



AZIENDA
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Santa Maria
della Misericordia
di Udine



UNIVERSITY
OF UDINE



BEYOND THE SLIDES 2015 1st UDINE ECMO WORKSHOP

DECEMBER 18-19, 2015

AUDITORIUM HYPO ALPE ADRIA

TAVAGNACCO (UD)

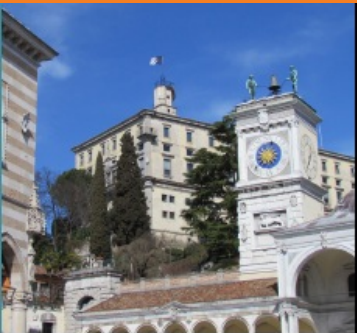
PROMOTED BY
CARDIOTHORACIC DEPARTMENT



SUPPORTED BY

MAQUET
GETINGE GROUP

Promed



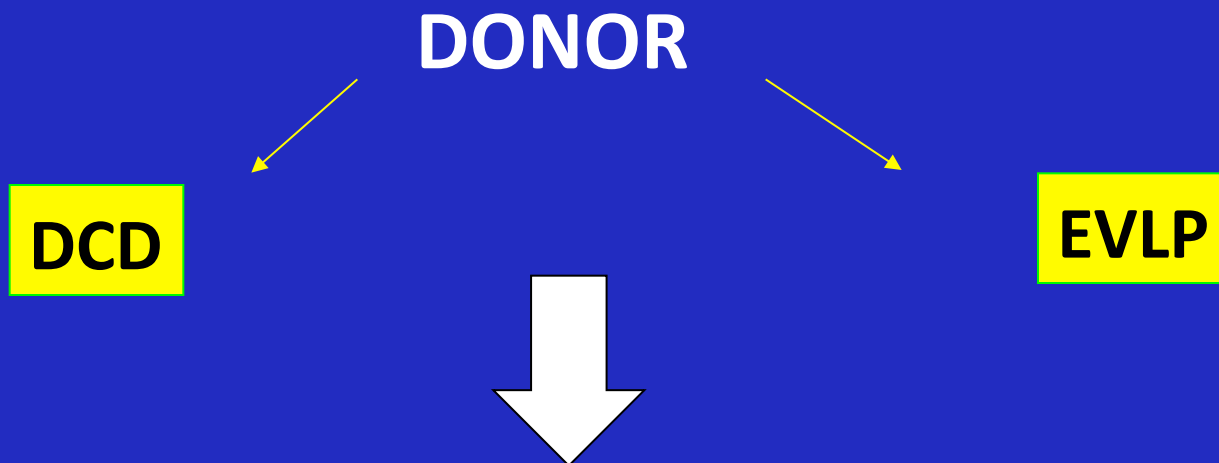
ECMO FOR RESPIRATORY SUPPORT

ECMO and pulmonary transplantation

PROF. FEDERICO REA
CHIRURGIA TORACICA
UNIVERSITA' DI PADOVA



ECMO support may participate to all lung transplant phases including harvesting and implantation



ECMO - Bridge

ECMO - Support

ECMO - Post Tx

Donor after cardiac death

NHBD categories	Alternative categorization	Potential donor status	Hospital Department	Death ascertainment
I	Uncontrolled	Death at hospital arrival	Outside hospital	Cardiac standard
II	Uncontrolled	Unsuccessful resuscitation attempt	Emergency Room	Cardiac standard
III	Controlled	Awaiting cardiac arrest	Intensive Care Unit	Cardiac standard
IV	Controlled	Cardiac arrest while brain death	Intensive Care Unit	Cardiac standard
V*	Uncontrolled	ICU sudden irreversible cardiac arrest	Intensive Care Unit	Cardiac standard
VI**	Partially controlled	Death in ECMO maintenance	Intensive Care Unit	Cardiac or neuro st.

* Madrid category, Sanchez-Fructuoso et al. *J Am Soc Nephrol* 11: 350, 2000;

** Pavia category

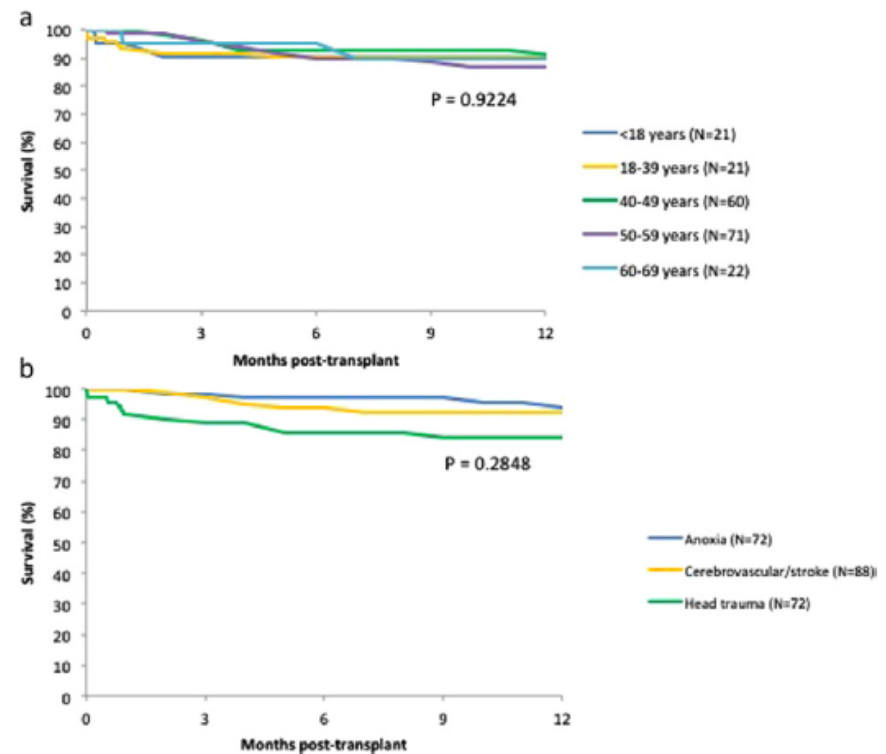
(N)ECMO for Organ Protection ?



International Society for Heart and Lung Transplantation Donation After Circulatory Death Registry Report

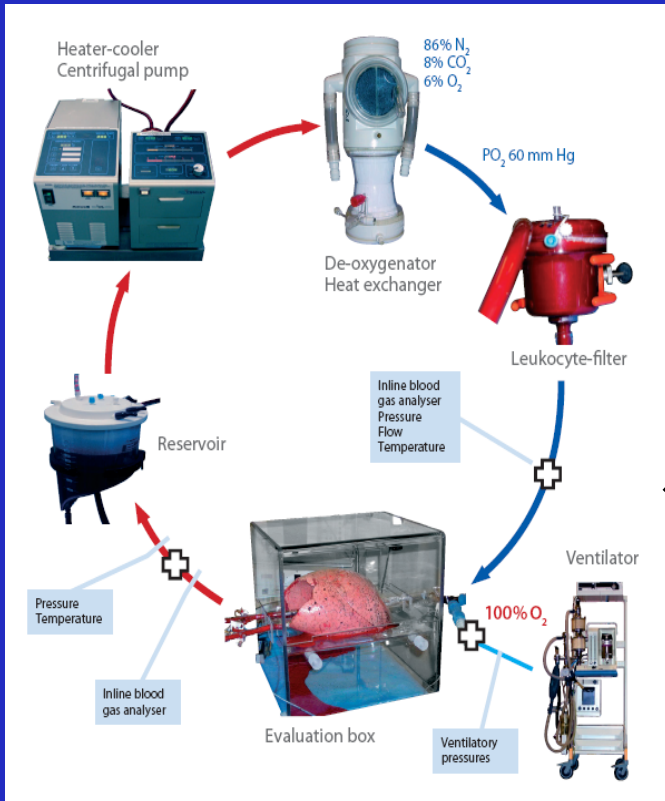


Marcelo Cypel, MD, Bronwyn Levvey, RN, Dirk Van Raemdonck, MD, Michiel Erasmus, MD, John Dark, MB, FRCS, Robert Love, MD, David Mason, MD, Allan R. Glanville, MD, Daniel Chambers, MD, Leah B. Edwards, PhD, Josef Stehlik, MD, Marshall Hertz, MD, Brian A. Whitson, MD, Roger D. Yusen, MD, Varun Puri, MD, Peter Hopkins, MD, Greg Snell, MD, and Shaf Keshavjee, MD; for the International Society for Heart and Lung Transplantation



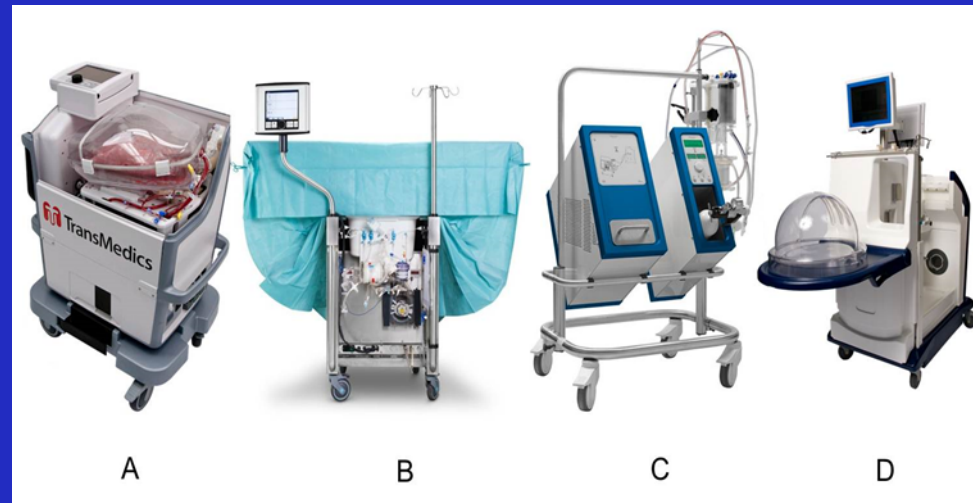
CONCLUSION: This large study of international, multi-center experience demonstrates excellent survival after lung transplantation using DCD donors. It should be further evaluated whether the mechanism of donor death influences survival after DCD transplant.

Ex Vivo Lung Perfusion (EVLP)



How could EVLP help to improve outcome?

- *by increasing the acceptance rate*
- *by decreasing the incidence of PGD (IRI)*
- *by decreasing the incidence of BOS (CR)*



PRESERVATION AND INCREASE POST-OPERATIVE RESULTS



The INSPIRE International Lung Trial With The Organ Care System Technology (OCS™)



[OLB05*] THE ORGAN CARE SYSTEM (OCS™) LUNG INSPIRE INTERNATIONAL TRIAL RESULTS

Abbas Ardehali, Marshall Hertz, Ken McCurry, Christian Bermudez, Marco Schiavon, Joren Madsen, Federico Rea, Gabiel Loor, Michael Smith, Jasleen Kureja, Gregor Warnecke, Dirk Van Raemdonck, Gilbert Massard, Andre R. Simon, Javier Moradiellos, Andres Varela, Igor Tudorache, Christian A. Kuehn, Murat Avsar, Wiebke Sommer, Bettina Wiegmann, Hermann Reichenspurner, Jaya Nagendran, Pascal A. Thomas, Nicola Santelmo, Pierre E. Falcoz, Anne Olland, Christoph Knosalla, Roland Hetzer, Steven Tsui, Kumud Dhital, Axel Haverich

Results: 306 subjects were treated per protocol, 141 OCS group and 165 SOC group patients. While the total out of body time was longer in the OCS group, the total ischemia time was significantly shorter vs. SOC group ($p < 0.001$). At day 30, survival and freedom of PGD 3 within 72 hours was 79.4% of the OCS vs. 70.3% of SOC patients (Primary effectiveness endpoint: Non-inferiority $p = 0.0045$ and superiority $p = 0.09$). For the composite of in hospital survival and freedom of PGD 3 within 72 hours, 80.1% of OCS patients met the endpoint vs. 66.7% of SOC arm (Non-inferiority $p = 0.0003$ and superiority $p = 0.01$). Freedom from PGD 3 within the first 72 hours post-transplant was 82.3% in OCS arm vs. 70.3% in the SOC arm (superiority test $p = 0.016$). The trial met the primary safety endpoint under the non-inferiority margin of 0.075; $p = 0.0035$.

Conclusions: This trial meets all its non-inferiority endpoints and multiple important superiority endpoints including a significant reduction of PGD grade 3 using the OCS Lung technology. These results provide evidence for new portable EVLP strategies in routine lung preservation to improve outcomes.

RECONDITIONING

NEW TECHNOLOGY

(Ann Thorac Surg 2007;83:2191-5)

First Human Transplantation of a Nonacceptable Donor Lung After Reconditioning Ex Vivo

Stig Steen, MD, PhD, Richard Ingemansson, MD, PhD, Leif Eriksson, MD, PhD, Leif Pierre, CPP, Lars Algotsson, MD, PhD, Per Wierup, MD, PhD, Qiuming Liao, MD, Atli Eyjolfsson, MD, Ronny Gustafsson, MD, PhD, and Trygve Sjöberg, PhD

Conclusions. Rejected donor lungs may be successfully transplanted after being reconditioned *ex vivo*.

ORIGINAL ARTICLE

N Eng J Med 2011;364(15):1431 - 1440 Normothermic Ex Vivo Lung Perfusion in Clinical Lung Transplantation

Marcelo Cypel, M.D., Jonathan C. Yeung, M.D., Mingyao Liu, M.D., Masaki Anraku, M.D., Fengshi Chen, M.D., Ph.D., Wojtek Karolak, M.D., Masaaki Sato, M.D., Ph.D., Jane Laratta, R.N., Sassan Azad, C.R.A., Mindy Madonik, C.C.P., Chung-Wai Chow, M.D., Cecilia Chaparro, M.D., Michael Hutcheon, M.D., Lianne G. Singer, M.D., Arthur S. Slutsky, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Marc de Perrot, M.D., Andrew F. Pierre, M.D., Thomas K. Waddell, M.D., Ph.D., and Shaf Keshavjee, M.D.



RECIPIENT

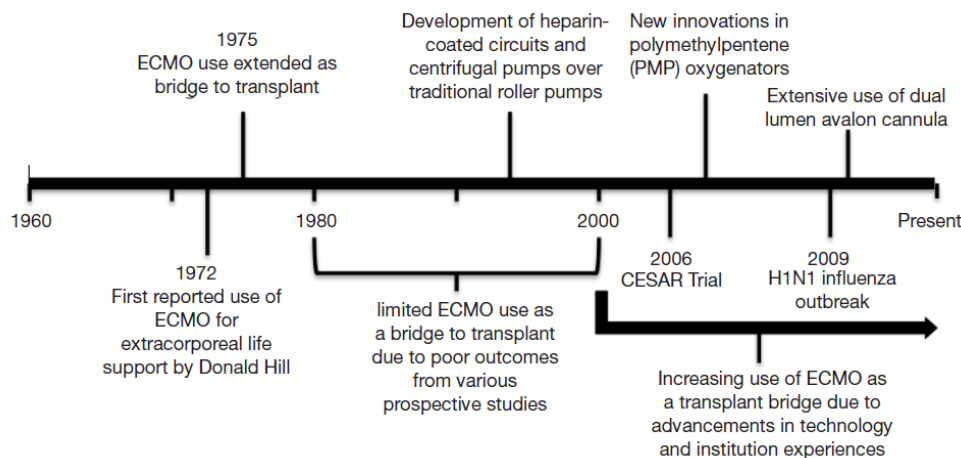
ECMO - Bridge

ECMO - Support

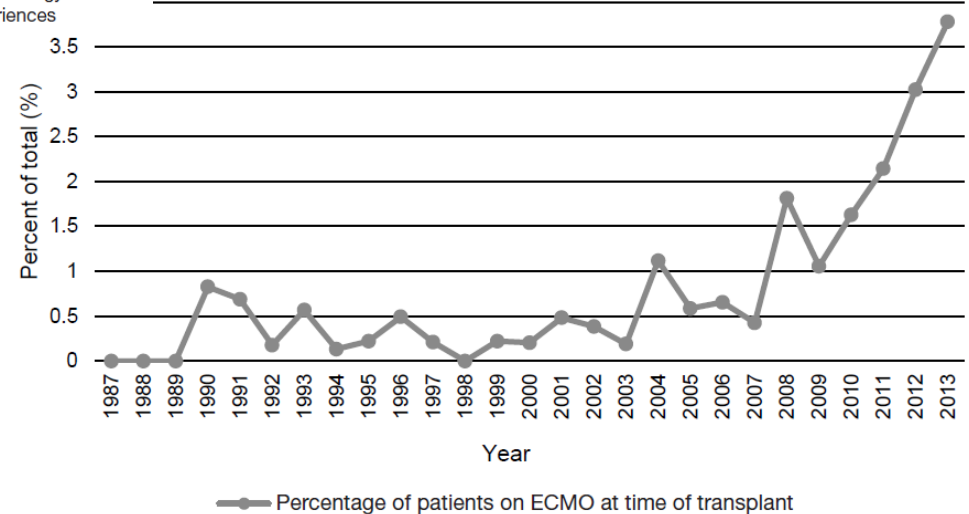
ECMO – Post tx

Bridge to lung transplantation and rescue post-transplant: the expanding role of extracorporeal membrane oxygenation

Brian C. Gulack, Sameer A. Hirji, Matthew G. Hartwig



Use of ECMO prior to lung transplant by year



Bridge to lung transplantation and rescue post-transplant: the expanding role of extracorporeal membrane oxygenation

Brian C. Gulack, Sameer A. Hirji, Matthew G. Hartwig

Table 1 Contraindications (both absolute and relative) to bridging to lung transplant with ECMO (9,10,37,39,40)

Absolute contraindication

- Untreated infection
- Organ failure (other than pulmonary)
- Recent malignancy
- Active substance abuse
- Poor social support system
- History of nonadherence

Relative contraindication

- Advancing age
- Small institutional experience
- Poor pre-ECMO functional status
- Severe obesity (BMI >30)

ECMO, extracorporeal membrane oxygenation.

Table 2 Overview of recent single and multi-institution studies reviewing outcomes following lung transplantation after ECMO

Study	Number of patients	1-year survival (%)
Toyoda <i>et al.</i> [2013] (9)	24	74
Hoopes <i>et al.</i> [2013] (12)	31	93
Anile <i>et al.</i> [2013] (44)	7	85.7
Nosotti <i>et al.</i> [2013] (43)	11	85.7
Lafarge <i>et al.</i> [2013] (10)	30	66.5
Bittner <i>et al.</i> [2012] (27)	27	33
Gottlieb <i>et al.</i> [2012] (42)	60	57
Lang <i>et al.</i> [2012] (38)	34	60
Hämmäinen <i>et al.</i> [2011] (13)	13	92

ECMO, extracorporeal membrane oxygenation.

Newer treatment modalities

Transplantation. 2015 Aug;99(8):1667-71.

Outcome of Extracorporeal Membrane Oxygenation as a Bridge To Lung Transplantation: An Institutional Experience and Literature Review.

Inci I, Klinzing S, Schneiter D, Schuepbach RA, Kestenholz P, Hillinger S, Benden C, Maggiorini M, Weder W.

CONCLUSIONS: Our data show significantly lower survival in this high-risk group compared to patients transplanted without preoperative ECLS. **Awake and ambulatory ECLS provides the best prognosis for these high-risk patients.**

Awake vs.Intubated

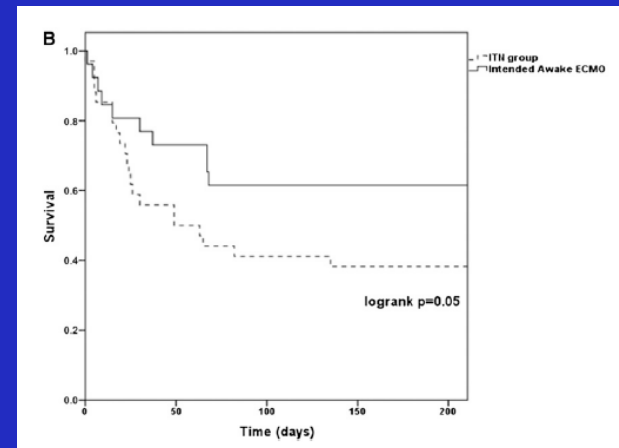
Am J Respir Crit Care Med Vol 185, Iss. 7, pp 763-768, Apr 1, 2012

Extracorporeal Membrane Oxygenation in Awake Patients as Bridge to Lung Transplantation

Thomas Fuehner¹, Christian Kuehn², Johannes Hadem³, Olaf Wiesner¹, Jens Gottlieb¹, Igor Tudorache², Karen M. Olsson¹, Mark Greer¹, Wiebke Sommer², Tobias Welte¹, Axel Haverich², Marius M. Hoyer¹, and Gregor Warnecke²

Survival at 6 months after LuTx was 80% in the awake ECMO group versus 50% in the MV group ($P = 0.02$). Patients in the awake ECMO group required shorter postoperative MV ($P = 0.04$) and showed a trend toward a shorter postoperative hospital stay ($P = 0.06$).

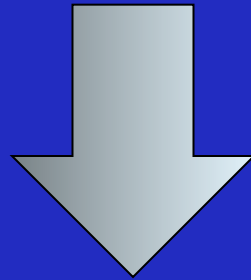
Conclusions: ECMO support in patients who are awake and nonintubated represents a promising bridging strategy, which should be further evaluated to determine its role in patients with end-stage lung disease awaiting LuTx.



ECMO bridge



Patient with high risk mortality



URGENT LUNG TRANSPLANT



Testo approvato in data 13 ottobre 2010



PROTOCOLLO NAZIONALE PER LE EMERGENZE DI POLMONE

1. Il protocollo nazionale per le emergenze di polmone si propone di diminuire il tempo di attesa in lista dei pazienti più critici.
2. I pazienti arruolabili devono essere di età ≤ 50 anni, in assistenza respiratoria invasiva e/o con device extracorporeo vascolare ad esclusione del DECAP, già inseriti in lista di attesa per trapianto di polmone e ricoverati presso la terapia intensiva di un centro trapianti di polmone.

Few conflicting papers

European Journal of Cardio-Thoracic Surgery 46 (2014) e41–e47
doi:10.1093/ejcts/ezu259 Advance Access publication 3 July 2014

ORIGINAL ARTICLE

High-emergency waiting list for lung transplantation: early results of a nation-based study[†]

Bastien Orsini^a, Edouard Sage^b, Anne Olland^c, Emmanuel Cochet^d, Mayeul Tabutin^e, Matthieu Thumerel^f,
Florent Charot^g, Alain Chapelier^b, Gilbert Massard^c, Pierre Yves Brichon^d, Francois Tronc^e, Jacques Jougon^f,
Marcel Dahan^g, Xavier Benoit D'Journo^a, Martine Reynaud-Gaubert^c, Delphine Trousse^a,
Christophe Doddoli^a and Pascal Alexandre Thomas^{a,*}

In-hospital mortality: 29.4%

CONCLUSIONS: The new allocation system aimed at lowering mortality on the RWL, but also offered an access to LTx for new patients with end-stage respiratory failure. The HEWL increased the likelihood of mortality after LTx, but permitted acceptable mid-term survival rates. The high mortality associated with the use of ECMO should be interpreted cautiously.

30-day mortality: 18%

Interactive CardioVascular and Thoracic Surgery Advance Access published August 18, 2014

Interactive CardioVascular and Thoracic Surgery (2014) 1–6
doi:10.1093/icvts/ivu257

ORIGINAL ARTICLE – ADULT CARDIAC

Urgent lung transplant programme in Italy: analysis of the first 14 months[†]

Massimo Boffini^{a,*}, Federico Venuta^b, Federico Rea^c, Michele Colledan^d, Luigi Santambrogio^e,
Andrea Maria D'Armini^f, Alessandro Bertani^g, Luca Voltolini^h, Francesco Parisiⁱ, Giuseppe Marinelli^j,
Alessandro Nanni Costa^k and Mauro Rinaldi^a

CONCLUSIONS: The urgent lung transplant programme allowed transplantation in a significant percentage of prioritized patients with acceptable 30-day and 1-year mortality rates. An accurate selection of recipients may further improve the clinical impact of this programme, reducing the ethical concerns about transplantation in high-risk patients.

URGENT LUNG TRANSPLANT PROGRAMME

PADOVA EXPERIENCE

PERIOD: JANUARY 2012 TO NOVEMBER 2014

POPULATION: 17 PATIENTS IN HEWL

16 ECMO-BRIDGE:

- 3 V-A ECMO (18.7%)
- 13 V-V- ECMO (81.3%)*

1 PATIENT ONLY INTUBATED

1 PATIENT DIED ON HEWL
(MORTALITY 5.8%)

16 BLTX

*2 SWITCH FROM ECMO VV TO ECMO VA (BOTH THESE PATIENTS DIED IN PERIOPERATIVE PERIOD)

URGENT LUNG TRANSPLANT PROGRAMME

PADOVA POPULATION GROUP

SEX (M/F)	2/15
AGE (yr)	27 ± 11.5
BMI	19.1 ± 3.3
DIAGNOSIS	
• CF	11
• IPF	2
• LIP	1
• BOS	1
• Other	2
Waiting list time(d)	6 (range:3-48)
Colonisation	8 (47%)
Mechanical ventilation (MV)	1 (5.9%)
Extracorporeal lung support (ECLS)	4 (23.5%)
MV + ECLS	12 (70.6%)

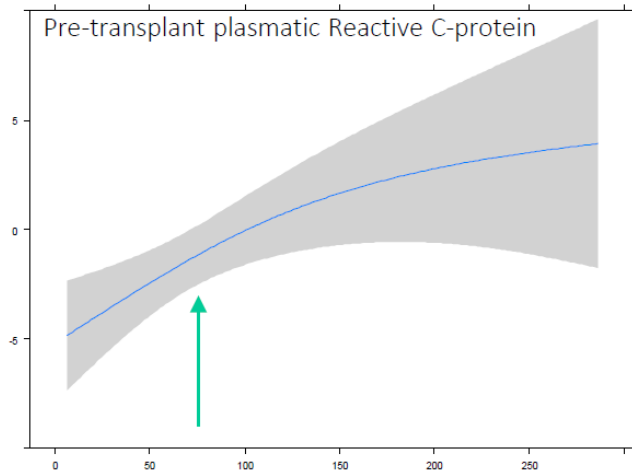
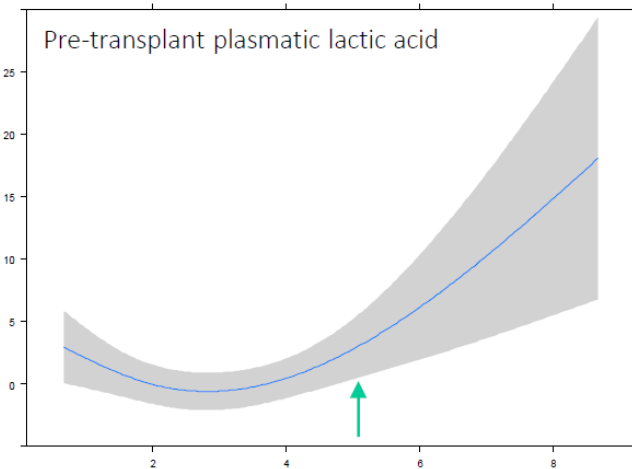
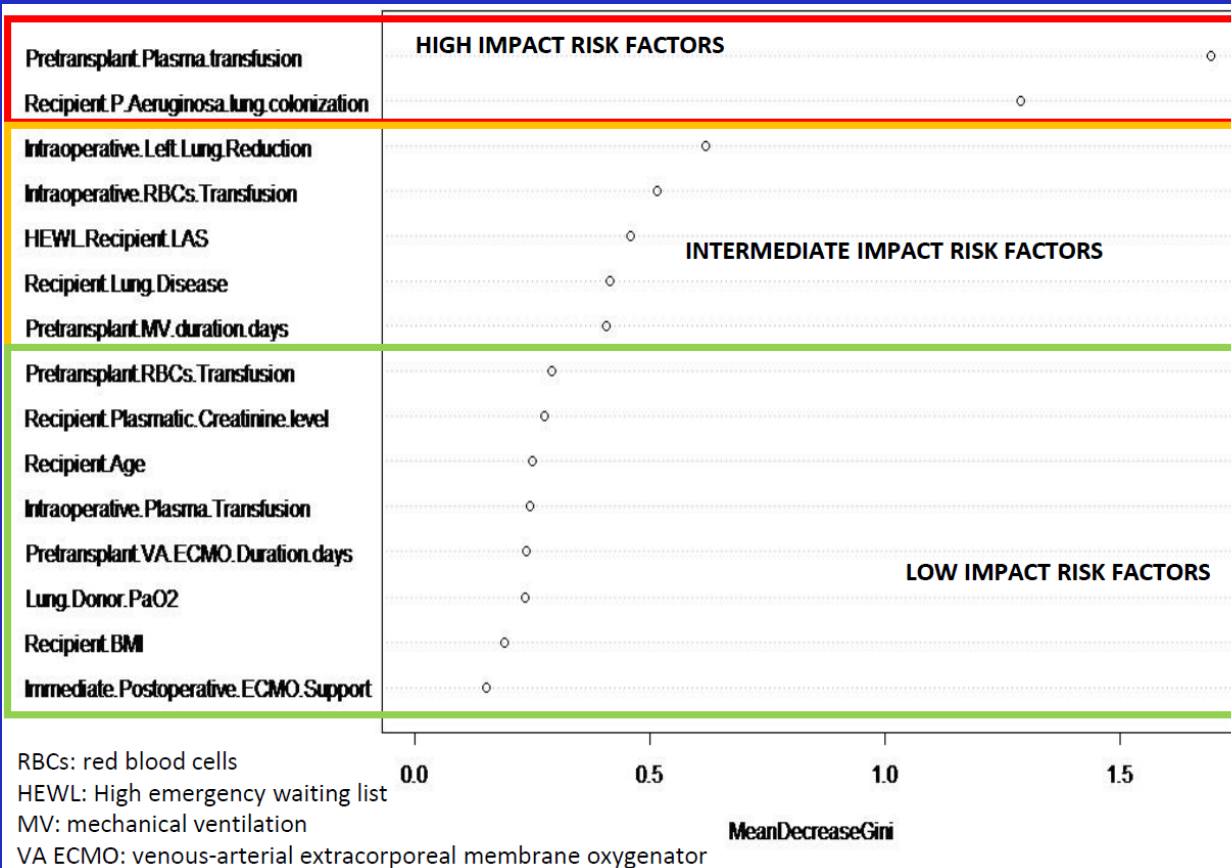
URGENT LUNG TRANSPLANT PROGRAMME

POST-TRANSPLANT RESULTS

ECMO	11 (68,7%)
ECMO duration (d)	4 ± 4,8
MV (d)	4 ± 19
ICU stay(d)	21,3 ± 17,9
30 day-mortality	5 (31,2%)
In-hospital mortality	6 (37,5%)
1 year-survival	9 (56,2%)

URGENT LUNG TRANSPLANT PROGRAMME

PRE-OPERATIVE RISK FACTORS OF IN-HOSPITAL MORTALITY



URGENT LUNG TRANSPLANT PROGRAMME

KEY POINTS

- Accurate selection of recipients to decrease the high in-hospital mortality in high-risk patients
- Necessity of further studies to evaluate risk factors of in-hospital mortality of these patients

RECIPIENT

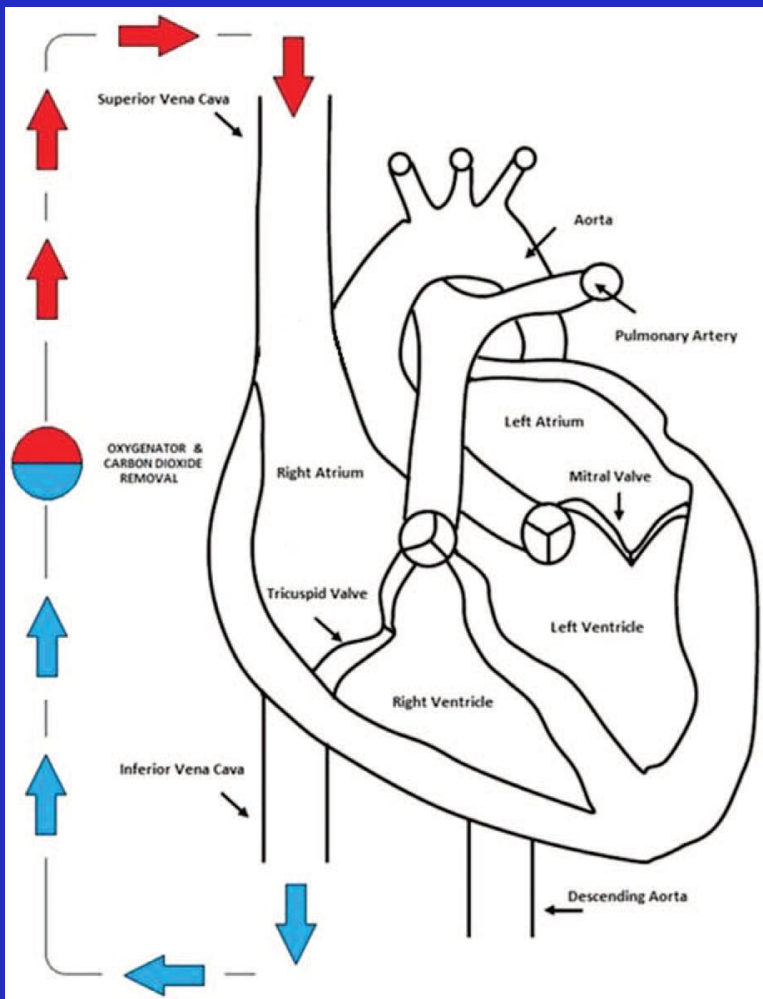
Hemodynamics
Hypoxia - Hypercapnia



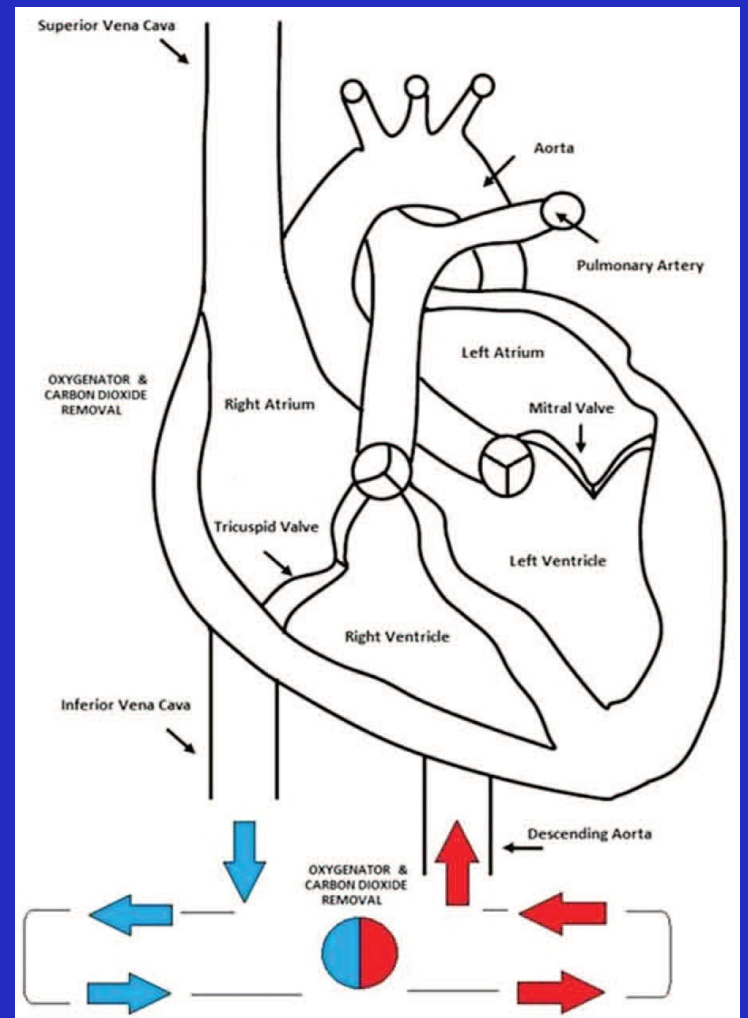
ECMO - Bridge

ECMO - Support

ECMO - Post-tx



Veno-venous ECMO



Veno-arterial ECMO

Institutional experience with extracorporeal membrane oxygenation in lung transplantation[☆]

Clemens Aigner, Wilfried Wisser, Shahrokh Taghavi, György Lang,
Peter Jaksch, Damian Czyzewski, Walter Klepetko^{*}

Department of Cardio-Thoracic Surgery, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria

European Journal of Cardio-thoracic Surgery 31 (2007) 468–474

ECMO is a valuable tool in lung transplantation providing the potential to bridge patients to transplantation, to replace CPB with at least equal results and to overcome severe postoperative complications. Favourable survival rates can be achieved despite the fact that ECMO is used in the more complex patient population undergoing lung transplantation as well as to overcome already established severe complications.

CARDIOTHORACIC TRANSPLANTATION: LUNG TRANSPLANTATION

Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

Tiago N. Machuca, MD, Stephane Collaud, MD, MSc, Olaf Mercier, MD, PhD, Maureen Cheung, MD, Valerie Cunningham, CCP, S. Joseph Kim, MD, PhD, Sassan Azad, CRA, Lianne Singer, MD, MSc, Kazuhiro Yasufuku, MD, PhD, Marc de Perrot, MD, MSc, Andrew Pierre, MD, MSc, Karen McRae, MD, Thomas K. Waddell, MD, PhD, Shaf Keshavjee, MD, MSc, and Marcelo Cypel, MD, MSc

J Thorac Cardiovasc Surg 2015;149:1152-7

Conclusions: Extracorporeal membrane oxygenation may be considered as the first choice of intraoperative cardiorespiratory support for lung transplantation. (J Thorac Cardiovasc Surg 2015;149:1152-7)

Five-year experience with intraoperative extracorporeal membrane oxygenation in lung transplantation: Indications and midterm results

Fabio Ius, MD,^a Wiebke Sommer, MD,^{a,b} Igor Tudorache, MD,^a
Murat Avsar, MD,^a Thierry Siemeni, MD,^a Jawad Salman, MD,^a
Ulrich Molitoris, MD,^a Clemens Gras, MD,^c Bjoern Juettner, MD,^c
Jakob Puntigam, MSc,^a Joerg Optenhoefel, MSc,^a Mark Greer, MD,^d
Nicolaus Schwerk, MD,^e Jens Gottlieb, MD,^{b,d} Tobias Welte, MD,^{b,d}
Marius M. Hoeper, MD,^{b,d} Axel Haverich, MD,^{a,b} Christian Kuehn, MD,^{a,1} and
Gregor Warnecke, MD^{a,b,1}

J Heart Lung Transplant. 2015 Sep 5.

CONCLUSIONS: Intraoperative ECMO filled the gap between pre-operative and post-operative ECMO in lung transplantation. Although complications and in-hospital mortality were higher in patients who received ECMO, survival was similar among patients who underwent transplantation with or without ECMO.

PADOVA EXPERIENCE

Design of the study

2012-2014: single-center,
retrospective analysis of
49 non-urgent lung transplant

14 ECMO
(13 BSLT)

6 months follow-up

35 NO-ECMO
(24 BSLT)

Venoarterial, femoro-femoral

Preoperative characteristics

Recipient

	ECMO	NO-ECMO	P
Age	55	47	0.29
Sex (M)	5/9	10/25	0.62
Pulmonar fibrosis	35.7%	48.6%	0.41
Cystic fibrosis	14.3%	37.1%	0.11
MDR Colonisation	7.1%	34.3%	0,04
Pulmonar hypertension	50%	22.8%	0,06

Donor

	ECMO	NO-ECMO	P
Age	50	35	<0.01
PaO2/FiO2	419.5	485	0.03
OTO score	3	1	0.054
Marginals	64.3%	51.4%	0.41

Transfusions

INTRAOPERATIVE			
	ECMO	NO-ECMO	P
pRBC	3 (0/5)	0 (0/2.5)	0.05
FFP	1 (0/3)	0 (0/0)	0.04
Platelets	0 (0/0.75)	0 (0/0)	<0.01

POST-OPERATIVE			
	ECMO	NO-ECMO	P
pRBC	2.5 (0/5.5)	2 (0/3)	0.20
FFP	0 (0/0)	0 (0/0)	0.44
Platelets	0 (0/0)	0 (0/0)	0.50

Data show median (1°/3° qt) of Unit per Patient

Post-operative: laboratory

	ECMO	NO-ECMO	P
Platelets (x 10 ⁹ /L)	161	224	0.12
aPTT (s)	29	26	0.01
INR	1.25	1.17	<0.01
PT (%)	47	59	0.03

Median first laboratory result after LT

Post-operative course

	ECMO	NO-ECMO	P
Duration of IMV (d)	2.5	2	0.01
ICU length of stay (d)	7.5	5	0.01
Hospital length of stay (d)	29	28	0,06
MDR Infections	50%	48.6%	0.93
Acute rejection	28.6%	54.3%	0.10
Bleeding	14.3%	5.7%	0.32
Thromboembolism	21.4%	0%	0.01
Cardiac arrest	14.3%	0%	0.02
Renal replacement therapy	14.3%	2.8%	0.13
6-month complication	64.3%	85.7%	0.09
6-month VC (%)	75	75	0.87

Survival

	ECMO	NO-ECMO	P
30 days	85.7%	100%	0.02
Hospital discharge	85.7%	97,2%	0.13
6 month	85.7%	91,4%	0.55

KEY POINTS

- ▶ Intraoperative ECMO seems a valuable resource for LT and, despite a higher transfusion rate, lead to similar mid-term outcomes to NO-ECMO LT.
- ▶ Need for a larger population analysis, possibly in a multicenter study.

RECIPIENT

ECMO - Bridge

ECMO - Support

ECMO - Post tx

Postoperative “*treatment*” tool

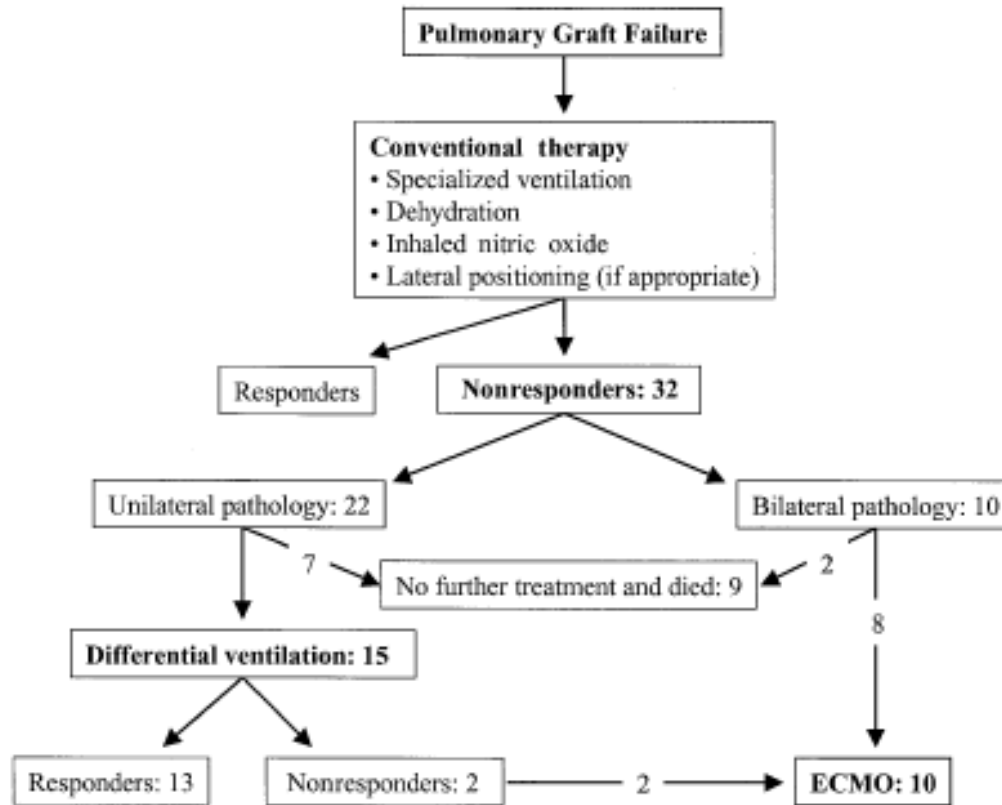


Fig 1. Algorithm for pulmonary graft failure after lung transplantation.

Bridge to lung transplantation and rescue post-transplant: the expanding role of extracorporeal membrane oxygenation

Brian C. Gulack, Sameer A. Hirji, Matthew G. Hartwig

Department of Surgery, Duke University Medical Center, Durham, NC, USA

Correspondence to: Matthew G. Hartwig, MD. Department of Surgery, Division of Thoracic Surgery, Duke University Medical Center, Box# 3863, Durham, NC 27710, USA. Email: matthew.hartwig@duke.edu.

a rescue post-transplant in the treatment of PGD.

The goal should be to avoid or minimize the detrimental effects of ventilator support for PGD secondary to elevated airway pressures or high inspired oxygen concentrations. Firm guidelines vary from center to center, but we recommend initiating ECMO support when ventilatory requirements reach a peak inspiratory pressure of 35 cm H₂O or F_iO₂ surpasses 60% in order to minimize lung injury from aggressive mechanical ventilation and oxidative stress.

Early Institution of Extracorporeal Membrane Oxygenation for Primary Graft Dysfunction After Lung Transplantation Improves Outcome

Christopher H. Wigfield, MD, FRCS,^a Joshua D. Lindsey, MBS,^a Thomas G. Steffens, CCP,^a
Niloo M. Edwards, MD, FACS,^a and Robert B. Love, MD, FACS^b

J Heart Lung

Transplant 2007;26:331-8. Copyright © 2007 by the International Society for Heart and Lung Transplantation.

Conclusions:

Our data suggest that, in addition to prolonged ventilation and pharmacologic support, ECMO should be considered as a bridge to recovery from PGD in lung transplantation. Early institution of ECMO may lead to diminished mortality in the setting of ALI despite the high incidence of MOF. Late institution of ECMO was associated with 100% mortality in this investigation.

Extended use of extracorporeal membrane oxygenation after lung transplantation

David P. Mason, MD,^a Daniel J. Boffa, MD,^a Sudish C. Murthy, MD, PhD,^a Thomas R. Gildea, MD,^b Marie M. Budev, DO,^b Atul C. Mehta, MD,^b Ann M. McNeill, RN,^a Nicholas G. Smedira, MD,^a Jingyuan Feng, MS,^c Thomas W. Rice, MD,^a Eugene H. Blackstone, MD,^{a,c} and B. Gösta Pettersson, MD, PhD^a

J Thorac Cardiovasc Surg 2006;132:954-60

Conclusions: ECMO can be extended beyond early severe graft failure to acute rejection and can be considered after the immediate postoperative period. -----

CONCLUSIONS

- **New prospective for ECMO (donor)**
- **Conventional use of ECMO (recipient)**
- **Increased use of ECMO bridge in awake patient**
- **ECMO is the first choice of intraoperative cardiorespiratory support for lung transplantation**
- **Similar survival among patients who underwent Lung Transplantation with or without ECMO**
- **Early institution of ECMO for PGD after transplantation**



THANK YOU

