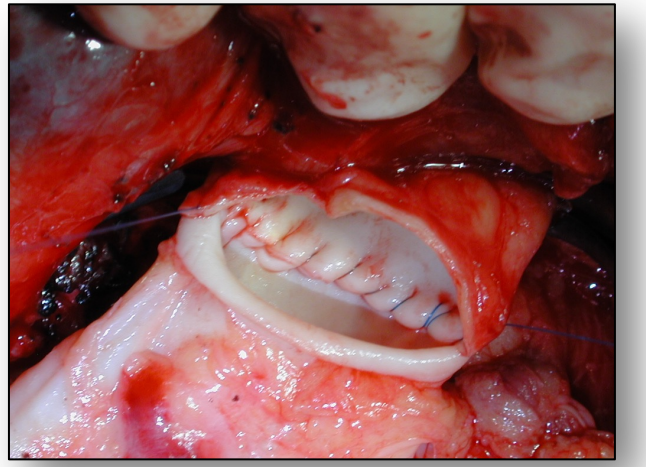
Matilla, Aigner, et al., Chest Surgery Atlas

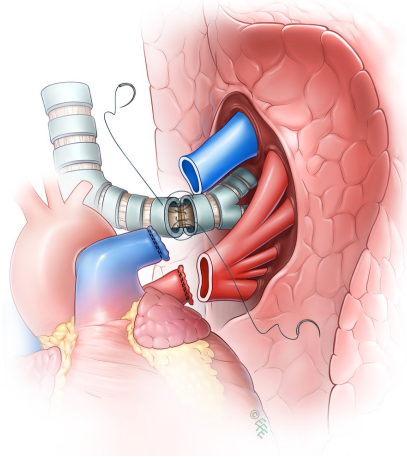
Anastomotic technique

- Bronchus
- Atrium
- Artery

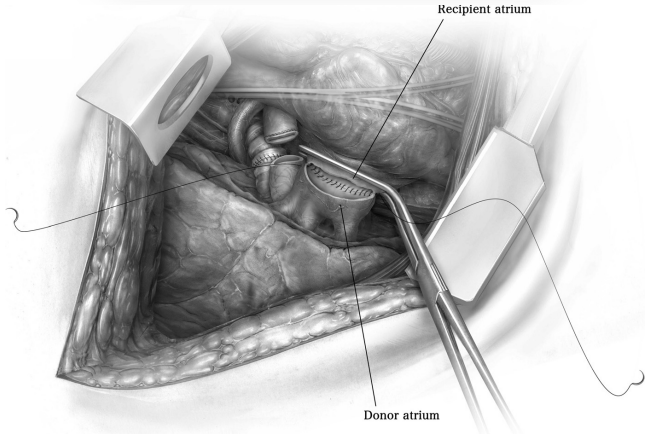




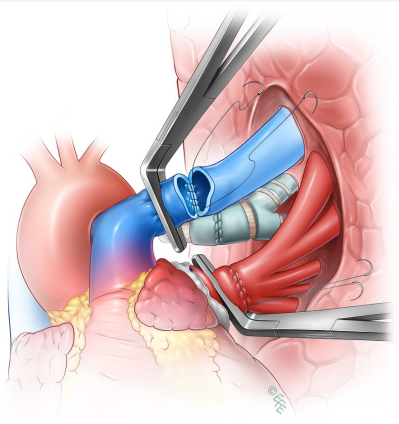


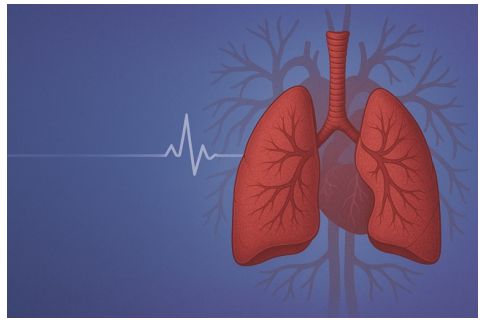


Matilla, Aigner, et al., Chest Surgery Atlas



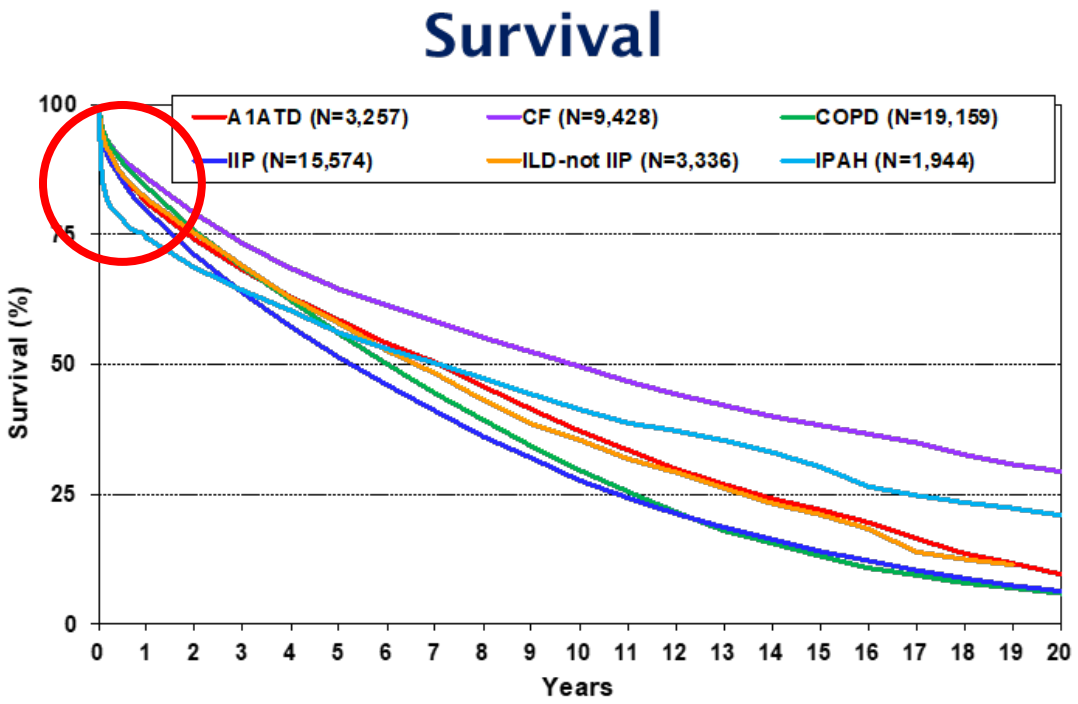
Aigner et al., Operative techniques in Thoracic and Cardiovascular Surgery

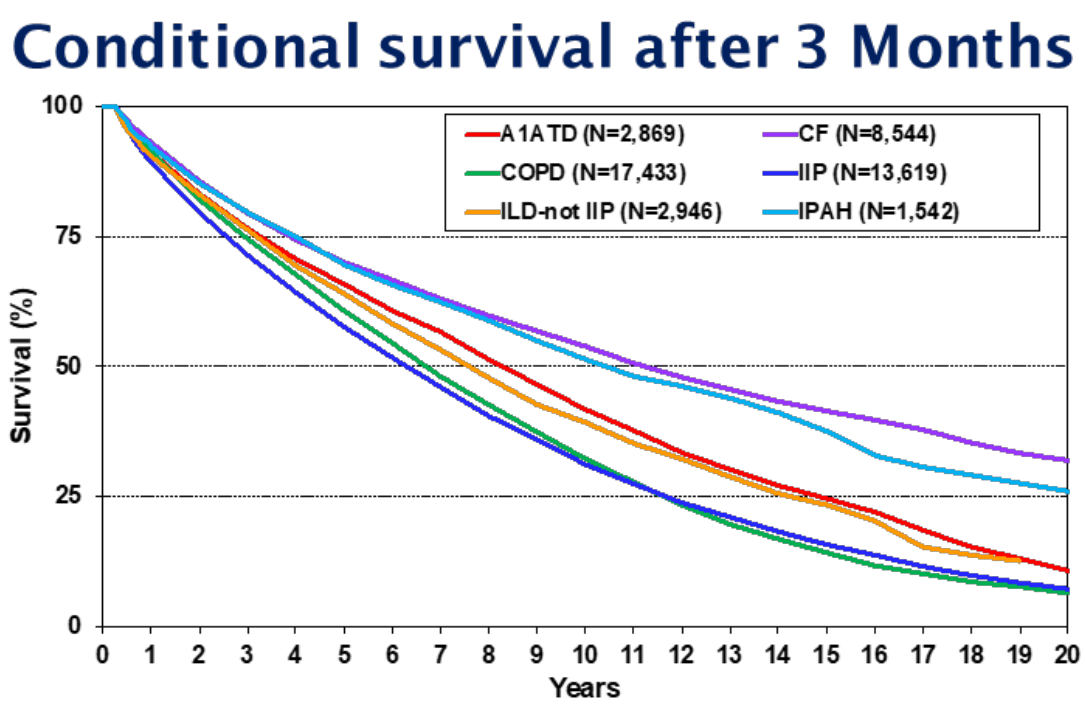




Postoperative challenges

Early postoperative management is critical



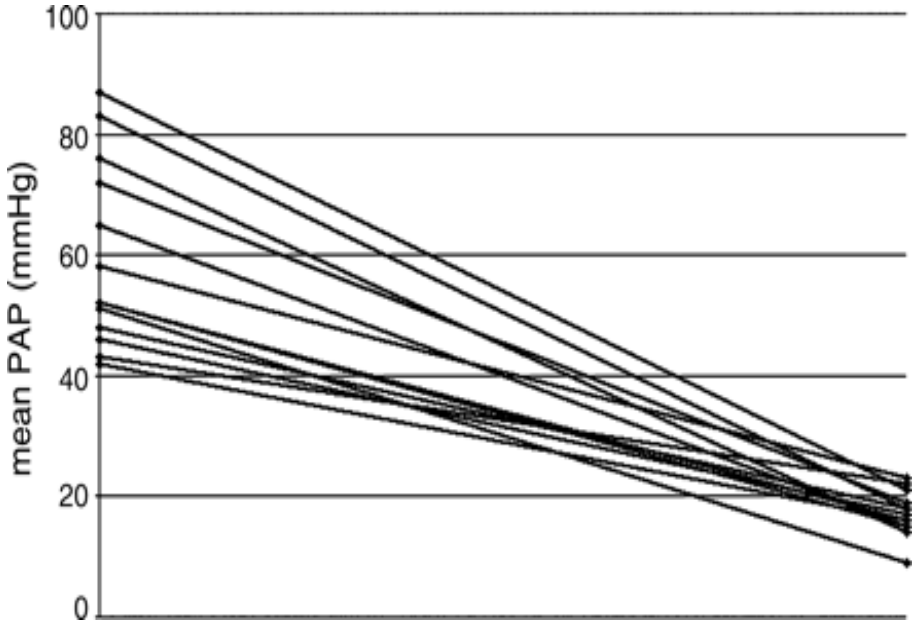


JHLT. 2019 Oct; 38(10): 1015-1066

Postoperative phase – RIGHT VENTRICLE

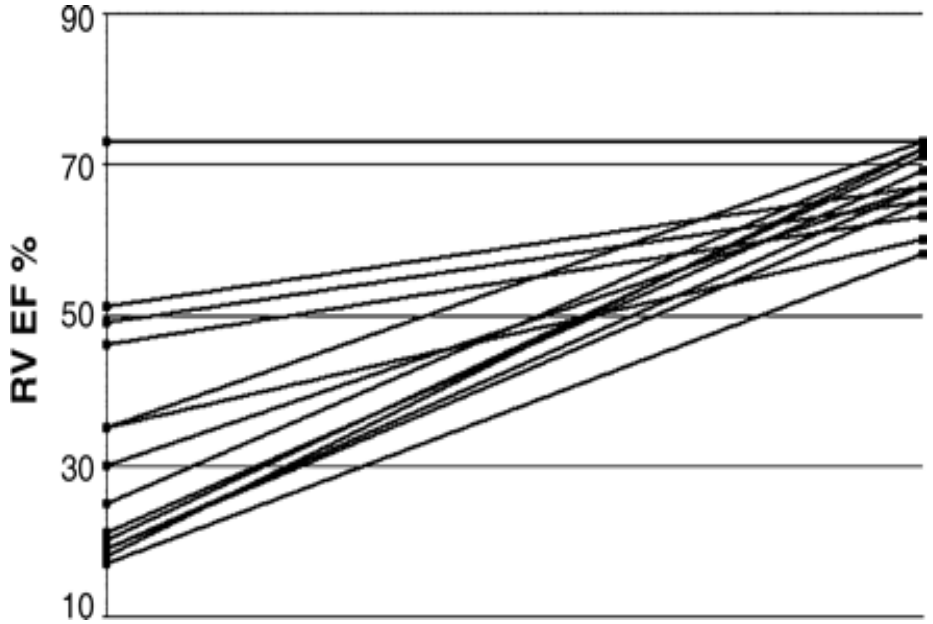
Pre-Tx failing RV … recovers after LuTx (PVR↓↓)

mPAP



before and after LuTx

RVEF



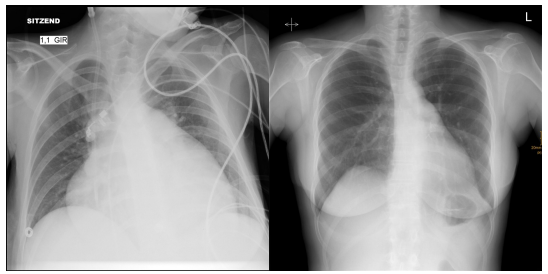
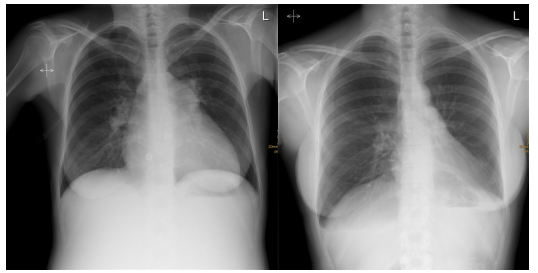
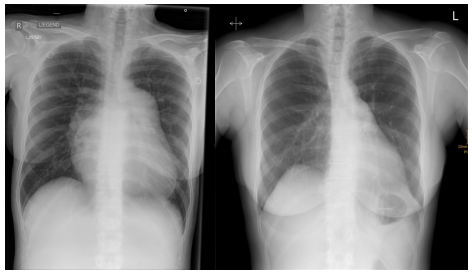
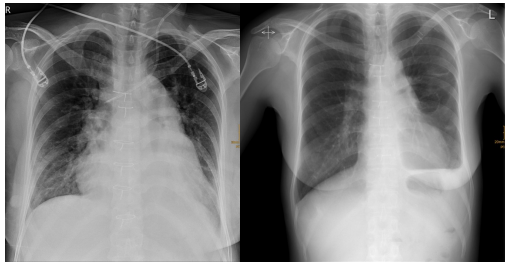
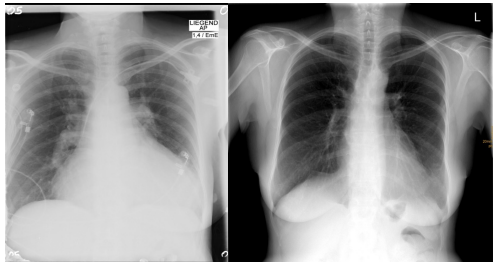
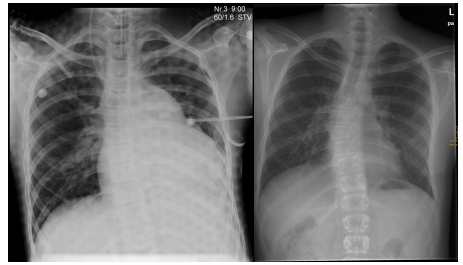
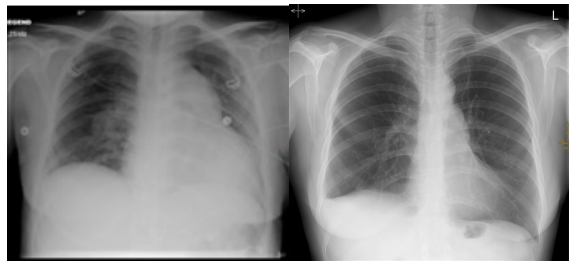
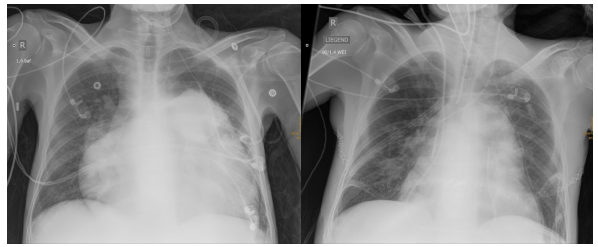
before and after LuTx

Kasimir MT et al., Eur J Cardiothorac Surg. 2004 Oct;26(4):776-81

Postoperative phase – RIGHT VENTRICLE

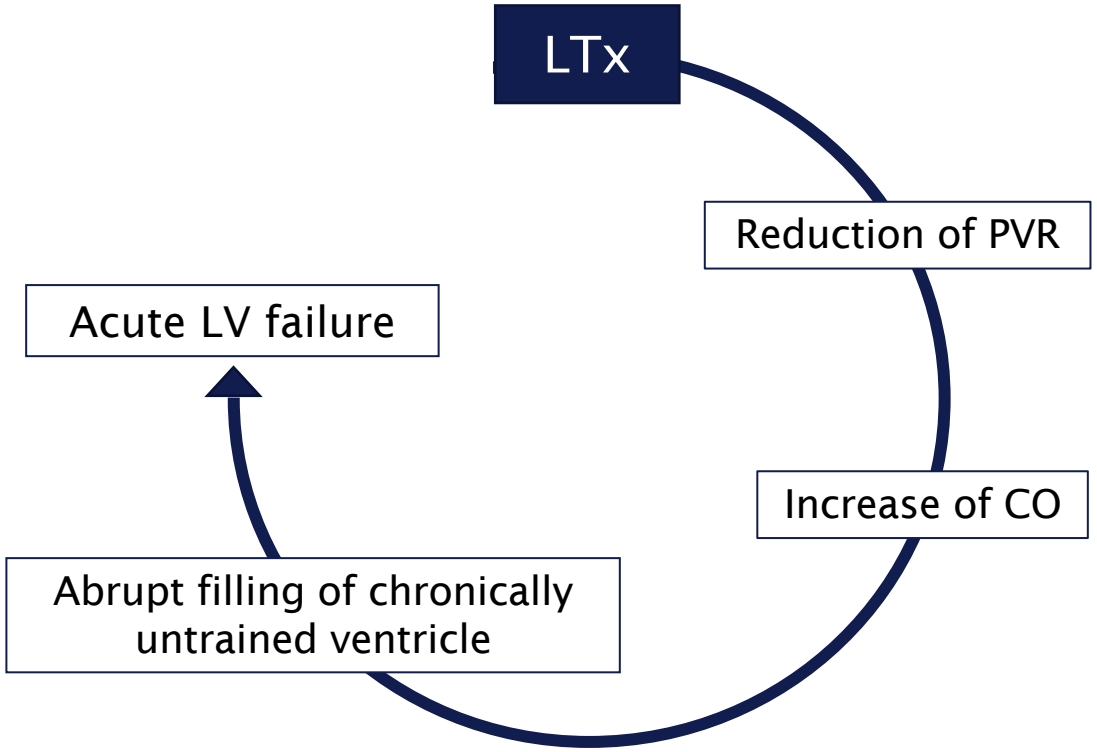
Reverse cardiac

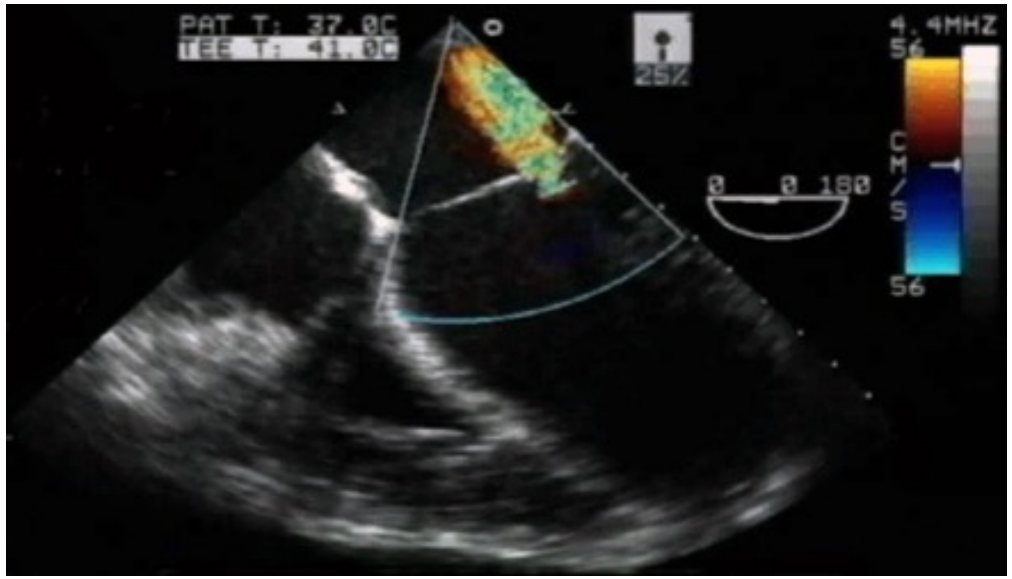
remodeling after BLTX

Acute changes after lung transplantation

LV





Transient Left Ventricular Failure Following Bilateral Lung Transplantation for Pulmonary Hypertension

Tudor Bîrsan, MD,[a] Alexander Kranz, MD,[b] Peter Mares, MD,[c] Omeros Artemiou, MD,[a] Shahrokh Taghavi, MD,[a] Andreas Zuckermann, MD,[a] and Walter Klepetko, MD[a]

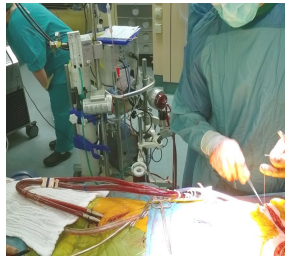
Prolongation of VA-ECMO

1. Preferred modality → peripheral femoral VA-ECMO with perfusion leg cannula

2. Two described strategies with comparable outcomes:

    I. Weaning from prolonged VA-ECMO, then gradual weaning from sedation and MV

    II. Weaning from MV, then awake VA-ECMO until LV readapts



Vienna approach – weaning from VA-ECMO then extubation

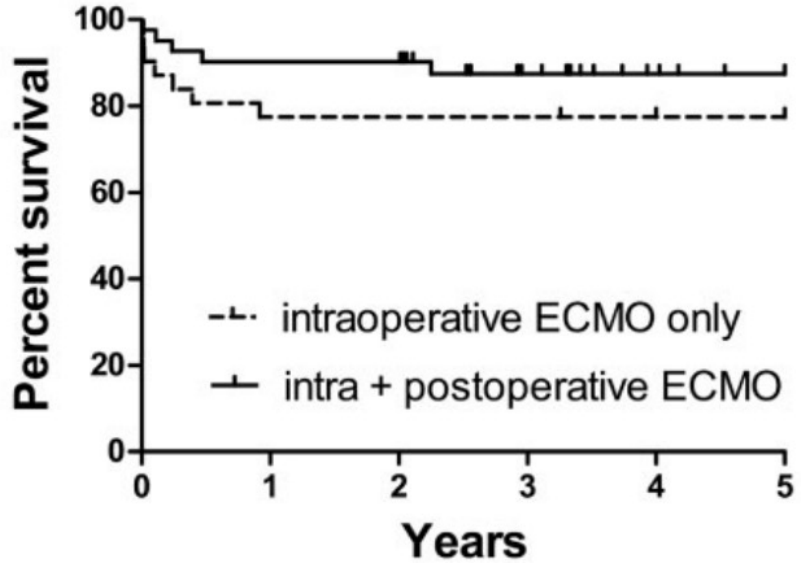
Retrospective analysis: January 2000 and December 2014

72 patients: Group A: 41 intra + postop ECMO

vs

Group B: 31 intraop ECMO only

Survival



Moser, Jaksch, Aigner, Klepetko et al. Eur J Cardiothorac Surg. 2018

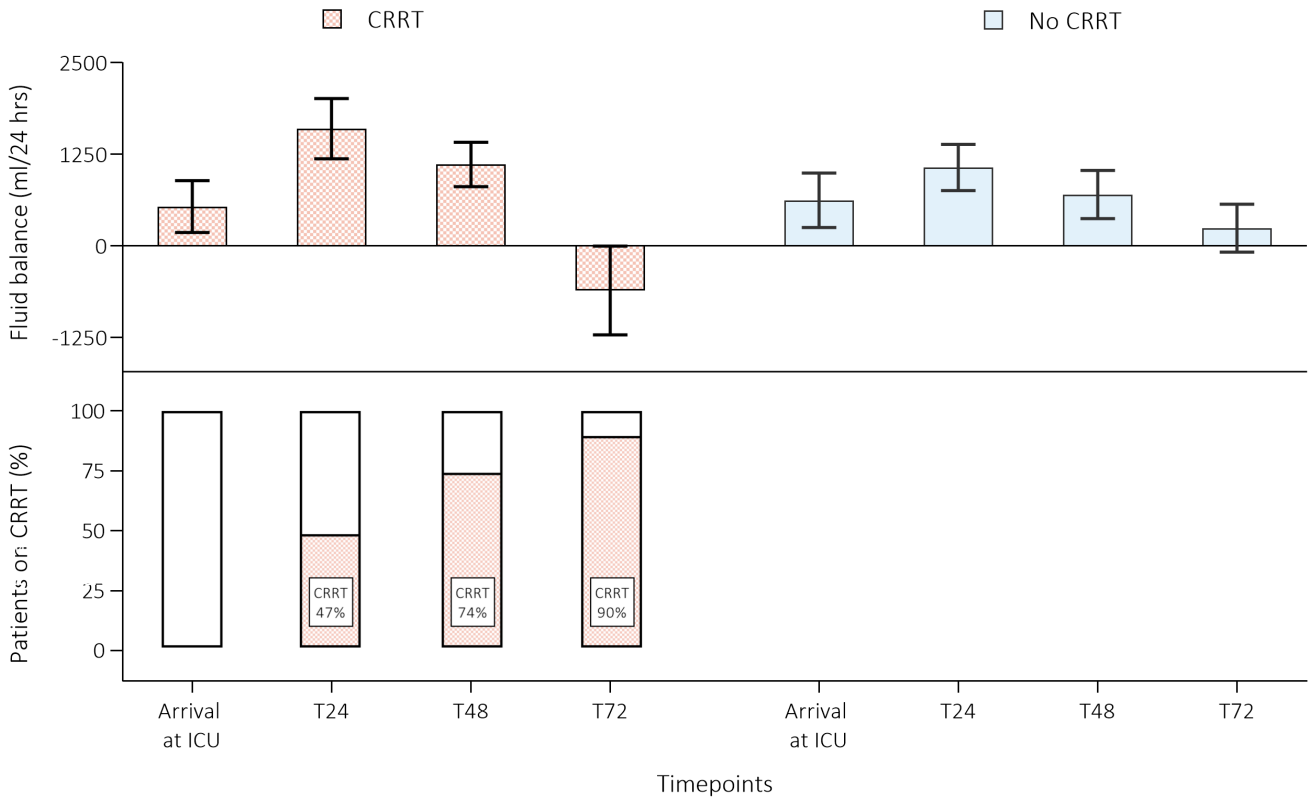
Fluid restriction/removal

1. Liberal use of loop diuretics and restrictive fluid management
2. If resistance to loop diuretics → Continuous Renal Replacement Therapy
3. Advantages of CRRT over diuretics:
    I. Highly effective
    II. Avoid neurohormonal activation
    III. Restore diuretic sensitivity
    IV. No long-term impairment of kidney function

Early implementation of renal replacement therapy after lung transplantation does not impair long-term kidney function in patients with idiopathic pulmonary arterial hypertension

THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY

- Study period: 2000 – 2018, 87 patients
- Criteria to start CRRT:
  - Resistance to diuretic therapy
  - Urine volume < 1000 ml/24 hrs
  - Fluid retention > 1500 ml/24 hrs
- 38 (43%) patients with CRRT for **16 d (10-22)**

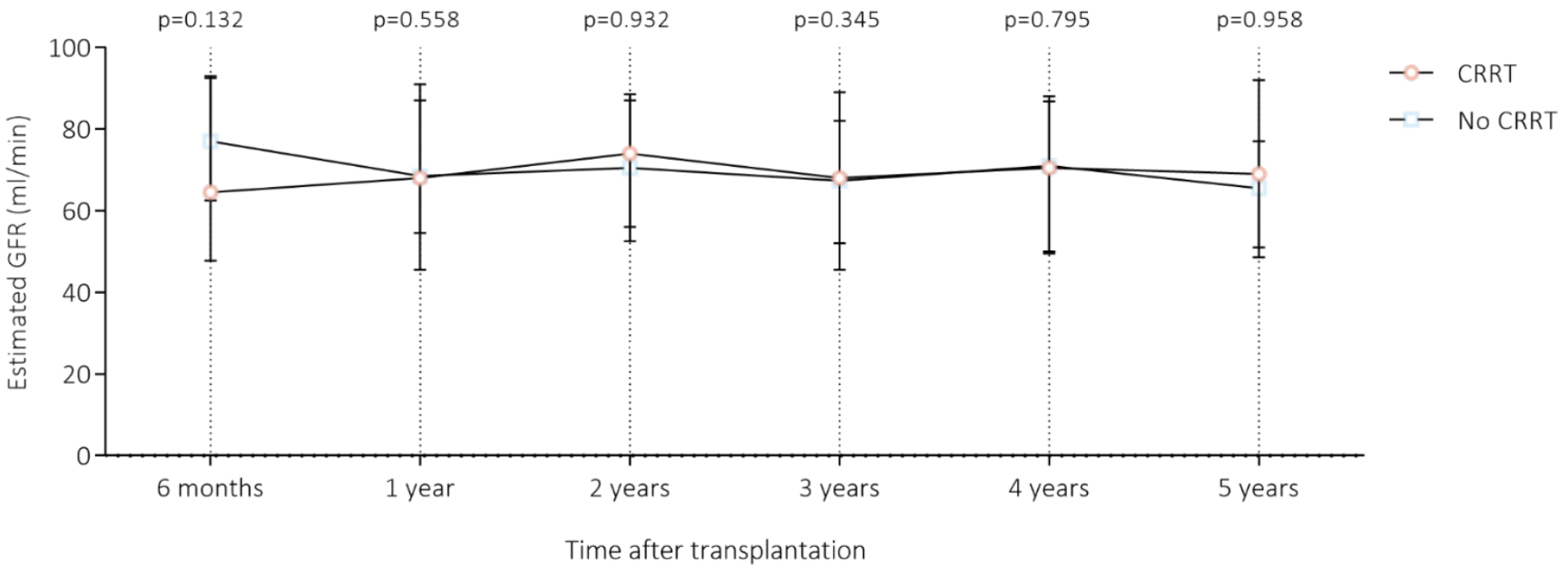


Benazzo et al. J Thorac Cardiovasc Surg. 2022 Feb;163(2):524-535.e3

Early implementation of renal replacement therapy after lung transplantation does not impair long-term kidney function in patients with idiopathic pulmonary arterial hypertension

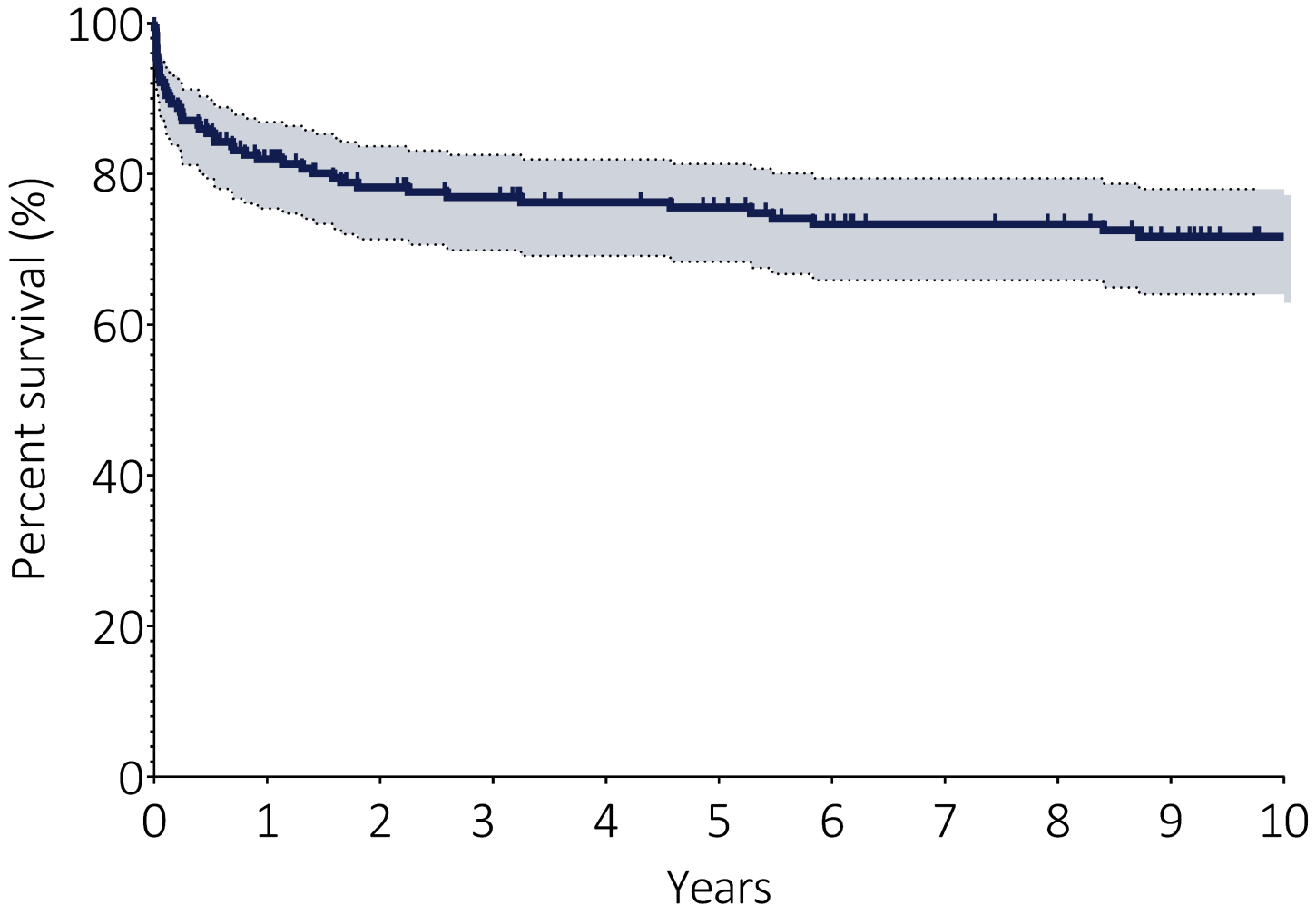
THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY

Long-term estimated GFR



Benazzo et al. J Thorac Cardiovasc Surg. 2022 Feb;163(2):524-535.e3

Vienna long-term survival of PAH



Conclusions

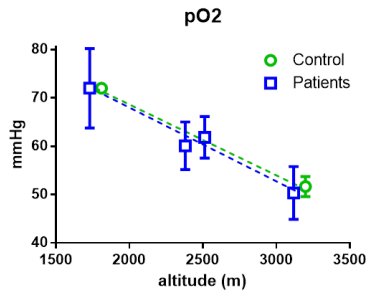
- **Double lung transplantation on intraoperative VA-ECMO** is associated with excellent outcomes
- **Acute left ventricular failure** represents the main challenge in the postoperative phase
- Excellent long term outcome and quality of life can be achieved after lung transplantation for PAH

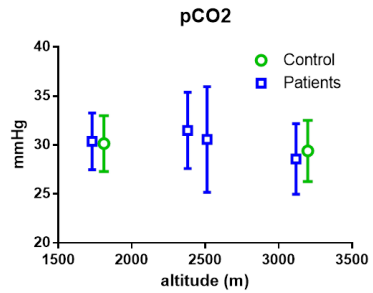
Lung Transplant Patients on Djebel Toubkal (4167m)

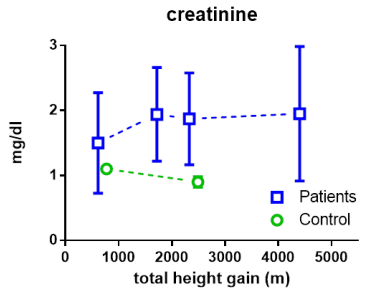
- 18 LuTX patients, 30 medical personell (Austria, Hungary, Germany, Italy, Greece)

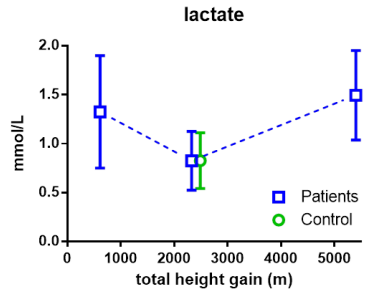
LuTX patients on Djebel Toubkal (4167m)

- 18 LuTX patients, 30 medical personell (Austria, Hungary, Germany, Italy, Greece)









2026....

Kontakt & Sponsoren

Projektleitung:
Dr. Peter Jaksch
Medizinische Universität Wien
E-Mail: peter.jaksch@meduniwien.ac.at

Spenden & Sponsoring:
Verein Lunge Aktiv
IBAN: AT65 12000 10018987577
BIC: BKAUATWW

Angefragte Partner & Sponsoren
- Medizinische Partner: ISHLT, ESOT, ERS, ÖGP, MUW, ATX
- Unternehmen: Sanofi, Chiesi, Novartis, Biotest, Paragonix, Therakos, bioMérieux
- Öffentliche Einrichtungen: Österreichisches Sportministerium, Krankenhaus Hochegg
- Expeditionsorganisation: Furtenbach Adventures GmbH

Medien & Öffentlichkeitsarbeit
- Professionelle TV-Dokumentation
- Umfangreiche Social-Media-Kampagne: @AktivLunge
- Internationale Presse- und Öffentlichkeitsarbeit
- Präsentationen auf medizinischen und wissenschaftlichen Konferenzen weltweit

Herzlichen Dank für Ihre Unterstützung und Zusammenarbeit!

LUNGEAKTIV

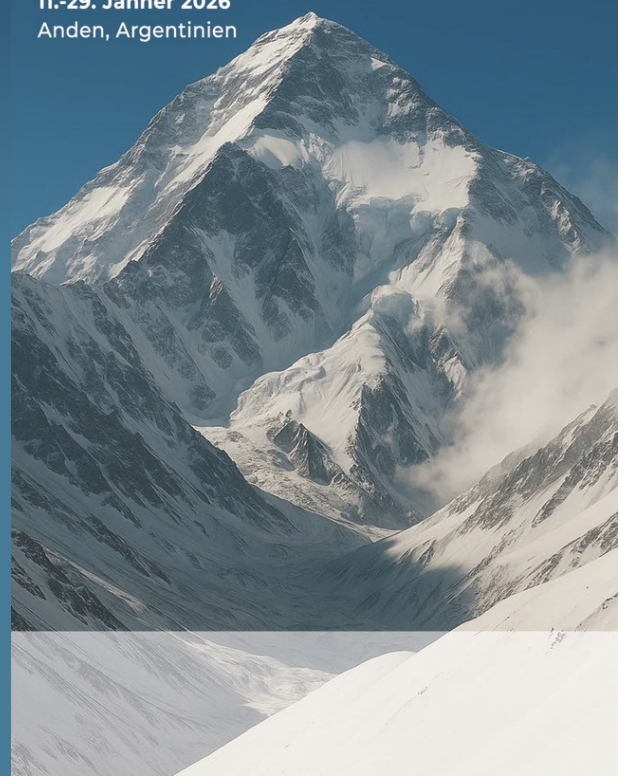
UPCOMING EXPEDITION

A Breath Above: Aconcagua 2026

Pioneering the Limits of Transplantation

6 961 M 22 838 FT

11.-29. Jänner 2026
Anden, Argentinien



Thank you!