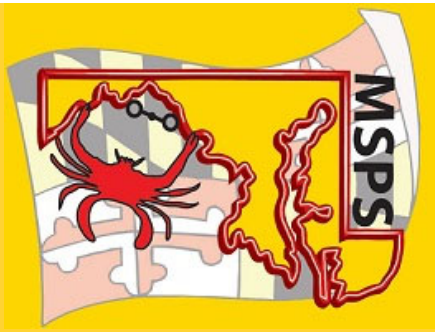
MAVES
Mid-Atlantic VAD and ECMO Symposium



Welcome to the 12th Annual MAVES

3 May 2020

MAVES
Mid-Atlantic VAD and ECMO Symposium

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Use of ECMO and Cardiopulmonary Bypass in Lung Transplantation

A. Sasha Krupnick
Surgical Director of Lung Transplantation
University of Virginia/University of Maryland as of July 2020

Disclosures

- I’m a surgeon (don’t ask complicated questions)

- Courier Therapeutics (no relation to current topic)

Outline

- Lung Transplantation
  - History and current data of lung transplantation
  - Limitations of the filed
  - Pre-operative use of extracorporeal oxygenation
  - Selective vs Elective vs. Emergent use of extracorporeal oxygenation /circulatory support intraoperatively
  - Pre-operative use of extracorporeal oxygenation/ circulatory support

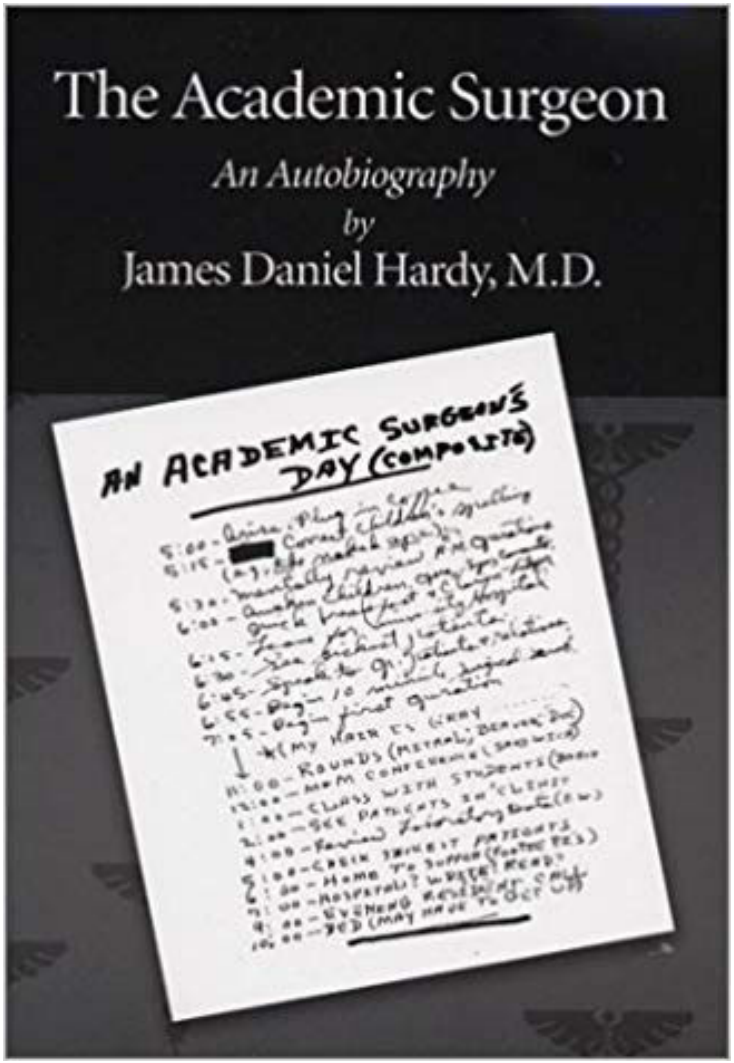
History of Human Lung Transplantation

James Hardy
1918-2003

First human lung transplant on June 11, 1963
Immunosuppression: thymic irradiation, azathioprine and prednisone

Patient died 3 weeks after due to renal failure

This event was over shadowed by death of civil rights advocate Medgar Evers



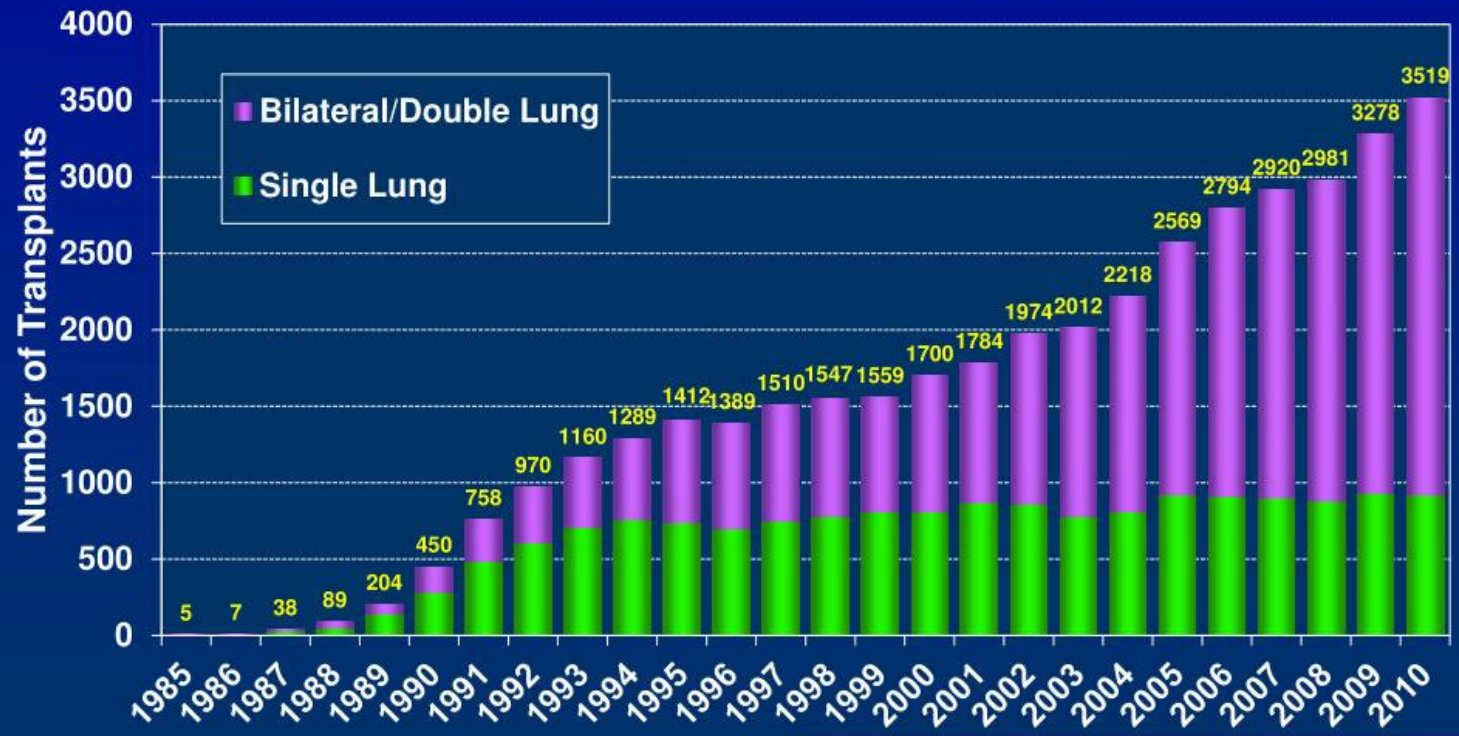
1964-First heart transplant in man/primate to human

Modern Era of Lung Transplantation

1963-1978 - 38 lung or heart/lung transplants performed-none left the hospital

1983 – University of Toronto: single lung TX ; Success
1983 – University of Toronto: double lung TX; success
1989 – Washington University: bilateral sequential lung TX

NUMBER OF LUNG TRANSPLANTS REPORTED BY YEAR AND PROCEDURE TYPE



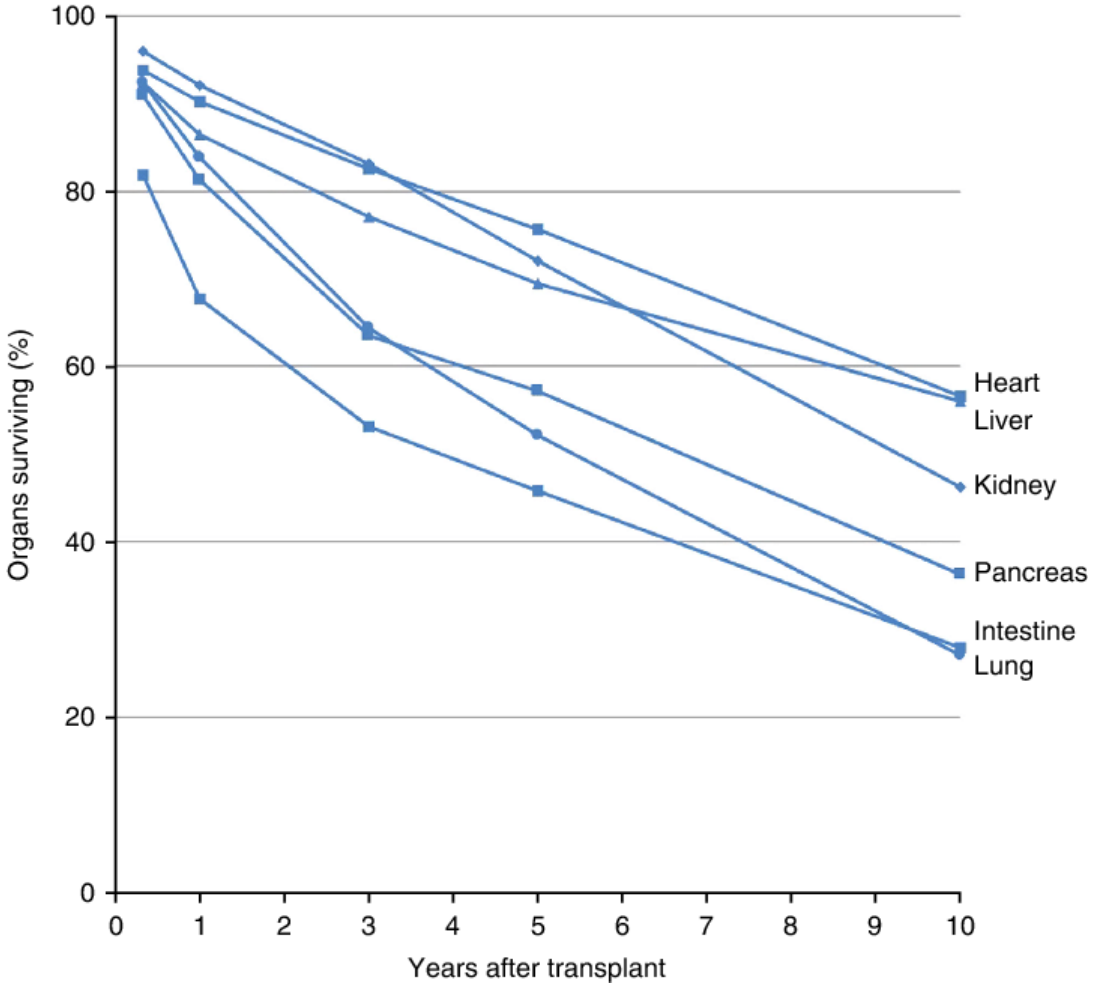
NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.

ISHLT

2012

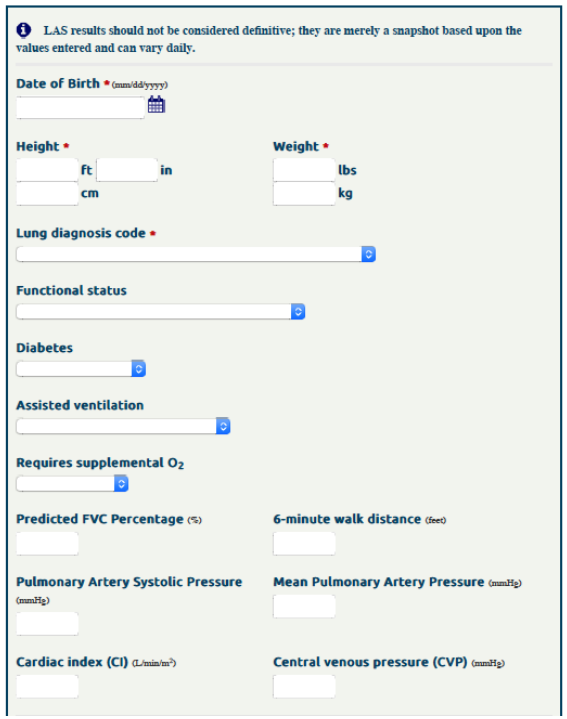
J Heart Lung Transplant. 2012 Oct; 31(10): 1045-1095

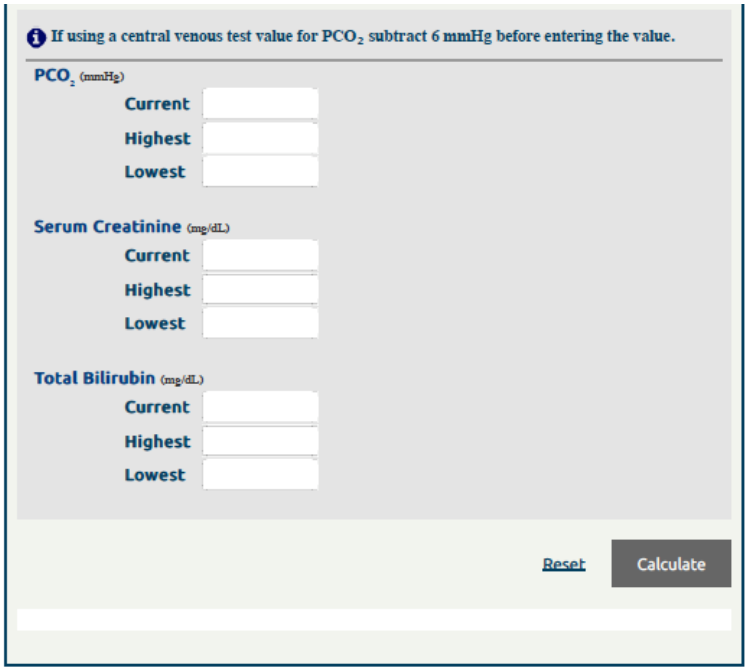
Solid Organ Survival



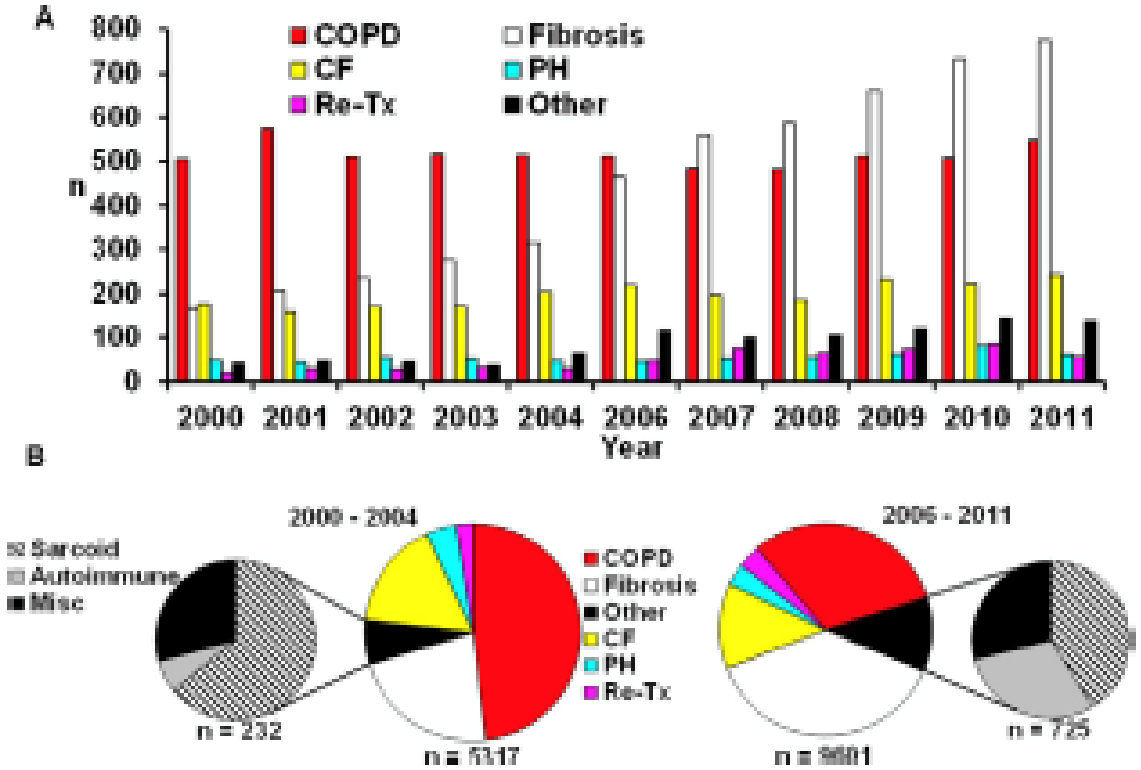
Use of ECMO as Bridge to Lung Transplantation

- 2005-LAS (Lung Allocation Score) System;
- 2017-Donation Service Area (DSA) as the first level of distribution with a 250 nautical mile circle around the donor hospital.





Use of ECMO as Bridge to Lung Transplantation



Effect of the lung allocation score on lung transplantation in the United States

Thomas M. Egan, MD, MSc,[a,1] and Leah B. Edwards, PhD[b]

The Journal of Heart and Lung Transplantation, Vol 35, No 4, April 2016

Use of ECMO as Bridge to Lung Transplantation

1987-2008

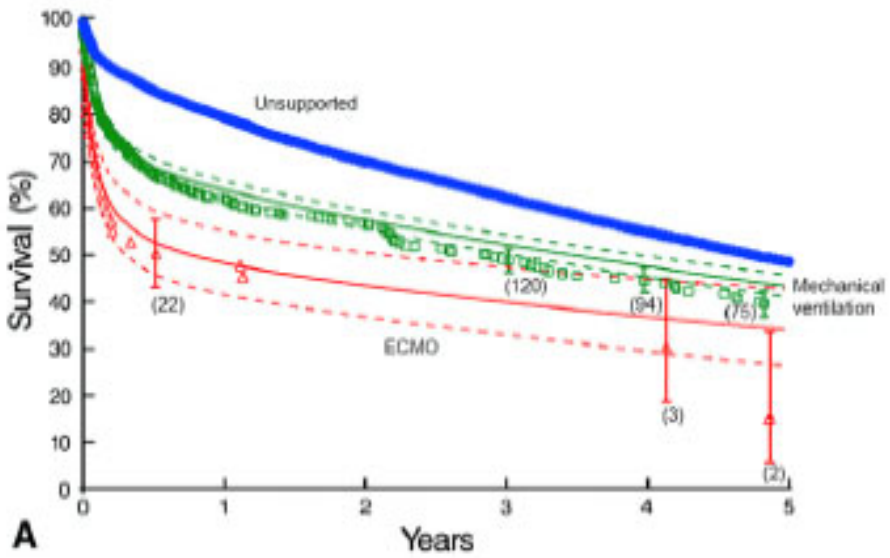
TABLE 2. Lung transplant recipient and donor characteristics, details of transplantation, and in-hospital posttransplant events in ventilatory-supported and unsupported patients (continuous variables)

Variable	Mechanical ventilation (n = 586) n*	Mean ± SD or 15th/50th/85th percentiles	ECMO (n = 51) n*	Mean ± SD or 15th/50th/85th percentiles	Unsupported (n = 15,297) n*	Mean ± SD or 15th/50th/85th percentiles	P
Recipient							
Demographic							
Age (y)	586	38 ± 21	51	39 ± 22	15,297	48 ± 14	<.0001
BMI (kg/m^2)	529	23 ± 5.3	42	25 ± 4.9	14,839	24 ± 4.8	<.0001

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

David P. Mason, MD,[a] Lucy Thuita, MS,[b] Edward R. Nowicki, MD, MS,[a] Sudish C. Murthy, MD, PhD,[a] Gösta B. Pettersson, MD, PhD,[a] and Eugene H. Blackstone, MD[a,b]

The Journal of Thoracic and Cardiovascular Surgery • Volume 139, Number 3



Use of ECMO as Bridge to Lung Transplantation

1987-2008

TABLE 2. Lung transplant recipient and donor char
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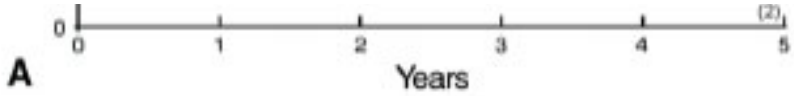
The Journal of Thoracic and Cardiovascular Surgery • Volume 139, Numb

Table 1
Recipient condition at the time of transplant

	2010		2015	
Medical condition				
Hospitalized in ICU	150	8.4%	276	13.0%
Hospitalized not in ICU	148	8.3%	242	11.8%
Not hospitalized	1487	83.3%	1530	74.5%
Hospitalization unknown	0	0.0%	16	0.8%
Vent/ECMO at transplant				
Vent + ECMO	22	1.2%	63	3.1%
Vent only	130	7.3%	64	3.1%
ECMO only	7	0.4%	33	1.6%
Neither	1626	91.1%	1895	92.2%

Abbreviation: ICU, intensive care unit.

From Valapour M, Skeans MA, Smith JM, et al. Optn/srtr 2015 annual data report: lung. Am J Transplant 2017;17(Suppl 1):413; with permission.



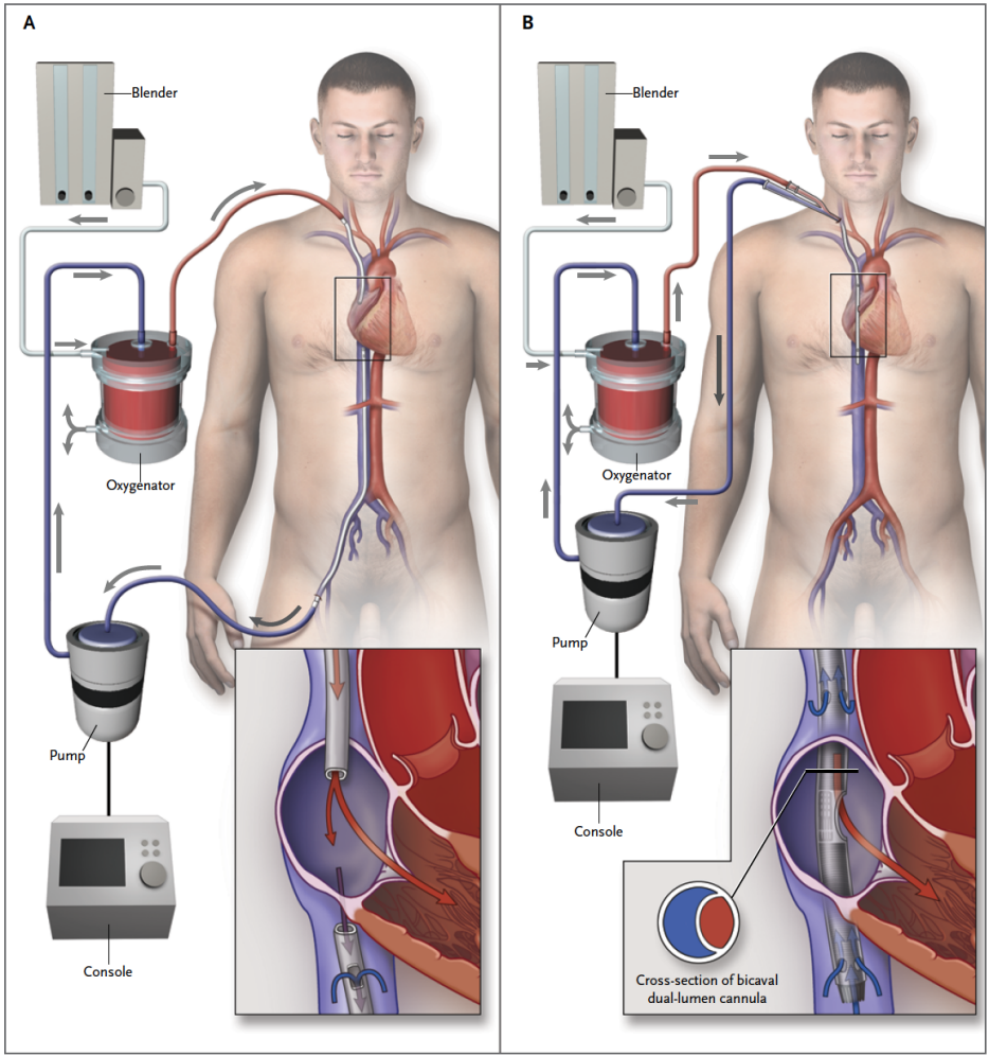
Use of ECMO as Bridge to Lung Transplantation

Absolute contraindications

Contraindications for the use of ECMO as a bridge to lung transplantation are as follows:

1. Ineligibility for lung transplant
2. Refractory bacteremia or septic shock
3. Irreversible multiorgan damage (other than lungs)
4. Severe arterial occlusive disease
5. Contraindications to systemic anticoagulation
6. Uncontrolled metastatic disease or other terminal illness that is not otherwise treatable with lung transplant
7. Acute intracerebral hemorrhage or stroke

Use of ECMO as Bridge to Lung Transplantation



Use of ECMO as Bridge to Lung Transplantation

The "Sport Model": Extracorporeal Membrane Oxygenation Using the Subclavian Artery

Mauer Biscotti, MD, and Matthew Bacchetta, MD

(Ann Thorac Surg 2014;98:1487–9)

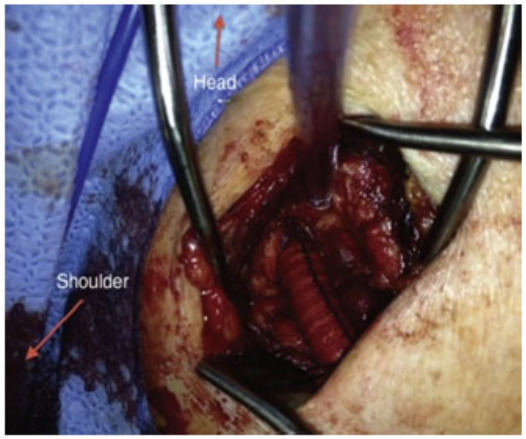


Fig 1. Hemashield graft and subclavian artery anastomosis shown during an operation. The arrows indicate the orientation of the patient as labeled.

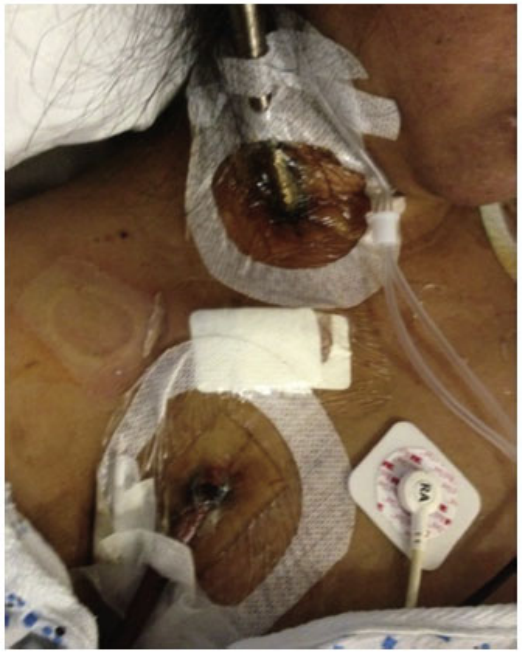


Fig 3. "Sport model" configuration. RA indicates right atrial electrocardiographic lead.

Use of ECMO as Bridge to Lung Transplantation

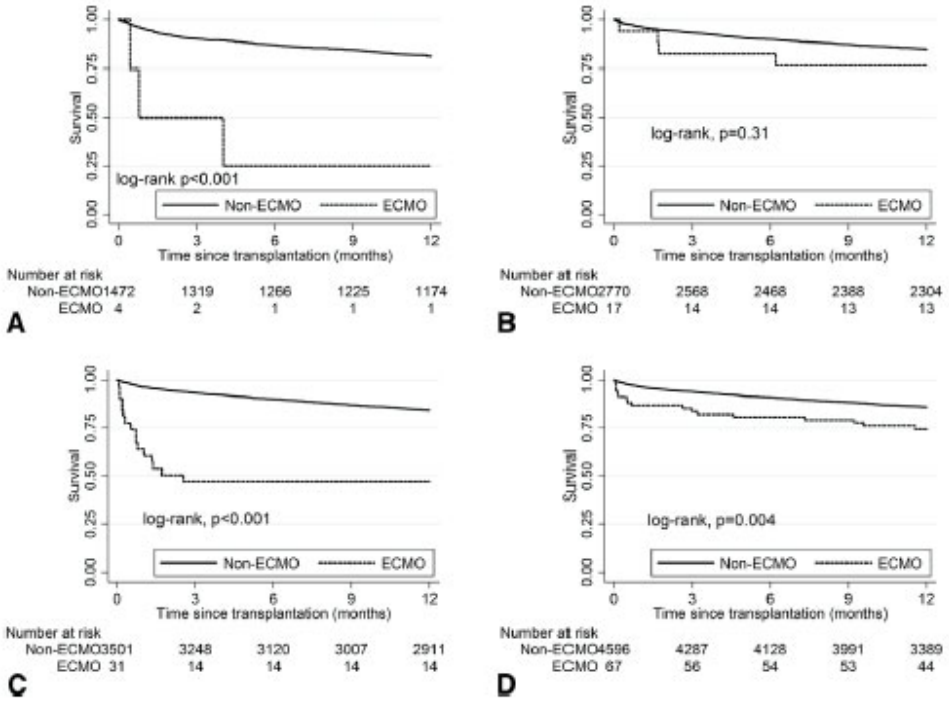


FIGURE 1. Kaplan–Meier curves comparing survival between patients with and without ECMO bridge to lung transplantation accord 2000 to 2002 (A), 2003 to 2005 (B), 2006 to 2008 (C), and 2009 to 2011 (D). *ECMO*, Extracorporeal membrane oxygenation.

Extracorporeal membrane oxygenation as a bridge to lung transplantation in the United States: An evolving strategy in the management of rapidly advancing pulmonary disease

Awori J. Hayanga, MD, MPH,[a] Jonathan Aboagye, MD, MPH,[b] Stephen Esper, MD, MBA,[c] Norihisa Shigemura, MD, PhD,[d] Christian A. Bermudez, MD,[d] Jonathan D'Cunha, MD, PhD,[d] and Jay K. Bhama, MD[e]

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Use of ECMO as Bridge to Lung Transplantation

Table 3
Summary of recent studies reviewing 1-year survival outcomes of ECMO bridging conditional on receiving a lung transplant after ECMO

Single Center Studies	Number of Patients	1-y Survival
Lang et al,[33] 2012	34	63%
Shafii et al,[17] 2012	19	79%
Weig et al,[34] 2013	26	54%
Crotti et al,[35] 2013	22	79%
Lafarge et al,[36] 2013	36	60%
Inci et al,[38] 2015	26	68%
Biscotti et al,[39] 2017	40	92%

FI
20

Norihisa Shigemura, MD, PhD,[a] Christian A. Bermudez, MD,[a] Jonathan D'Cunha, MD, PhD,[a] and Jay K. Bhama, MD[c]

Use of ECMO as Bridge to Lung Transplantation

Box 1
Factors that affect posttransplant survival in patients on ECMO support

Favorable factors
- Age less than 50 years
- Normal or marginally elevated total bilirubin
- Normal or mildly elevated pulmonary artery pressures
- Less than 14-day duration on ECMO
- Low SOFA score (<6)
- Noninvasive ventilation
- Ability to participate in physical therapy (ie, "awake ECMO")

Unfavorable factors
- Age greater than 60 years
- Total bilirubin greater than 3
- Severe pulmonary hypertension
- Prolonged ECMO (>14 days)
- Prolonged mechanical ventilation
- Prolonged immobility on ECMO
- SOFA score greater than 9
- Major bleeding, infectious complications, or end-organ perfusion
- Complications on ECMO
- Retransplant with a retransplant interval less than 1 year

Abbreviations: ECMO, extracorporeal membrane oxygenation; SOFA, sequential organ failure assessment.

Adapted from Loor G, Simpson L, Parulekar A. Bridging to lung transplantation with extracorporeal circulatory support: when or when not? J Thorac Dis 2017;9:3352–61; with permission.

Use of ECMO as Bridge to Lung Transplantation

Box 1
Factors that affect posttransplant survival in patients on ECMO support

Favorable factors
- Age less than 50 years
- Normal or marginally elevated total bilirubin
- Normal or mildly elevated pulmonary artery pressures

Two fundamental questions are important when deciding to place a patient on ECMO:

I. Is this patient a potential candidate for a lung transplant?
II. Is the prognosis reasonable for surviving to transplant and having quality of life and survival after transplant?

- Prolonged ECMO (>14 days)
- Prolonged mechanical ventilation
- Prolonged immobility on ECMO
- SOFA score greater than 9
- Major bleeding, infectious complications, or end-organ perfusion
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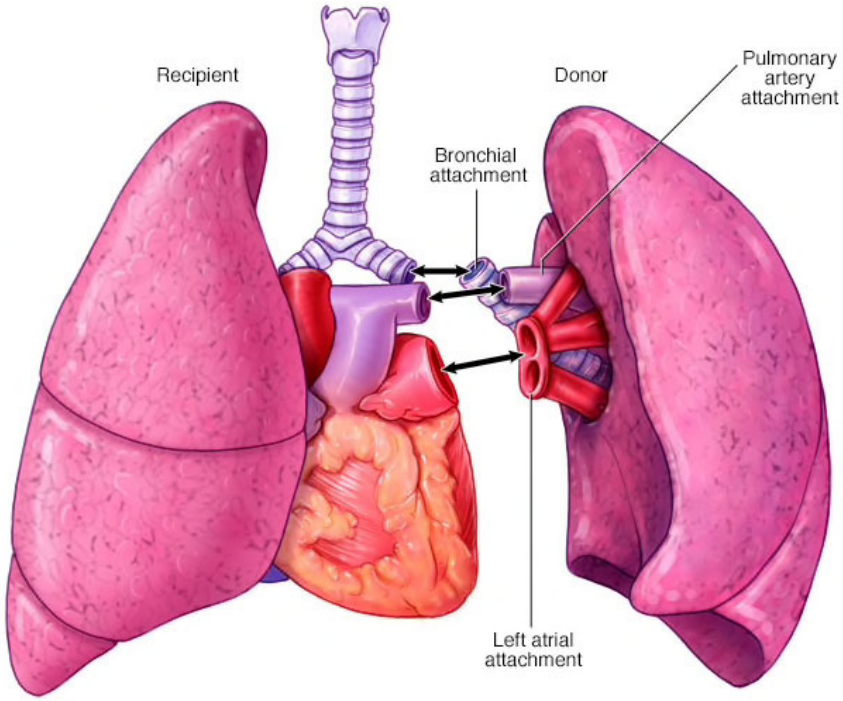
Intraoperative Circulatory Support for Lung Transplantation



No extracorporeal support

Partial support

Full support

Intraoperative Circulatory Support for Lung Transplantation

Globally, interoperative use of mechanical circulatory/ventilatory support for lung transplantation ranges from 30 to 50% with variations between centers regarding type of device and timing.

Off Pump-Pros: no heparin, no risk of cannulation, circuit activation of inflammatory mediators

Off Pump-Cons: hemodynamic instability during dissection, poor oxygenation due to single lung ventilation of bad lung, after implantation the new lung gets 100% of the blood flow right away.

ECMO vs. full CPB: use of pump suction for tough dissection, different degree of anticoagulation, full vs partial support

Intraoperative Circulatory Support for Lung Transplantation

In God we trust; all others must bring data. W. Edwards Deming

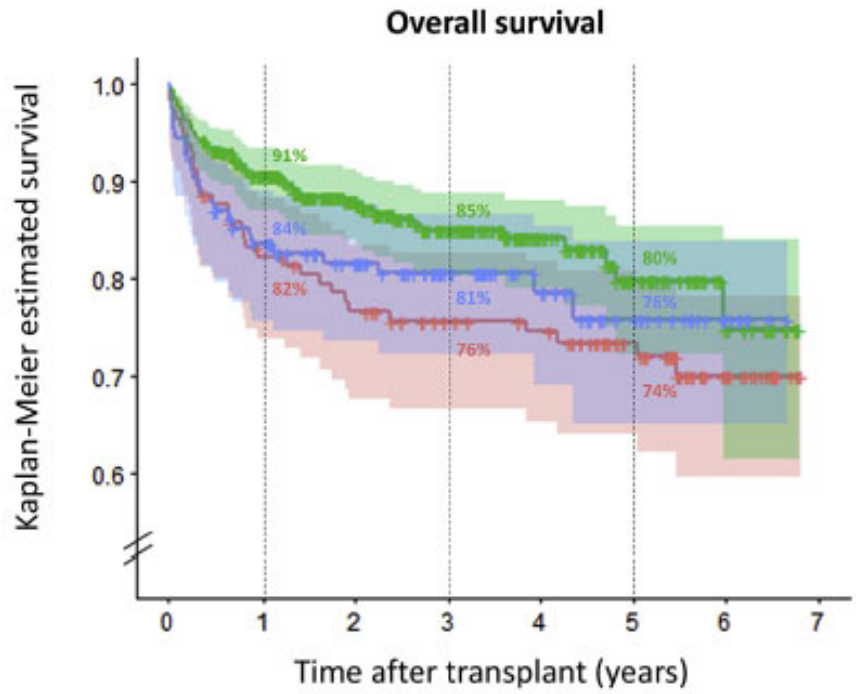
Early days prior to LAS-most COPD patients

Cardiopulmonary bypass for bilateral sequential lung transplantation in patients with chronic obstructive pulmonary disease without adverse effect on lung function or clinical outcome

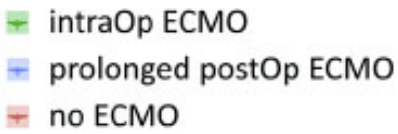
Wilson Y. Szeto, MD[a]

The Journal of Thoracic and Cardiovascular Surgery • August 2002

Intraoperative Circulatory Support for Lung Transplantation



intraOp ECMO	340	272	194	136	77	40	14	0
prolonged postOp ECMO	123	97	80	56	38	21	7	0
no ECMO	114	90	82	72	68	48	20	0



Intraoperative extracorporeal membrane oxygenation and the possibility of postoperative prolongation improve survival in bilateral lung transplantation

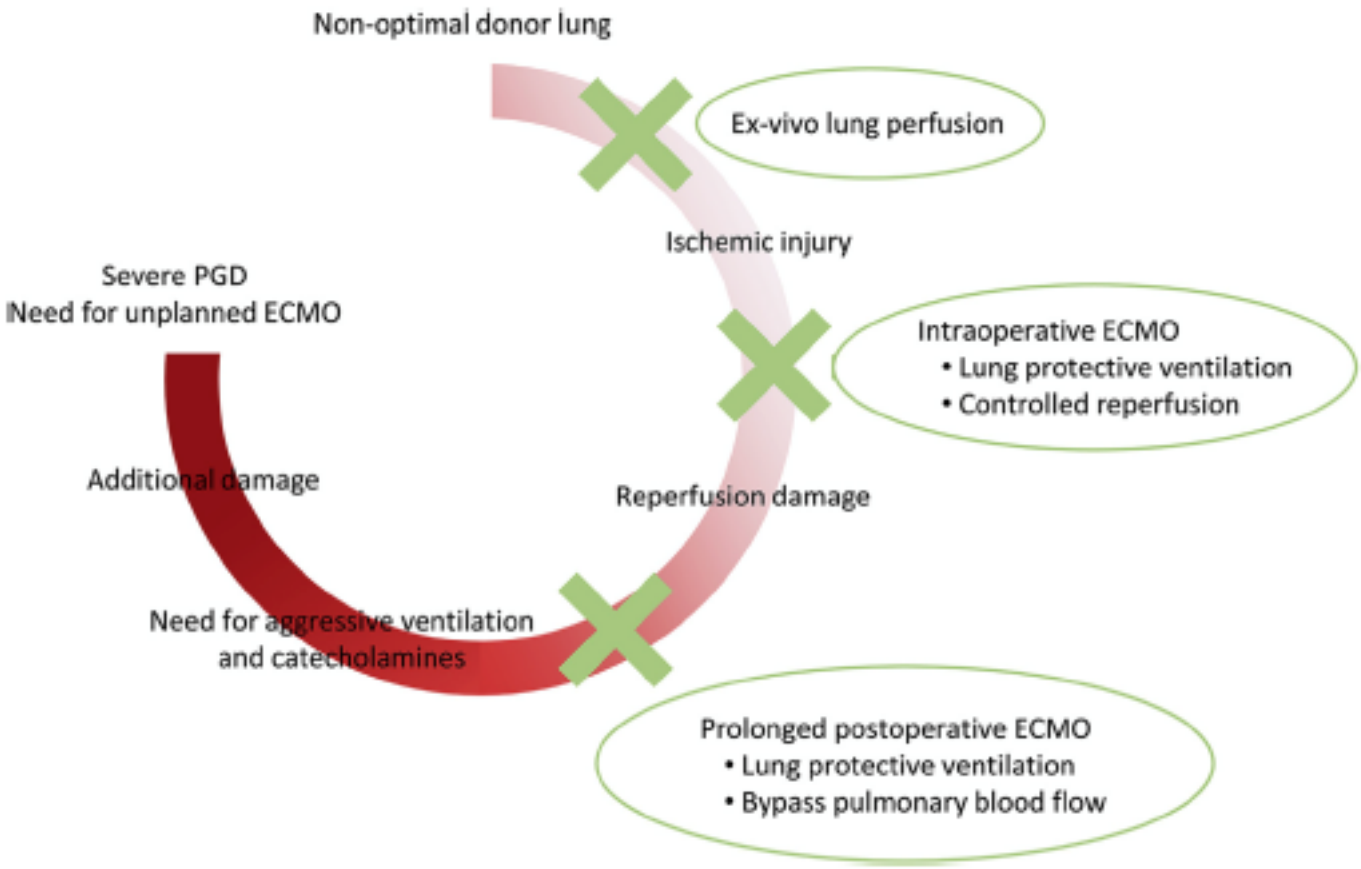
Konrad Hoetzenecker, MD, PhD,[a] Stefan Schwarz, MD,[a] Moritz Muckenhuber, MD,[a] Alberto Benazzo, MD,[a] Florian Frommlet, PhD,[b] Thomas Schweiger, MD, PhD,[a] Orsolya Bata, MD,[c] Peter Jaksch, MD,[a] Negar Ahmadi, MD,[d] Gabriella Muraközy, MD,[a] Helmut Prosch, MD,[e] Helmut Hager, MD,[f] Georg Roth, MD,[f] György Lang, MD, PhD,[a,g] Shahrokh Taghavi, MD,[a] and Walter Klepetko, MD[a]

The Journal of Thoracic and Cardiovascular Surgery • Volume 155, Number 5

Intraoperative Circulatory Support for Lung Transplantation

UVA Protocol
-elective central ECMO for all cases
-hep 50U/kg with goal of ACT180-220
-analyzing data now

Postoperative Circulatory Support for Lung Transplantation



Postoperative Circulatory Support for Lung Transplantation

Table 3 Published case series on secondary ECMO implant after lung transplantation

Study	N patients	Survival	Weaned patients	Time ECMO-weaning (days)
Meyers *et al.*, 2000 (64)	12 (2.7)	–	8 (66.6)	4.2 (mean)
Dahlberg *et al.*, 2004 (65)	16 (9.3)	46% at 2 years	–	–
Oto *et al.*, 2004 (66)	10 (2.1)	–	4 (40.0)	4 (mean)
Mason *et al.*, 2006 (67)	22 (4.0)	41% at 1 year[†]	–	4 (median)
Fischer *et al.*, 2007 (68)	151	42% at hospital discharge	–	6 (mean)
Bermudez *et al.*, 2009 (69)	58 (7.6)	40% at 1 year	39 (67.2)	5.5 (mean)
Hartwig *et al.*, 2012 (15)	28 (6.0)	64% at 1 year	27 (96.4)	3.6 (mean)
Marasco *et al.*, 2012 (70)	24	25% at hospital discharge	14 (58.3)	4.5 (median)
Mulvihill *et al.*, 2018 (71)	107 (5.1)	62% at 6 months	–	–

Values are reported as n (%). [†], survival was 41% at 1 year in patients with early graft failure and acute rejection and only 3% in patients with sepsis and pneumonia.

Postoperative Circulatory Support for Lung Transplantation

Table 3 Published case series on secon

Study
Meyers *et al.*, 2000 (64)
Dahlberg *et al.*, 2004 (65)
Oto *et al.*, 2004 (66)
Mason *et al.*, 2006 (67)
Fischer *et al.*, 2007 (68)
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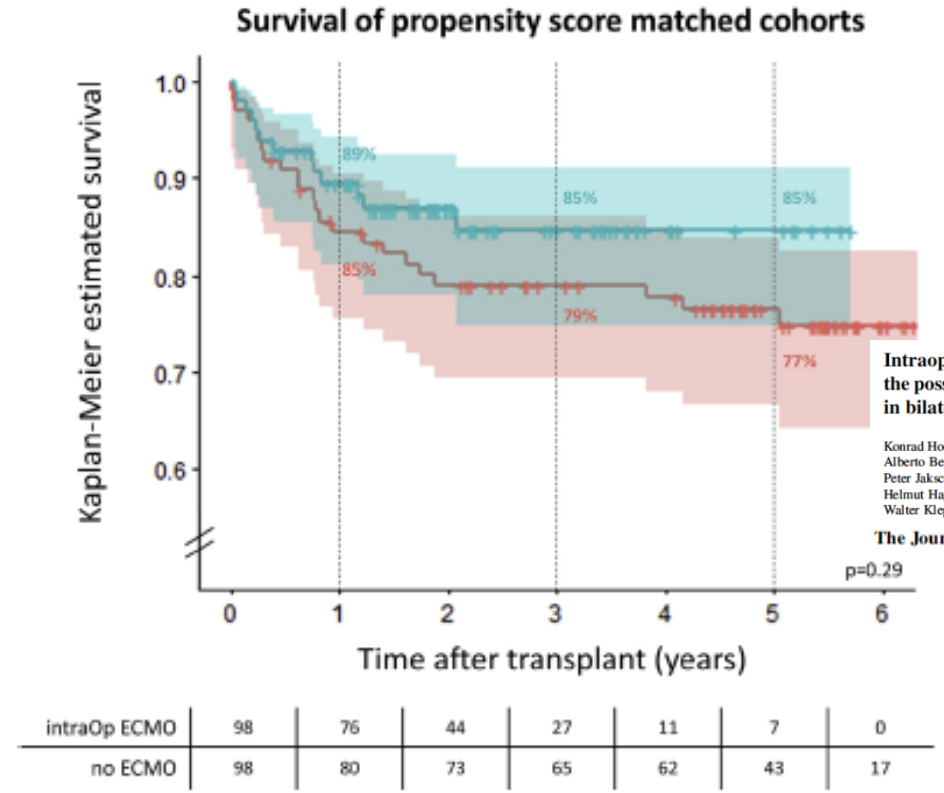

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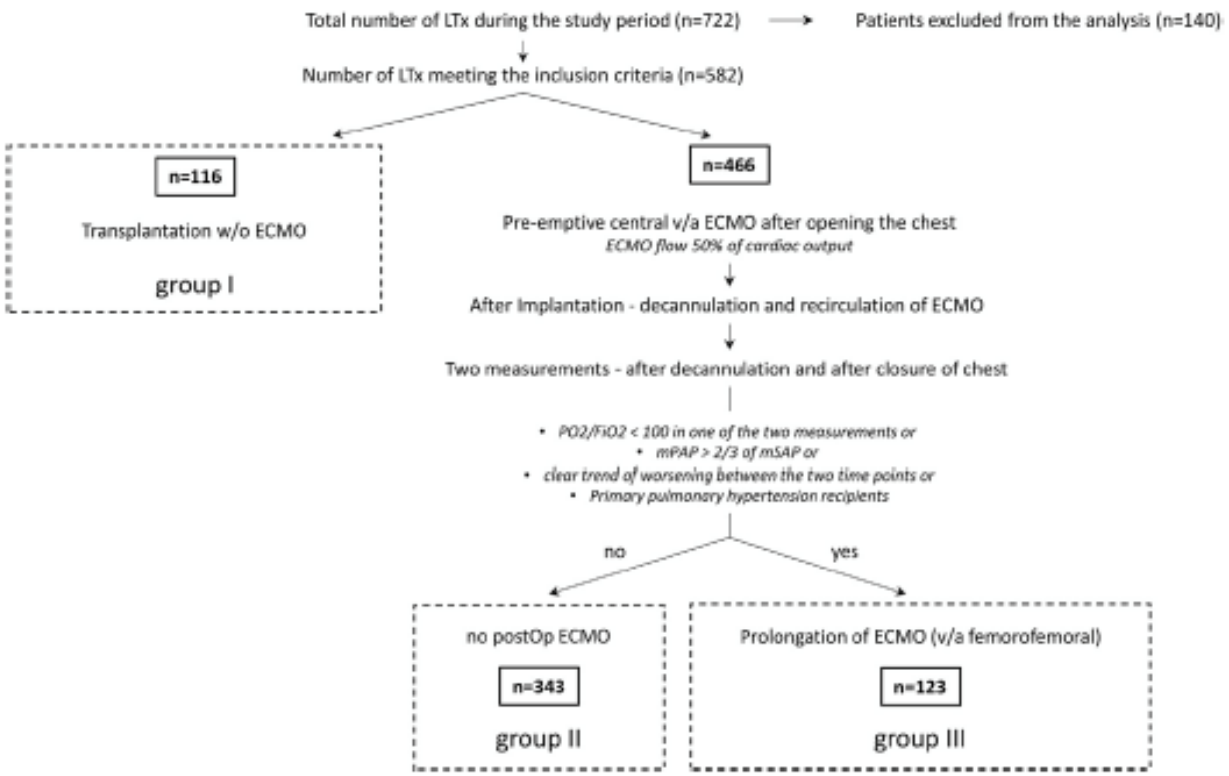
FIGURE 4. Intraoperative extracorporeal membrane oxygenation (*intraOp ECMO*) and patients not undergoing ECMO were matched to balance pretreatment characteristics using propensity score matching. Patients who were supported by ECMO had better survival compared with patients not undergoing ECMO, although this was not statistically significant. *ECMO*, Extracorporeal membrane oxygenation; *intraOp*, intraoperative.

Postoperative Circulatory Support for Lung Transplantation



Summary

Lung transplantation is evolving as a therapy for end stage lung failure

Intraoperative circulatory support gaining favor as we transplant sicker patients (anecdotal data supports this)

Post Operative support when used rationally can improve survival