

# **Ambulatory system: fiction or reality**

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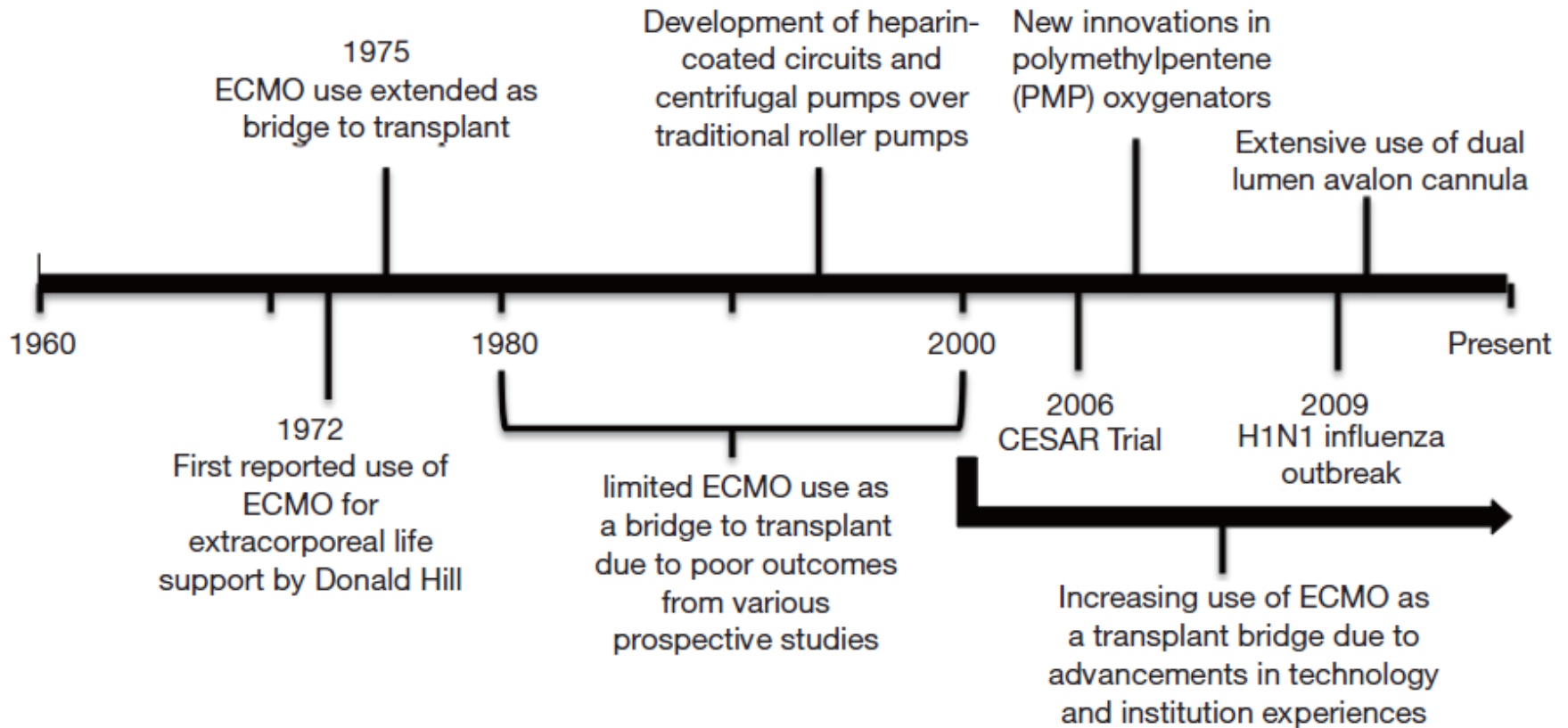
**Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico**

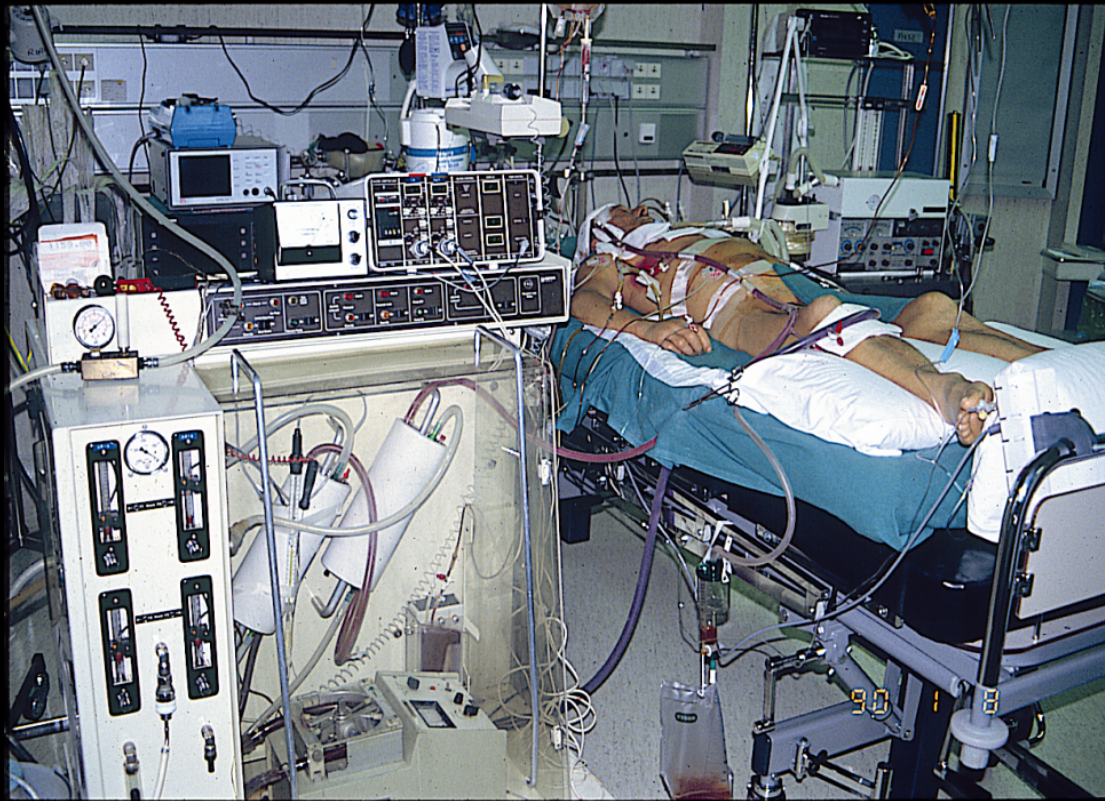
## **Ambulatory system: fiction or reality**

**No conflict of interest**

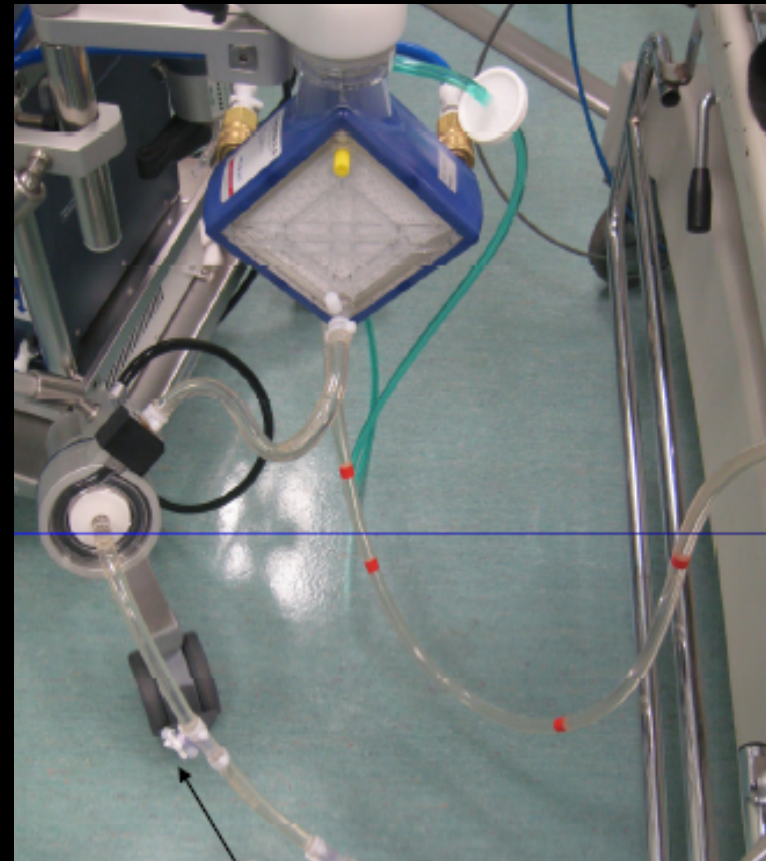
# **Ambulatory system: fiction or reality**

**Evolution of ECMO**  
**Indications and Outcome**  
**Modalities**  
**Donor-Recipient match**





**Advances in  
Technology**



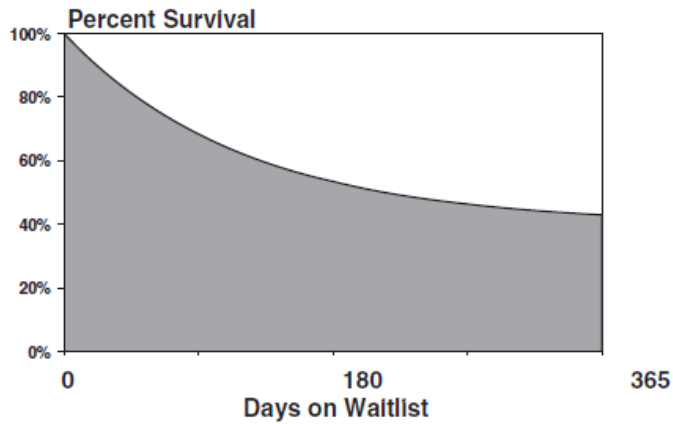
# Lung Allocation Score



**High Risk Recipients**

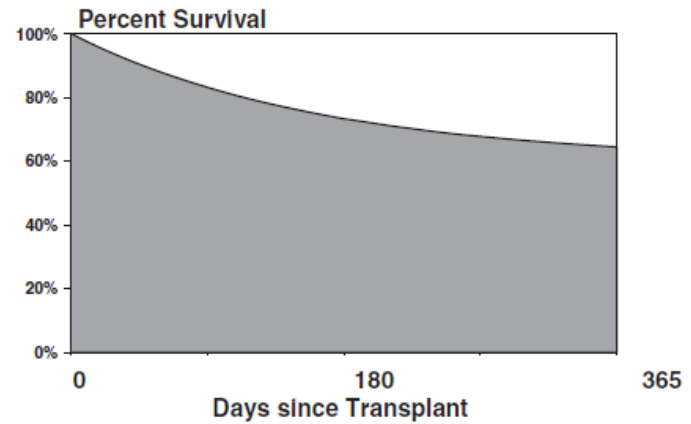
## Waitlist Urgency Measure

Shaded area under curve =  
Expected number of days lived  
without a transplant during an  
additional year on the waitlist



## Post-Transplant Survival Measure

Shaded area under curve =  
Expected number of days lived  
during the first year  
post-transplant



**Lung Allocation Score**



**High Risk Recipients**



**ECMO Lung Transplantation**

**Advances in  
Technology**

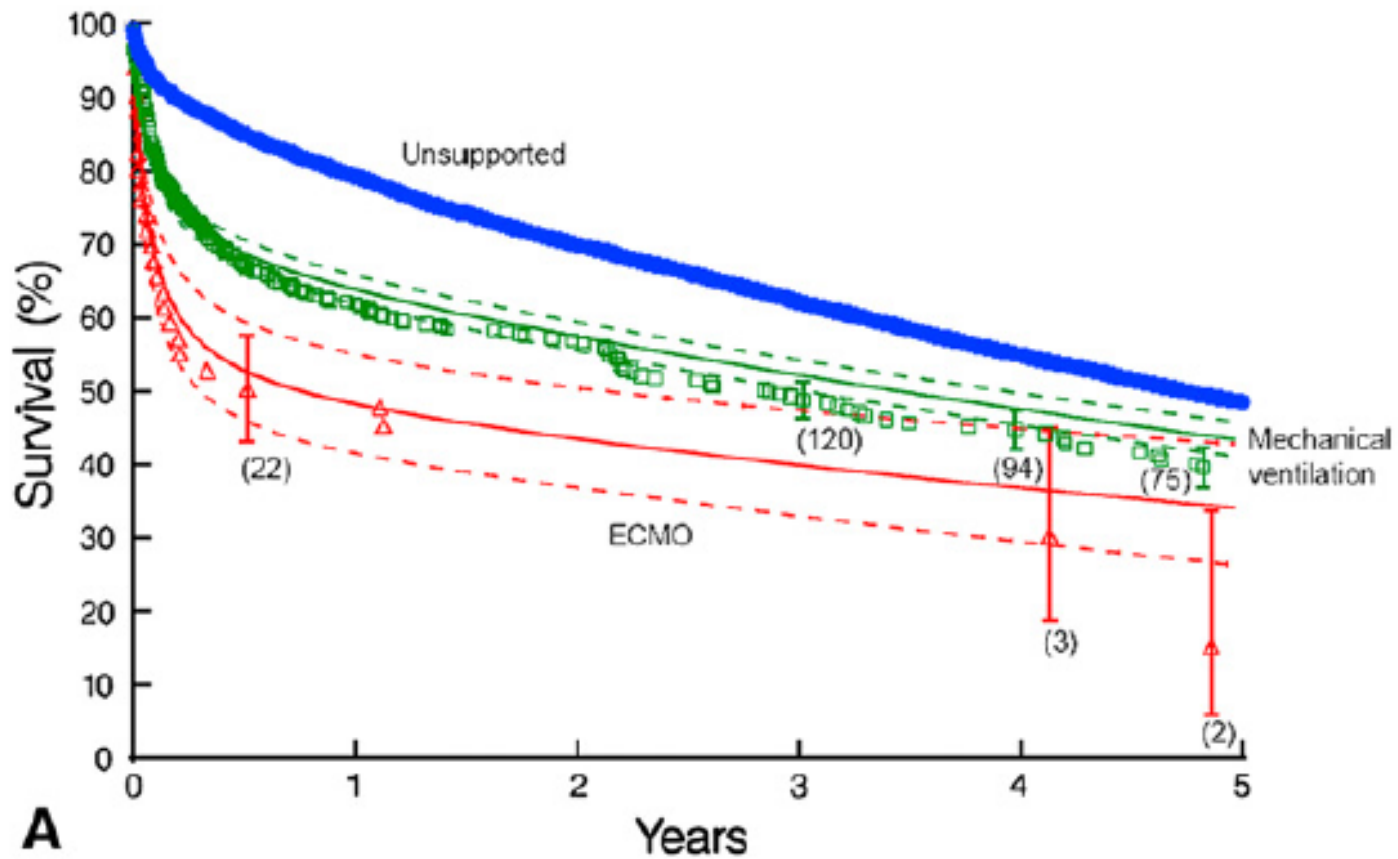


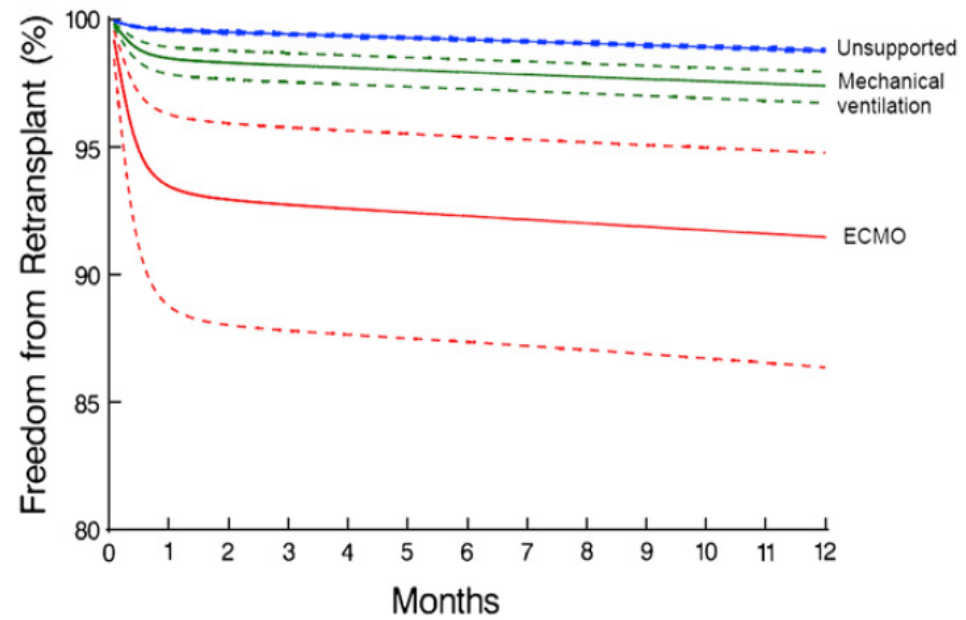
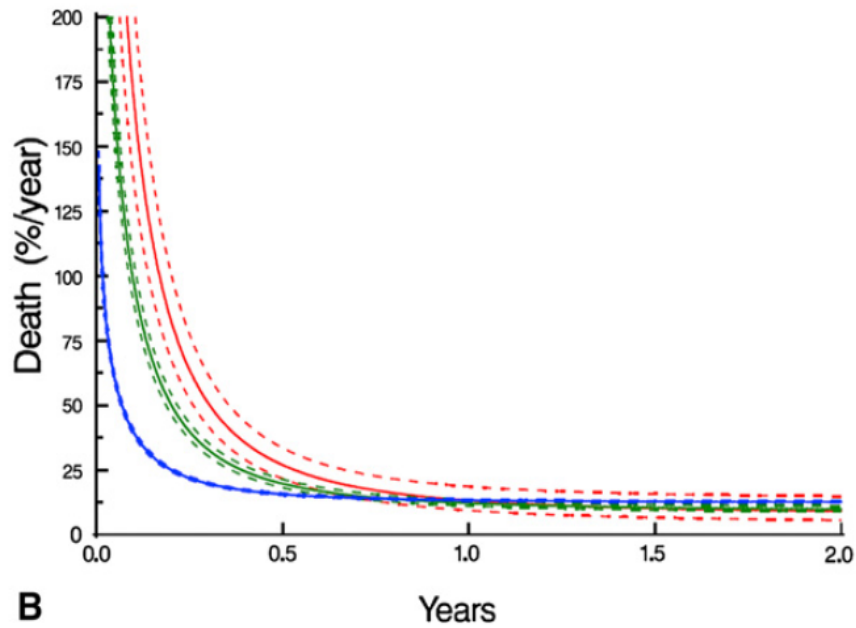
**CESAR trial  
H1-N1 influenza**



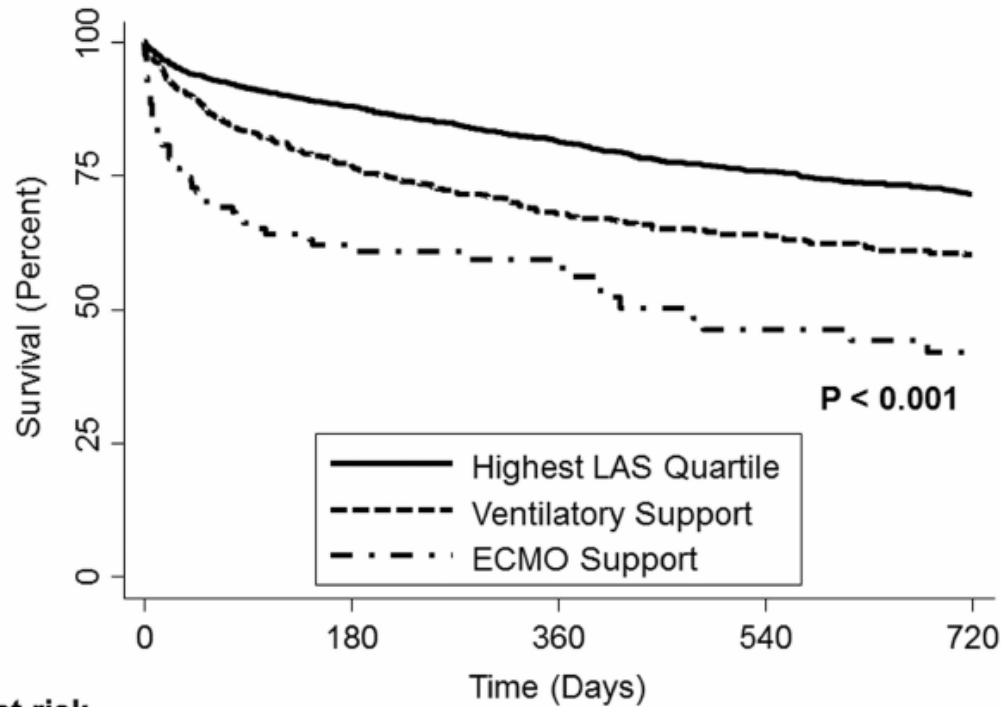
<b>Autore</b>	<b>Anno</b>	<b>Rivista</b>	<b>anno di reclutamento</b>	<b>Ltx tot</b>	<b>ECMO</b>	<b>% ECMO</b>	<b>30 Days</b>	<b>6 Months</b>	<b>1 Year</b>
Mason	2010	J Thorac Cardiovasc Surg	1987-2008	15'934	51	0.32	72	53	50
Bermudez	2011	Ann Thorac Surg	1991-2010	1'305	17	1	81		74
Hammemainen	2011	J Heart and lung transplant	2005-2009		16		81	75	75
Fuehner	2012	Am J Respir Crit Care Med	2006-2011	60	26	43		80	
George	2012	J Heart and lung transplant	2005-2011	9'267	122	1.3	76.4		57.6
Javidfar	2012	J Thorac Cardiovasc Surg	2007-2012	250	18	7.2	56	39	33
Shafii	2012	ASAIO Journal	2008-2011	424	19	4			52
Lang	2012	Transplantation	1998-2011		38				60
Bittner	2012	Ann thorac Surg	2002-2009	108	27	25	63	44	33
Anile	2013	Transplant Proc	1991-2012	197	12	6	100		85,7
Crotti	2013	Chest	2007-2011		25				52
Hoopes	2013	J Thorac Cardiovasc Surg	2003-2012		31				93
Toyoda	2013	J Thorac Cardiovasc Surg	2005-2011	715	31	4	96	83	74
Weig	2013	Clin Transplant	2005-2011	259	26	10		30	27
Lang	2014	J Heart and lung transplant	2008-2012	39	5	13		100	60
Inci	2015	Transplantation	2007-2013	186	30	16	89		68
Hayanga	2015	J Thorac Cardiovasc Surg	2000-2011	12'458	119	1			





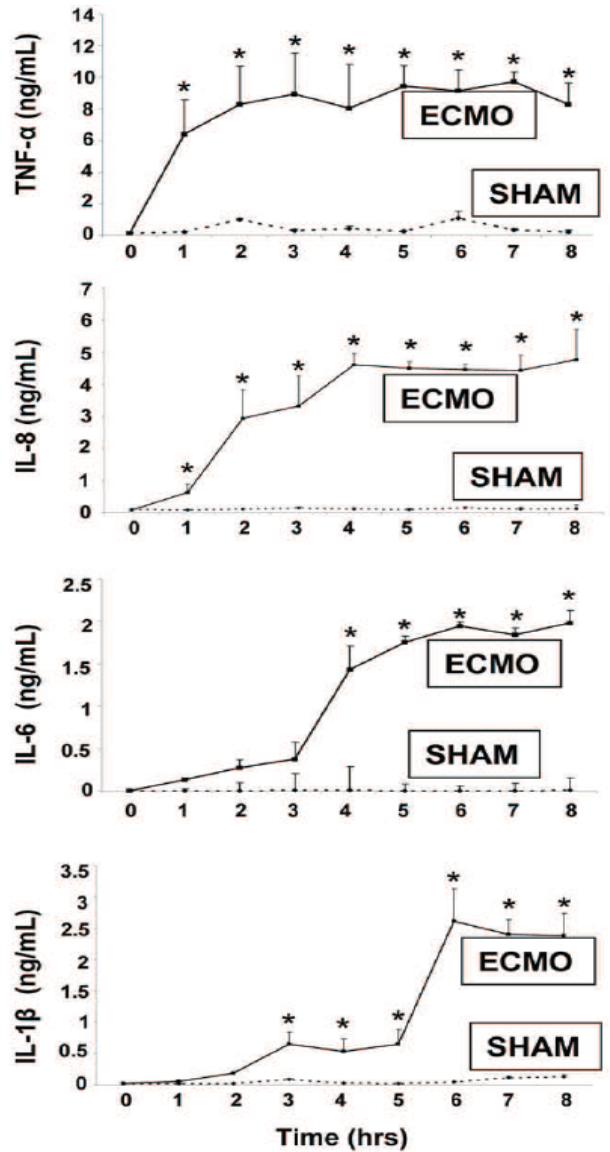


A

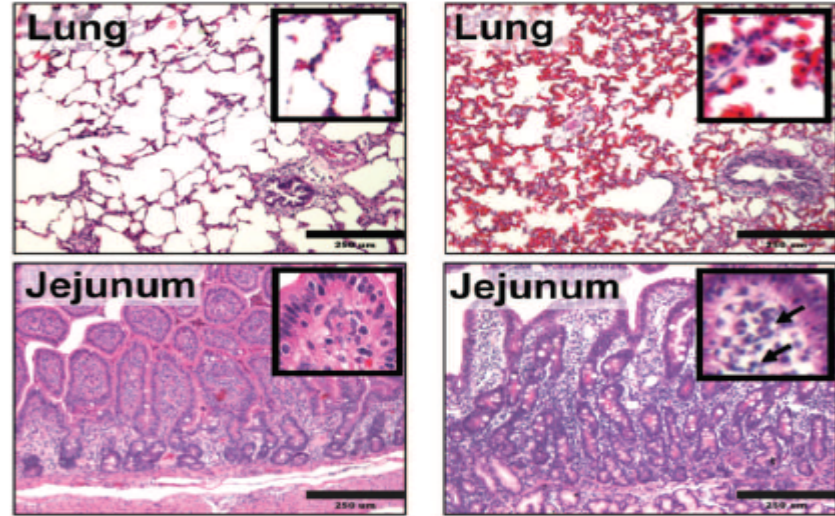


	<u>Number at risk</u>				
Highest LAS Quartile	1858	1367	1080	789	647
Ventilatory Support	525	358	262	184	163
ECMO Support	122	52	35	23	18

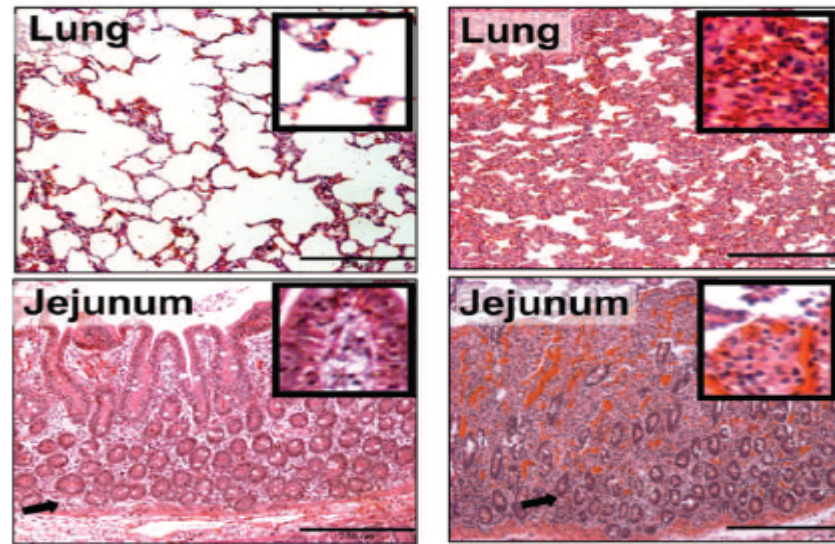
## B. PLASMA CYTOKINES



## A SHAM 2 hrs ECMO 2 hrs

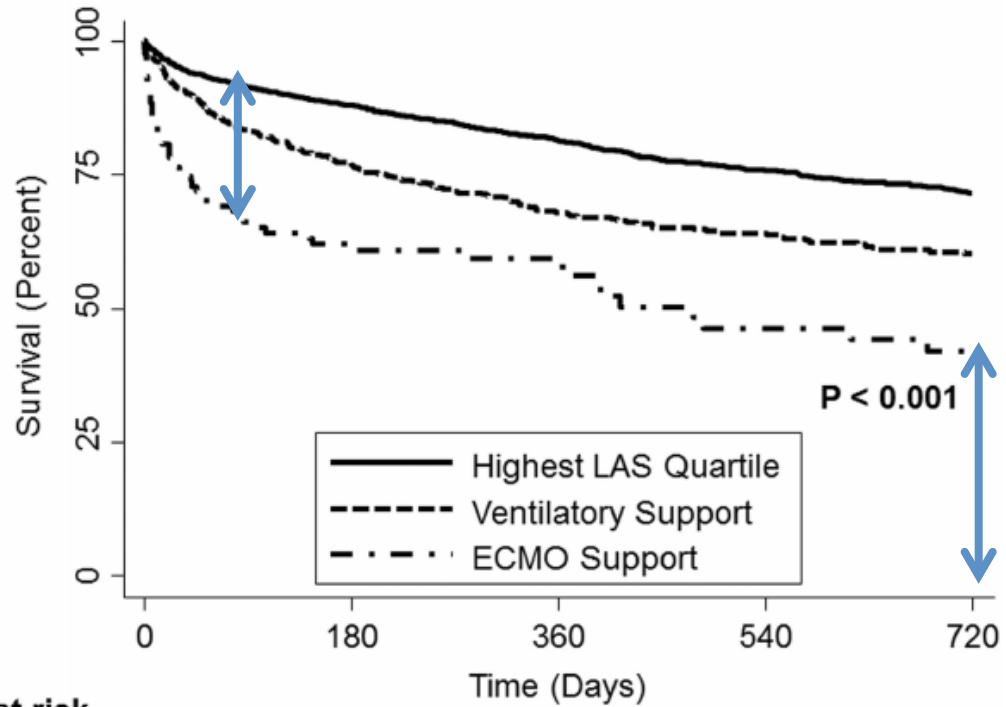


## SHAM 8 hrs ECMO 8 hrs

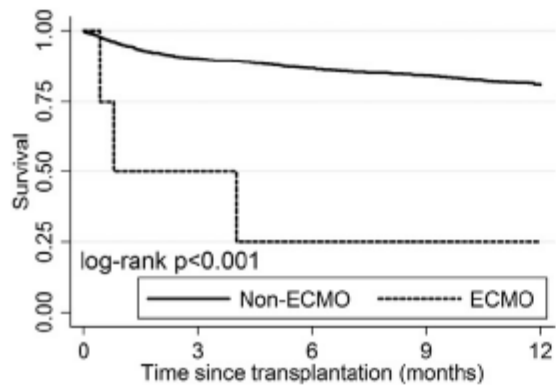


**... why are we using ECMO?**

A



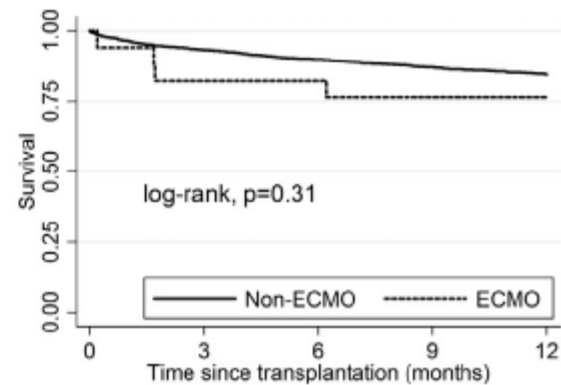
	<u>Number at risk</u>				
Highest LAS Quartile	1858	1367	1080	789	647
Ventilatory Support	525	358	262	184	163
ECMO Support	122	52	35	23	18



Number at risk

Non-ECMO	1472	1319	1266	1225	1174
ECMO	4	2	1	1	1

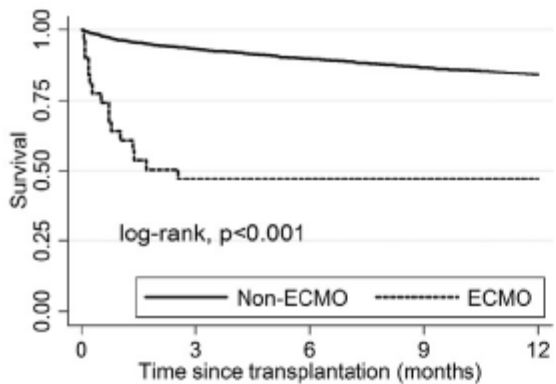
**A**



Number at risk

Non-ECMO	2770	2568	2468	2388	2304
ECMO	17	14	14	13	13

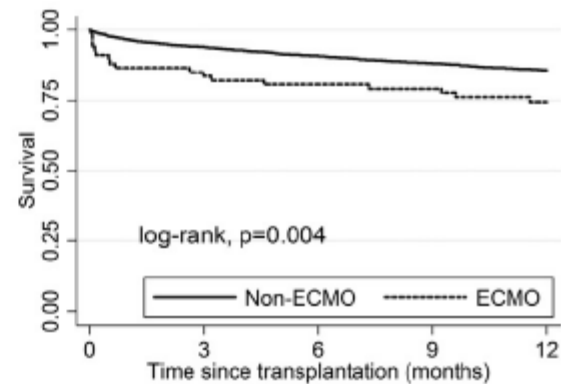
**B**



Number at risk

Non-ECMO	3501	3248	3120	3007	2911
ECMO	31	14	14	14	14

**C**



Number at risk

Non-ECMO	4596	4287	4128	3991	3389
ECMO	67	56	54	53	44

**D**

## International Society of Heart and Lung Transplantation

- Mechanical ventilation. Carefully selected candidates on mechanical ventilation without other acute or chronic organ dysfunction, who are able to actively participate in a meaningful rehabilitation program, may be successfully transplanted.
- Mechanical ventilation and/or extracorporeal life support (ECLS). However, carefully selected candidates without other acute or chronic organ dysfunction may be successfully transplanted.

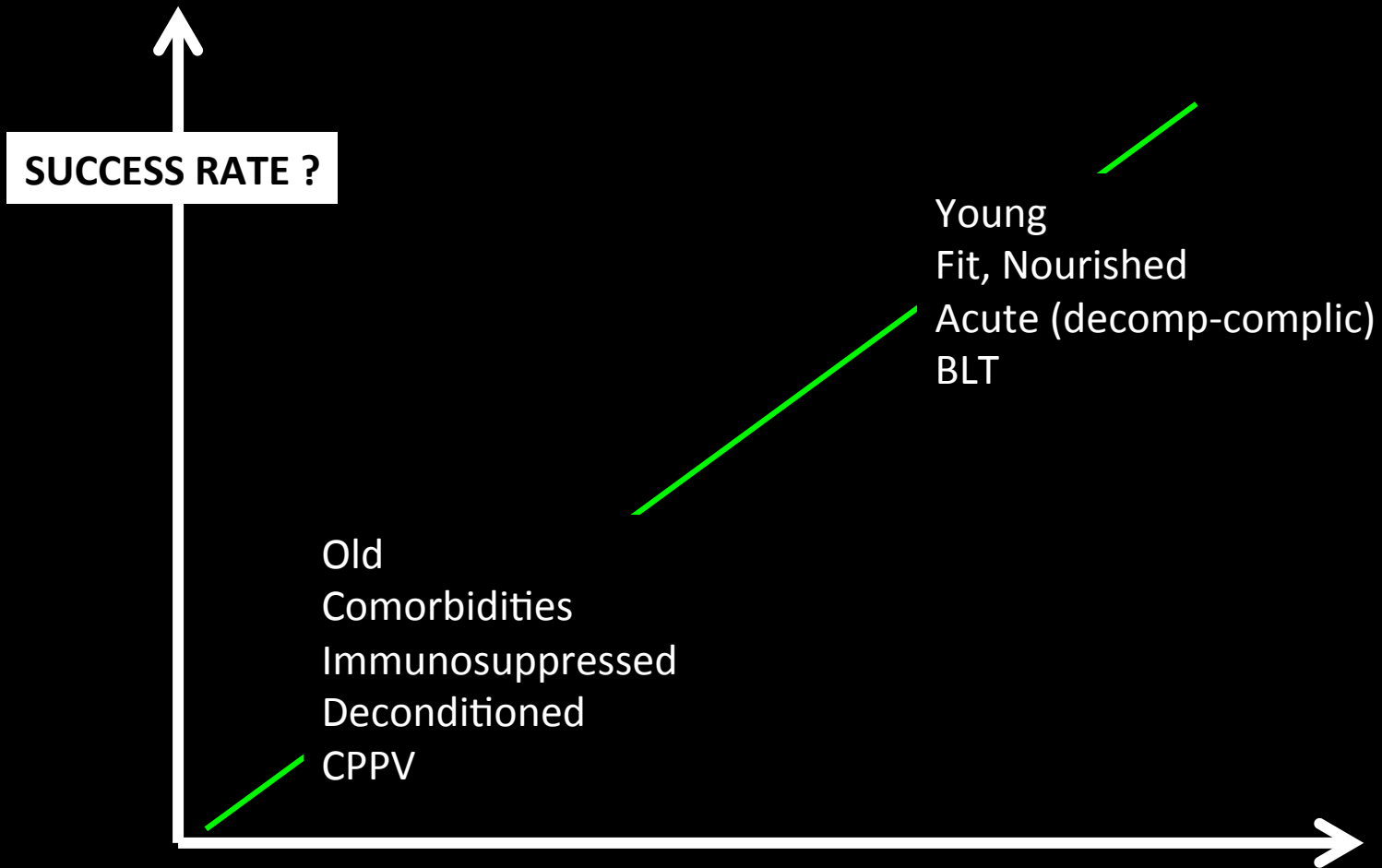


## Retrospective, single centers, case mix

**Table 1 Characteristics of patients who underwent ECMO bridge to lung transplant and were enrolled in the selected studies**

Author, year	Patients, number	Age, years	Sex male, n (%)	Diagnosis	Ventilation strategy	Bridge time, days	Severity score pre-bridge
Mason, 2010 [11]	51	39 ± 22	25 (49%)	PF 27%; COPD 19%; CF 12%; PH 9.8%; sarcoidosis 2%; other 20%	na	na	LAS 54 ± 21
Bermudez, 2011 [34]	17	40 ± 14	7 (41%)	PF 35%; Re-LTx 35%; CF 23%; COPD 6%	MV	3.2 (0 to 49)	na
Hammainen, 2011 [38]	16	41 ± 8 <sup>a</sup>	7 (58%) <sup>a</sup>	PF 37% <sup>a</sup> ; PH 15% <sup>a</sup> ; CF 8% <sup>a</sup> ; ARDS 8% <sup>a</sup> ; IP 8% <sup>a</sup> ; PVOD 8% <sup>a</sup> ; BOS 8% <sup>a</sup> ; PGD 8% <sup>a</sup>	na	12 (1 to 59)	na
Shafii, 2012 [41]	19	44 (23 to 60)	10 (53%)	IP 68%; CF 16%; PH 16%	MV 13	6 ± 5	LAS 87 (64 to 95)
Nosotti, 2012	11	34 ± 13	5 (45%)	na	Awake 7 MV 4	12.1 ± 14.7	SOFA 4.9 ± 1.4
Javidfar, 2012 [20]	18	34 (22 to 50)	8 (45%)	CF 44%; PF 33%; PH 11%; Other 11%	Awake 6	11.5 (6 to 18)	LAS 93 (90 to 94)
George, 2012 [10]	122	48 ± 16	74 (60%)	PF 29.5%; CF 11.5%; COPD 10.7%; PH 2.5%; other 45.8%	na	na	LAS 73.9 ± 21.4
Fuehner, 2012 [26]	26	44 (23 to 62)	21 (81%)	PF 35%; PH 27%; CF 19%; BOS 12%; sarcoidosis 4%	Awake 19 MV 7	9 (1 to 45)	SOFA 7 (6 to 12)
Hoopes, 2013 [32]	31	45 ± 15	21 (67%)	PF 29%; CF 23%; ILD 13%; ARDS 10%; PVOD 10%; PH 6%; BOS 3%; IP 3%; CWP 3%	Ambulatory 18 13 VM	11 (2 to 53)	LAS >50
Anile, 2013 [36]	12	na	na	CF 92%; histiocytosis 8%	Awake 2 MV 10	6 ± 2.1	na
Toyoda, 2013 [33]	31	46 ± 15 <sup>a</sup>	10 (42%) <sup>a</sup>	PF 33% <sup>a</sup> ; CF 21% <sup>a</sup> ; Re-LTx 13% <sup>a</sup> ; scleroderma 13% <sup>a</sup> ; bronchiectasis 8% <sup>a</sup> ; COPD 4% <sup>a</sup> ; sarcoidosis 4% <sup>a</sup> ; PH 4% <sup>a</sup>	MV <sup>a</sup>	7.1 ± 10	LAS 87 ± 9 <sup>a</sup>
Weig, 2013 [39]	26	36 (30 to 51) <sup>a</sup>	14 (54%)	PF 62%; CF 23%; COPD 4%; Re-LTx 4%; Lung cancer 4%; sarcoidosis 4%	na	16 (8.8 to 25) <sup>a</sup>	SOFA 9 (8.5 to 10.5) <sup>a</sup>
Crotti, 2013 [35]	25	41 ± 12	na	PF 52%; CF 16%; PH 16%; Re-LTx 12%; ARDS 4%	Awake 10 MV 15	5.8 ± 4.5 versus 29.8 ± 11.5 <sup>b</sup>	SOFA 5.6 ± 1.9
Lafarge, 2013 [40]	36	31 (22 to 48)	19 (53%)	CF 56%; PF 30%; other 14%	MV	3.5 (2 to 7)	na

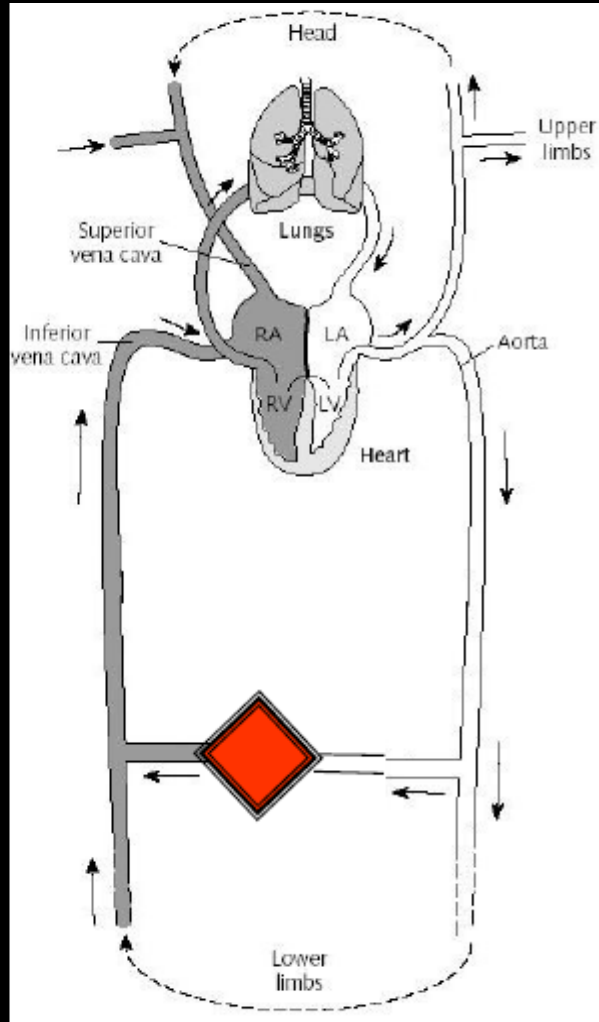
Data presented in this table refer to patients underwent ECMO support with the intention to bridge to lung transplantation. <sup>a</sup>Transplanted patients (when data for all enrolled patients are not available; Hammainen *et al.*, all data; Toyoda, all data; Weig *et al.*, age, ECMO bridge time and SOFA; Anile, diagnosis). ECMO bridge time (days) and the pre-bridge severity score are expressed as mean ± standard deviation or median and range. When no descriptive cumulative data for the overall population are provided, they are calculated from raw data presented in the original papers. <sup>b</sup>Data refer to patients divided according to waiting time on ECMO: up to 14 days or longer. Pts, patients; ECMO, extracorporeal membrane oxygenation; PF, pulmonary fibrosis; COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; PH, Pulmonary hypertension; Re-LTx, Re-lung transplantation; ARDS, acute respiratory distress syndrome; IP, interstitial pneumonia; PVOD, pulmonary veno-occlusive disease; BOS, bronchiolitis obliterans syndrome; PGD, primary graft dysfunction; ILD, interstitial lung disease; CWP, coal workers pneumoconiosis; MV, mechanical ventilation; LAS, lung allocation score; SOFA, sequential organ failure assessment; na, not available.



Hayes. JHLT 2015 Jun;34(6):832-8

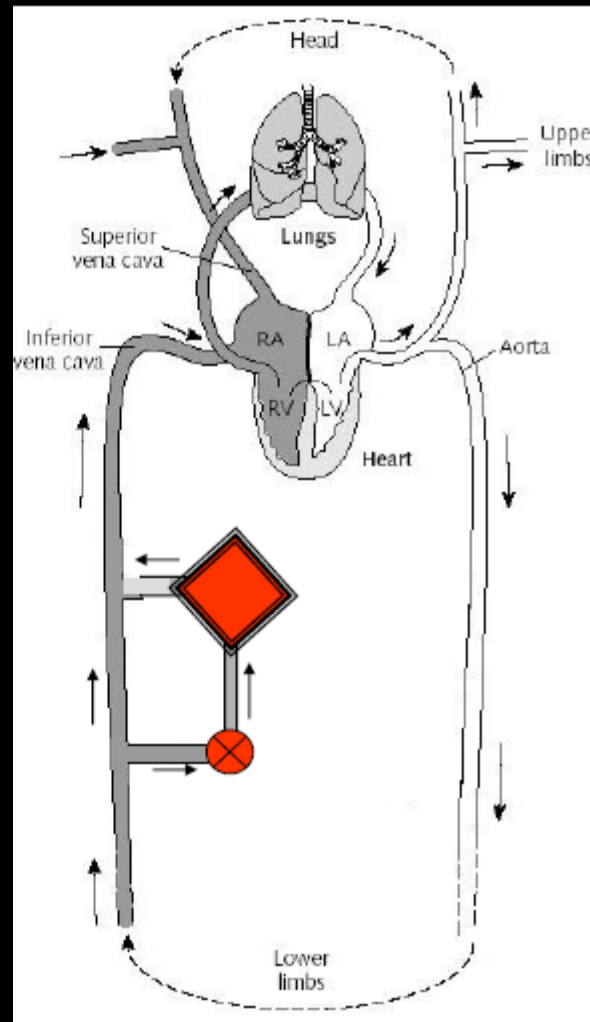
Hayanga, J Thorac Cardiovasc Surg 2015;149:291

# iLA



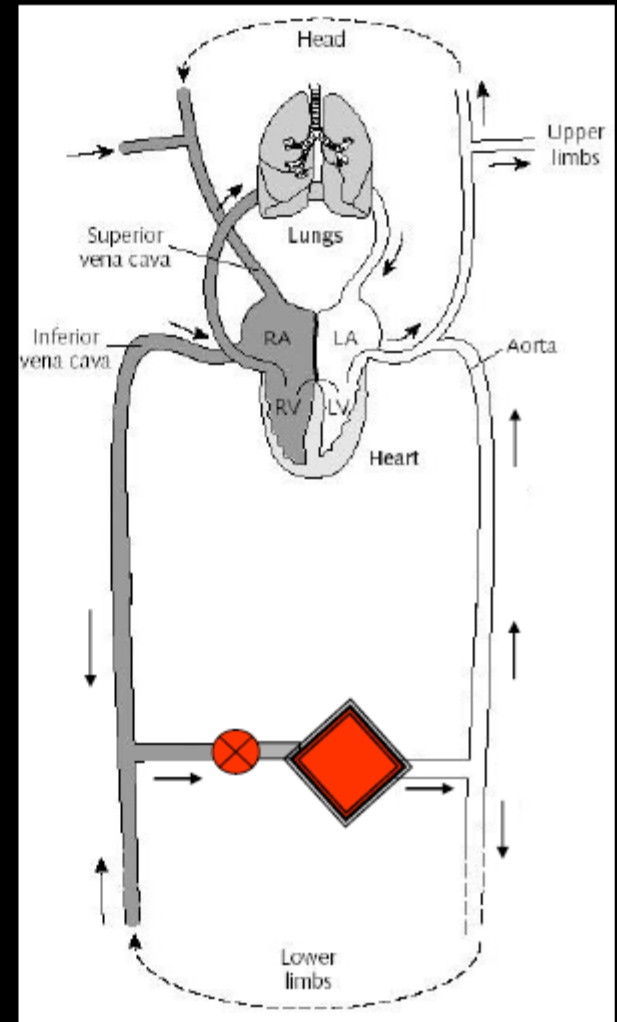
CO<sub>2</sub> removal

# VV ECMO



CO<sub>2</sub> removal  
Oxygenation

# VA ECMO



CO<sub>2</sub> removal  
Oxygenation  
Cardiovascular

# Lung Transplantation

before

during

after

ECMO - Bridge

ECMO - Support

ECMO - PGD



# Intraoperative “*prevention*”

## Low perfusion pressure

Bhabra, Ann Thor Surg 1996;61:1631

Bhabra, Ann Thor Surg 1998;65:187

Pierre, J Thorac Cardiovasc Surg 1998;116:932

Clark, J Thorac Cardiovasc Surg 1998;115:1335

Halldorsson, J Thorac Cardiovasc Surg 1998;115:415

## Protective ventilation

De Perrot, J Thorac Cardiovasc Surg 2002;124:1137

Crimi, Am J respir Crit Care Med 2005;174:178

Chiang, Resuscitation 2008;79:147

# Postoperative "treatment"

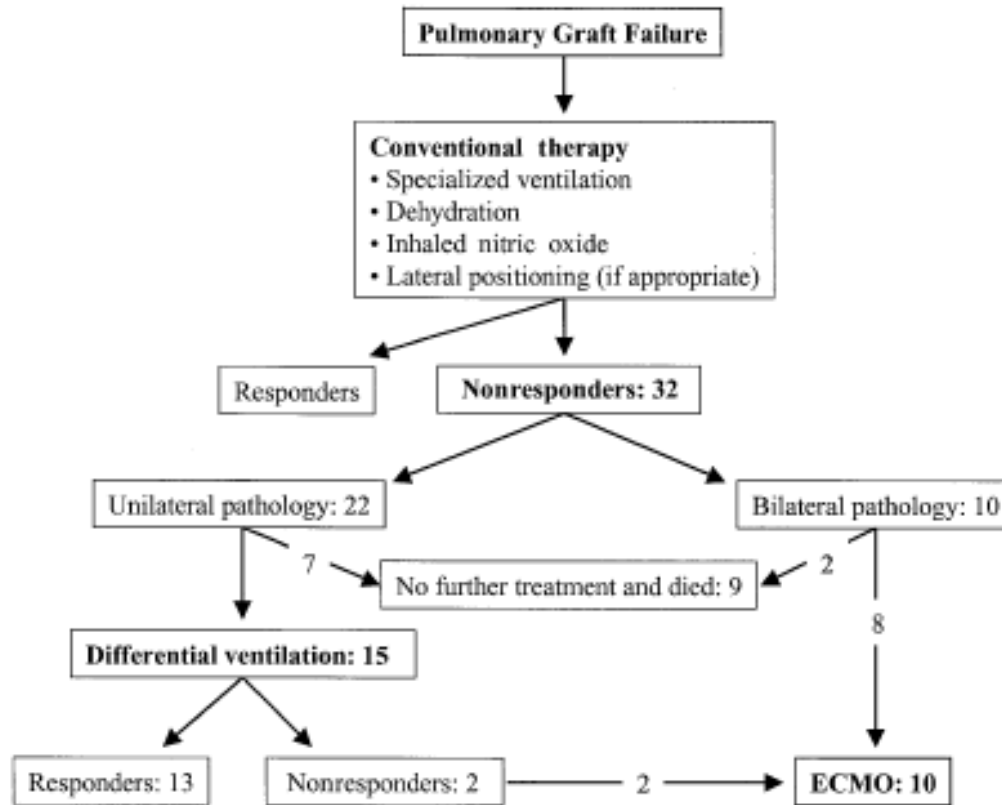
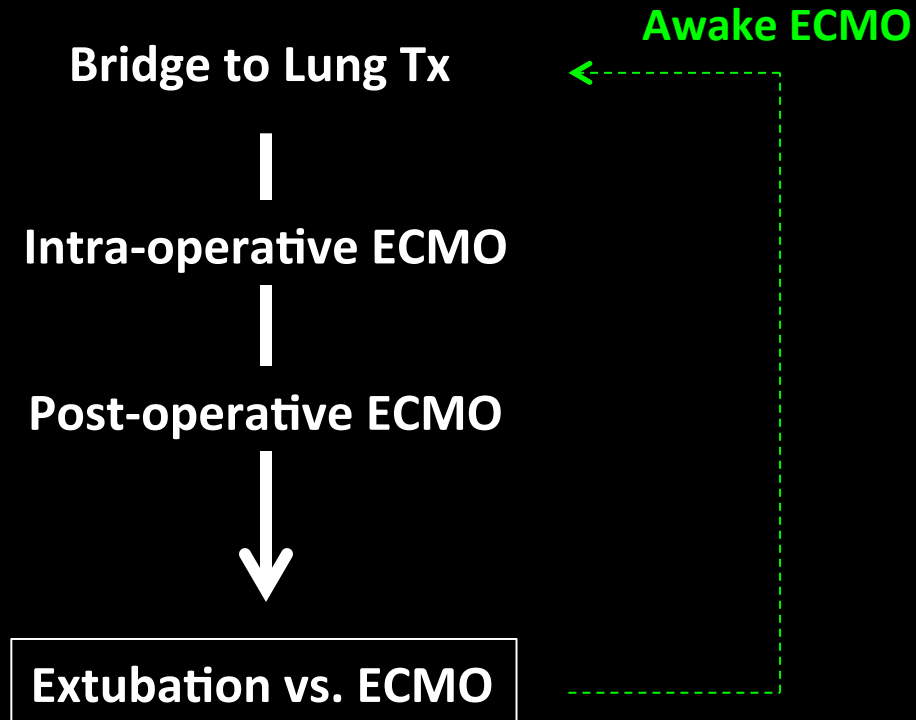


Fig 1. Algorithm for pulmonary graft failure after lung transplantation.

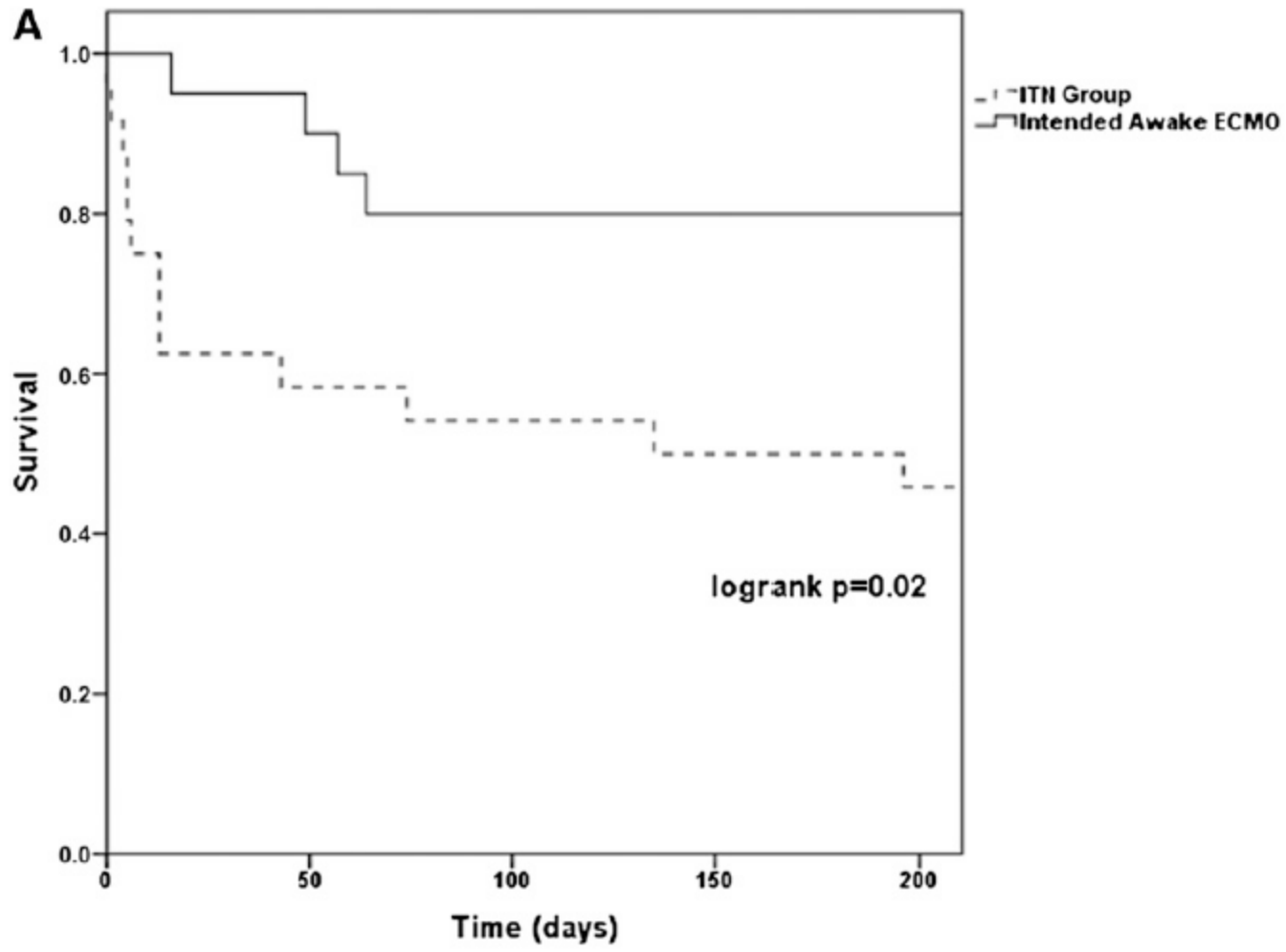
# Postoperative “management”



**TABLE 1. COMPARISON OF PATIENT CHARACTERISTICS AND OUTCOMES IN THE AWAKE ECMO GROUP AND THE MECHANICAL VENTILATION GROUP**

	Mechanical Ventilation Group	Awake ECMO Group	P Value
<b>Baseline characteristics</b>			
Patients, n	34	26	
Age, yr, median (range)	36 (18–59)	44 (23–62)	0.13
Age ≥55 yr, n (%)	5 (15)	5 (19)	0.64
Sex, female, n (%)	20 (59)	15 (58)	0.93
BMI, median (range)	20 (13–29)	24 (16–30)	0.07
Cystic fibrosis, n (%)	10 (29)	5 (19)	0.37
Pulmonary fibrosis, n (%)	7 (21)	9 (35)	0.22
PAH/CTEPH, n (%)	4 (12)	7 (27)	0.13
BOS, n (%)	9 (26)	3 (12)	0.15
Sarcoidosis, n (%)	0 (0)	1 (4)	0.25
PAPm ≥30 mm Hg, n (%)	8 (24)	11 (42)	0.12
Renal replacement therapy before bridging, n (%)	0 (0)	1 (4)	0.25
SAPS II 12 h before bridging (MV or ECMO), median (range)	30 (22–51)	45 (25–68)	0.003
SOFA 12 h before bridging (MV or ECMO), median (range)	7 (6–10)	7 (6–12)	0.2
SaO <sub>2</sub> immediately before bridging (MV or ECMO), median (range)	86 (70–92)	79 (58–92)	<0.001
Paco <sub>2</sub> immediately before bridging (MV or ECMO), median (range)*	76 (36–116)	80 (36–120)	0.89
<b>Bridging to Tx</b>			
Bridging time, median, range	15 (1–71)	9 (1–45)	0.25
Death before Tx, n (%)	10 (29)	6 (23)	0.58
<b>Post-transplant period</b>			
Transplantation, n (%)	24 (71)	20 (77)	
DLTx, n (% of transplant patients)	21 (84)	20 (100)	0.06
Death after LuTx, n (% of transplant patients)	12 (50)	4 (20)	0.02
Days on MV after LuTx (survivors only), median (range)	37 (1–72)	14 (0–64)	0.04
Extubation within 24 h after LuTx, n (%)	1 (4)	5 (25)	0.10
Renal failure requiring hemodialysis after Tx (survivors only), n (%)	2 (6)	1 (4)	0.66
Days on ICU (survivors only), median (range)	39 (4–74)	18 (1–69)	0.07
Days in hospital stay (survivors only), median (range)	67 (23–90)	38 (20–87)	0.06





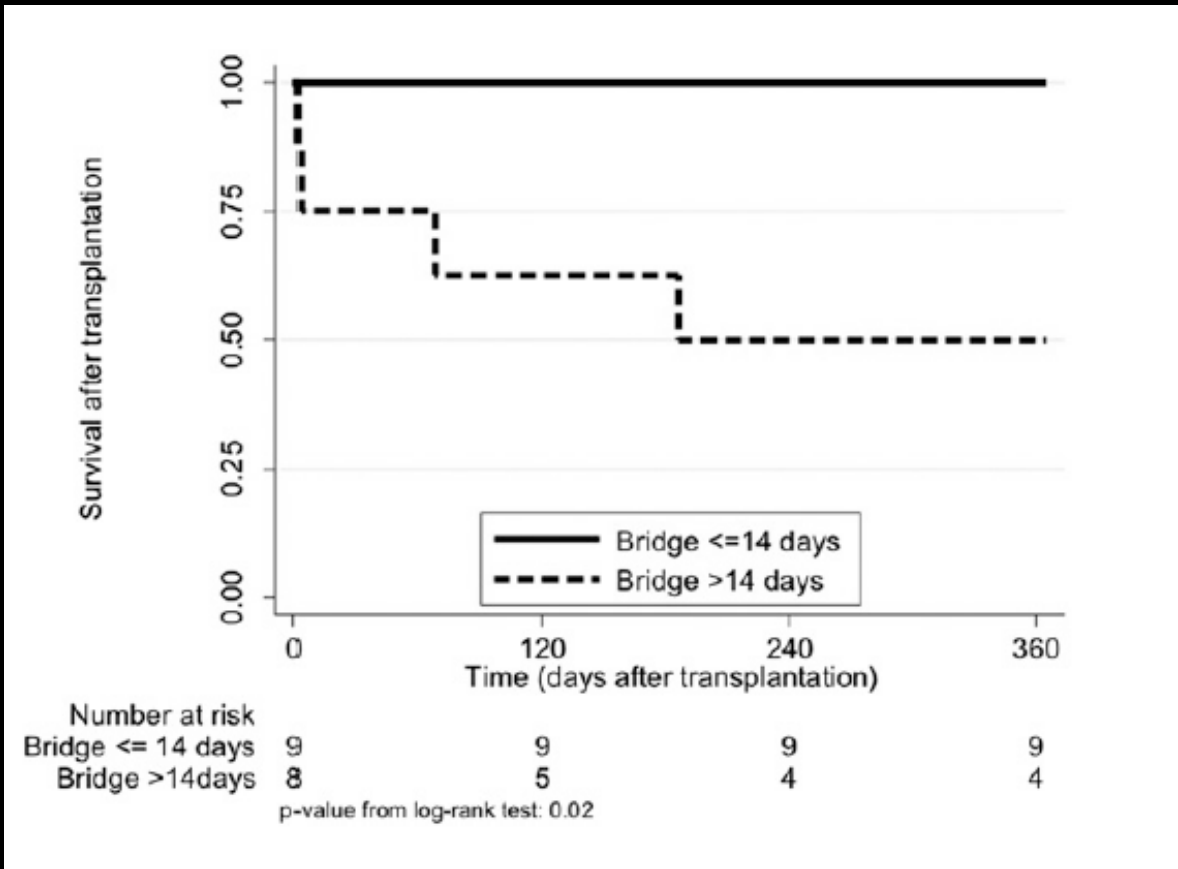
**Table 2:** Reported extracorporeal membrane oxygenation support in spontaneously breathing patients

Year	Author [reference]	Number of patients	Bridging time [median (days)]	Diagnosis (number of patients)	Outcome
2008	Broomé <i>et al.</i> [15]	1	54	Dermatomyositis	Alive
2008	Schmid <i>et al.</i> [16]	1	62	Pulmonary hypertension	Alive
2010	Garcia <i>et al.</i> [17]	1	19	COPD	Alive
2010	Nosotti <i>et al.</i> [5]	1	2	Pulmonary fibrosis	Alive
2010	Mangi <i>et al.</i> [18]	1	3	Pulmonary fibrosis	Alive
2011	Haneya <i>et al.</i> [19]	2	70	Pulmonary hypertension, cystic fibrosis	Alive
2011	de Perrot <i>et al.</i> [20]	3	30	Pulmonary hypertension	2 alive, 1 dead after LTx
2012	Reeb <i>et al.</i> [21]	1	11	Cystic fibrosis	Alive
2012	Fuehner <i>et al.</i> [8]	26	9	Cystic fibrosis (5), pulmonary fibrosis (10), pulmonary hypertension (7), BOS (3), sarcoidosis (1)	16 alive, 4 dead after LTx, 6 dead before LTx

COPD: chronic obstructive pulmonary disease; BOS: bronchiolitis obliterans syndrome; LTx: lung transplantation.

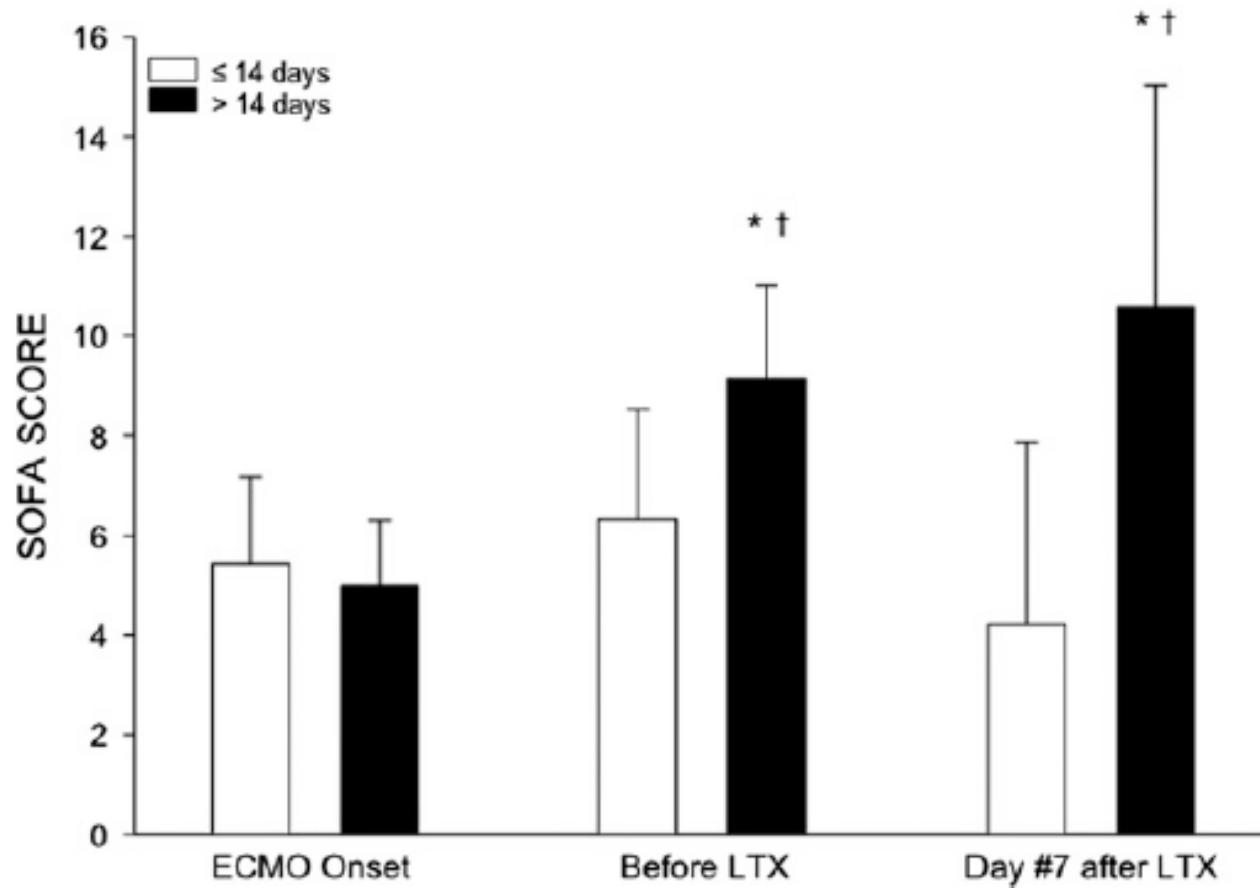
## Bridging in Retransplantation

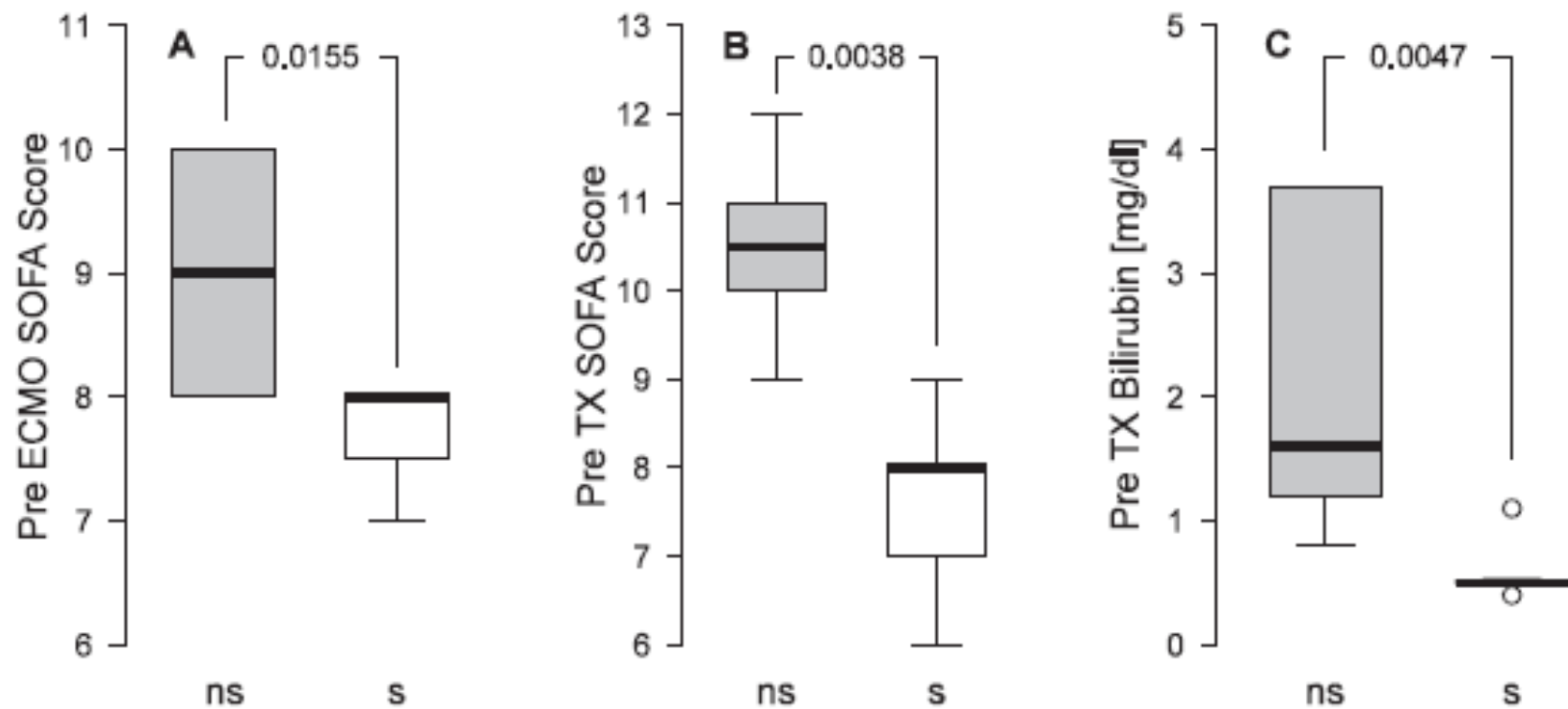
Lang G, J Heart Lung Transplant. 2014 ; 33(12):1264-72.



Hoopes, J Thorac Cardiovasc Surg 2013;145:862

Crotti, Chest 2013; 144(3):1018





...walking while waiting.



Lehr, Chest 2015 May;147(5):1213-8.

**... this observation should inform subsequent discussion as to whether the “ECMO bridge” is an evolving standard of care or a specialty practice limited to regional referral centers .**

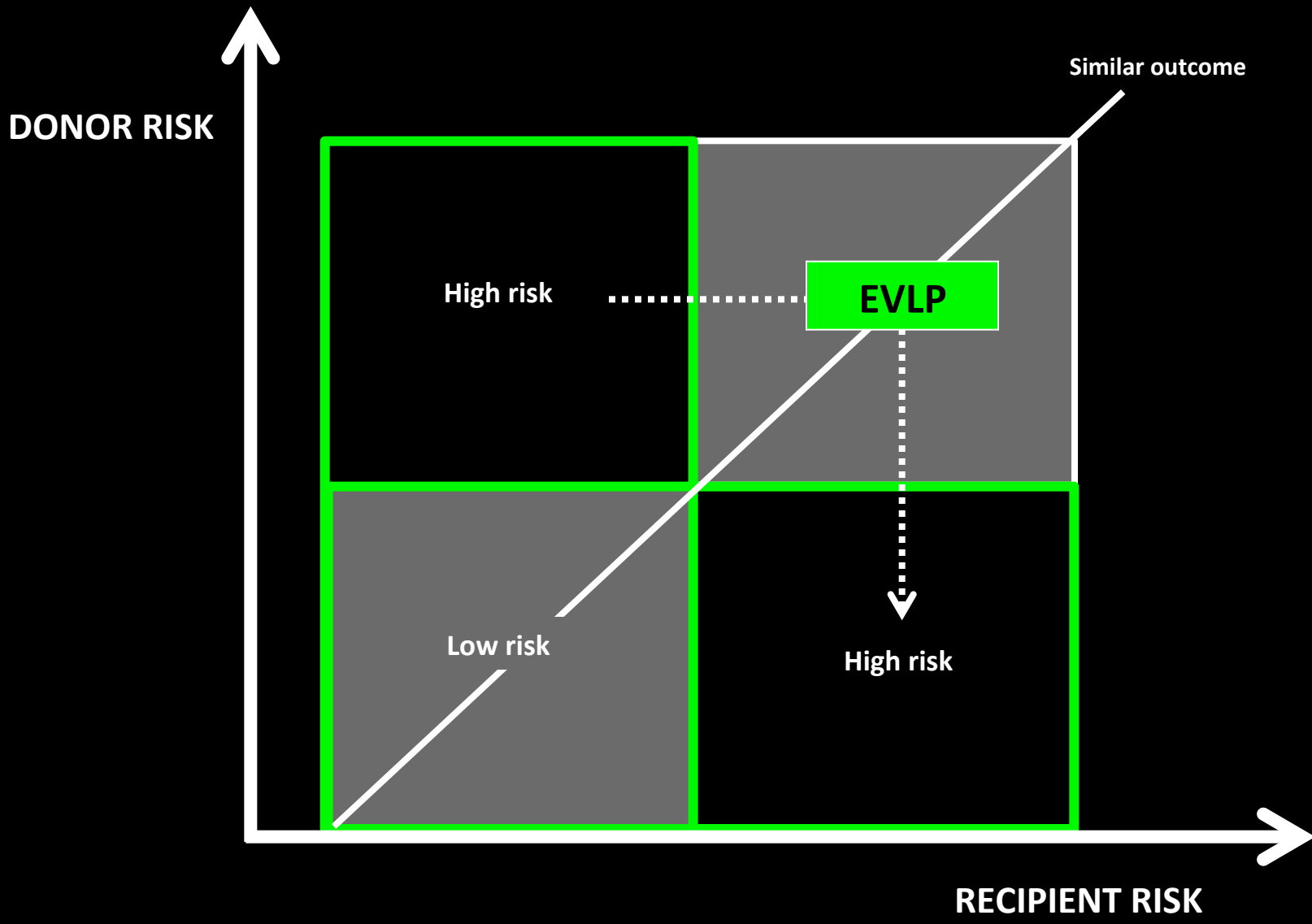
Hoopes, J Thorac Cardiovasc Surg 2013;145:862

**... an “awake” patient who does not meet the viability criteria for subsequent transplantation presents a significant logistic and ethical dilemma**

Hoopes, J Thorac Cardiovasc Surg 2013;145:862

**... balancing maximal individual patient survival against benefits to the maximum number of patients**

Mason, J Thorac Cardiovasc Surg 2010;139:765





## .... In conclusion

**The use of extracorporeal technology to salvage, rehabilitate, and bridge to transplantation high risk recipients is technically and logistically feasible.**

**Ambulatory system: yet to be *fully* explored**

**Thanks for your attention**