ECMO in Cancer Patients

RENCONTRE EVELINE MARKIEWICZ - 18^{ème} édition

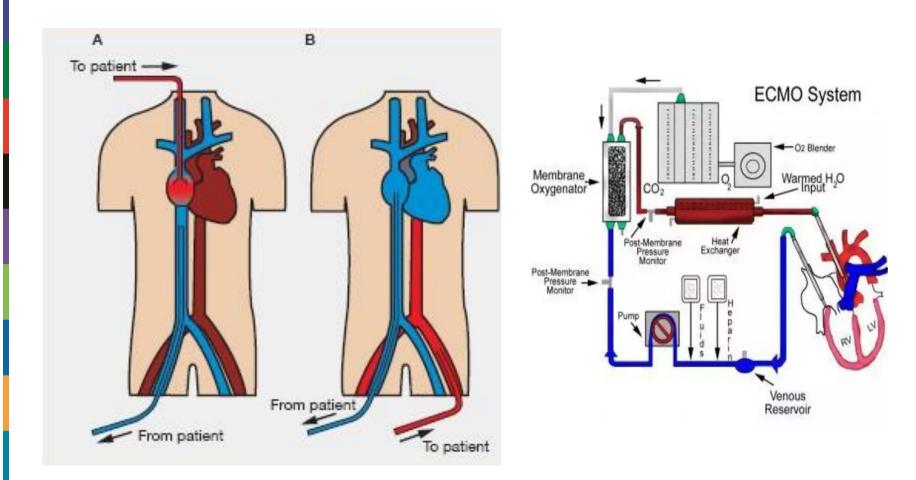
URGENCES ET COMPLICATIONS SÉVÈRES CHEZ LE PATIENT CANCÉREUX

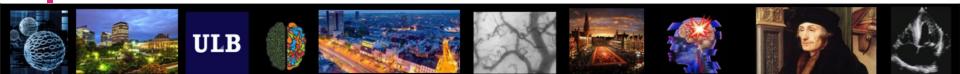
CRAPANZANO MINICHELLO VANES

Fabio Silvio TACCONE, MD, PhD **Dpt. of Intensive Care** Hôpital Erasme – ULB **Brussels** (BE)







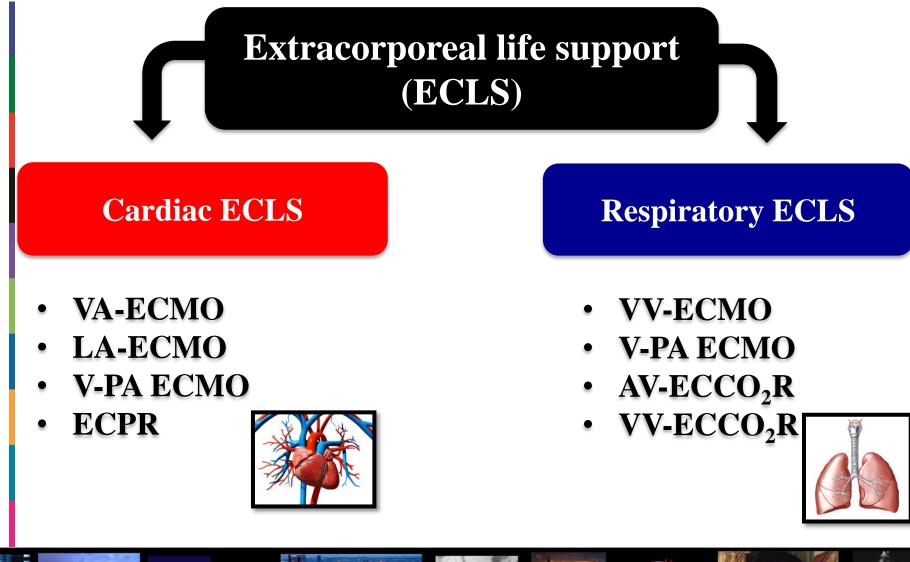




ULB





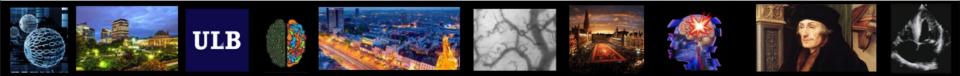






	Total Runs	Survived	ECLS	Survived	to DC or Transfer
Neonatal					
Pulmonary	26,719	22,394	83%	19,252	72%
Cardiac	7,266	4,727	65%	2,987	41%
ECPR	1,613	1,089	67%	666	41%
Pediatric					
Pulmonary	8,287	5,608	67%	4,812	58%
Cardiac	9,593	6,620	69%	4,941	51%
ECPR	3,615	2,078	57%	1,508	41%
Adult					
Pulmonary	13,712	9,174	66%	8,040	58%
Cardiac	12,566	7,181	57%	5,222	41%
ECPR	3,995	1,572	39%	1,144	28%
Total	87,366	60,443	69%	48,572	55%

July 2017

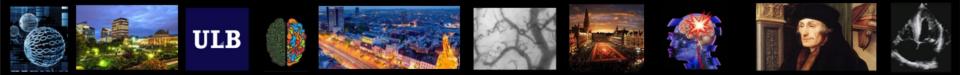






Centers Centers by year 400 10000 320 8000 240 6000 Centers Cases 160 4000 80 2000 0 0 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 1999 200 201 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 83 86 98 111 111 112 115 112 115 111 114 115 119 117 117 129 131 134 149 163 181 200 239 266 303 323 329 251 Centers Cases 1644 1775 1933 1910 1879 1876 1868 1743 1720 1722 1859 1855 1908 1974 1977 2183 2346 2564 2802 3260 3443 4009 5076 6098 7545 8529 9127 2807

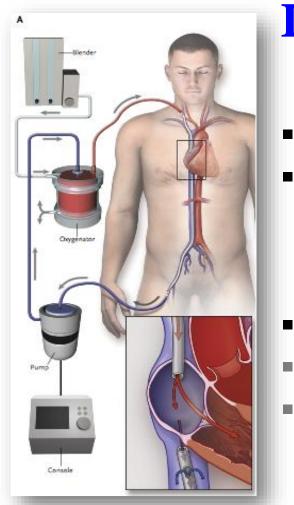
July 2017





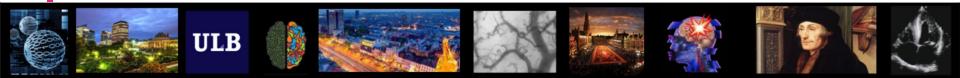
VV-ECMO





INDICATIONS

- Hypoxemic Respiratory Failure
- Lung Transplantation
 - $\blacktriangleright \quad Bridge \ to \ Tx$
 - Surgery
 - > PGD
- Trauma
- Interventional procedures
- **Obese patients** with severe respiratory failure (to promote spontaneous breathing)





VV-ECMO: HRF



ARDS Aspiration/Smoke inhalation Pneumonia **RECOVERY** Alveolar nemorrhage Alveolar proteinosis

Status asthmaticus *
 LUNGREST
 Pulmonary contusion

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- First successful implantation of ECMO by Robert Bartlett in 1972 (motor vehicle accident with severe respiratory failure)
- Used commonly at several specialized hospitals for the treatment of <u>infants</u> and, less frequently, for adults with respiratory or cardiac failure in 70-90
- Its use in adults remained controversial for some time due to lower survival rates
 - 1974 (Zapol): 90 patients, 42 of them treated with VA-ECMO High Pplt and low PEEP with low RR and high Vt; 9 days of MV to ECMO RBCT: 2.5 L/day 90% of mortality in both groups
 - 1994 (Morris): 40 patients treated with low-flow ECMO and PCIRV, no "lung rest" large inexperience RBCT 2.7 L/day Mortality: 67% ECMO vs. 56% CTRL

ECMO devices have markedly evolved – MV has improved

VV-ECMO: HRF / Evidence



ELIGIBLE PATIENTS

Severe potentially reversible HRF • Murray ≥ 2.5 • High PaCO2 / pH ≤ 7.2 Age: 18-65 yrs

High Pplt / FiO2 \leq 7 days No ICH, CI to UFH No Limitation of therapy

REGISTRATION

Referring ICU physician confirms:

- Patients is eligible
- Beds available

RANDOMIZATION

Patient is eligible Consent Prognostic factors Central Phone Randomization Allocation If necessary, arrange transport Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

180 randomized patients (90 vs. 90) out of 766 over 5 years (2001-2006) in 69 centers

90 ECMO patients (12 hours of optimized MV)

- <u>68</u> underwent ECMO ("LUNG REST")
- <u>22</u> not treated (24%)



 \geq 16 = Improvement



Mortality 18%

- > 3 = Death before transport
- \triangleright 2 = Death during transport
- \succ 1 = Amputation















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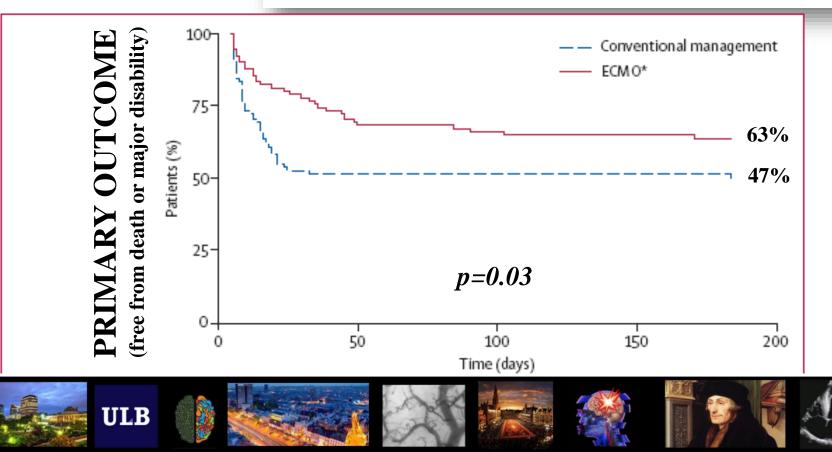
VV-ECMO: HRF / Evidence





Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

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VV-ECMO: HRF / Evidence

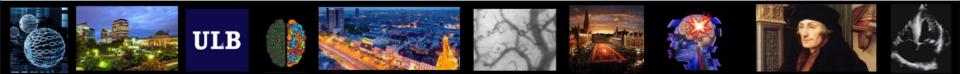




Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

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- Difference in **mortality** was not significant (p=0.07)
- In **PP analysis**, difference became even less significant
- Long recruitment period (mortality of ARDS changed)
- Expected mortality in the CTRL group of 70% (too high?)
 - ✓ "conventional centers" provided poor ARDS management?
- System with **ONE or FEW** dedicated centers = not generalizable !!!!
- What about "adverse events"???





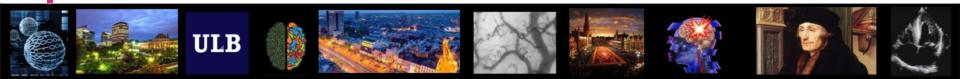
Several **case-series** reporting survival rate > 60% in severe ARDS patients on ECMO, while overall mortality in the same condition without ECMO was estimated < 35%

> Lewandoski, ICM 1997; Linden, ICM 2000; Mols G, Am J Surg 2000; Ullrich, Am Thorac Surg 1999; Kolla, Am Surg 1997; Bartlett, Clin Chest Med 2000

Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand

The ANZIC Influenza Investigators*

- 722 patients admitted to the ICUs; 462 (64%) treated with MV; 14% mortality
- 68 patients (15%) treated with VV-ECMO (PF 56-PEEP 18); 71% survival





Extracorporeal Membrane Oxygenation in Severe Influenza Infection with Respiratory Failure: A Systematic Review and Meta-analysis

Study	VV ECMO (%)	Pre-ECMO MV	Pre-ECMO	Medi	an (day	s)	Mortality (%)
		Median (days)	PaO ₂ /FiO ₂ ratio	ECMO duration	MV	ICU LOS	
Kutleša, 2014	100	2	58	8	NA	NA	35
Michaels, 2013	46	3.5	62	9.8	NA	21	40
Pham, 2013	87	2	63	11	28	33	36
Weber-Carstens, 2013	NA	2.6	87	NA	32	33	54
Roncon-Albuquerque, 2012	90	9.3	69	22	32	36	60
Takeda, 2012	100	5	50	8.5	NA	NA	65
Beutel, 2011	100	NA	85	10	19	NA	48
Forrest, 2011	94	2	57	10	NA	36	19
Noah, 2011	84	4	55	9	NA	NA	29
Patroniti, 2011 7	98	2	63	10	18	22	32
Schellongowski, 2011	80	NA	56	13	17	21	50
Holzgraefe, 2010	92	1	53	16	NA	NA	8
Davies, 2009	93	2	56	10	18	27	29

Table 3: Key procedural details and outcomes

13 studies (n=494 patients) – overall use of ECMO was **42%** and mortality was **37%** (significant heterogeneity) - Duration of ECMO was 10 days; of MV was 19 days

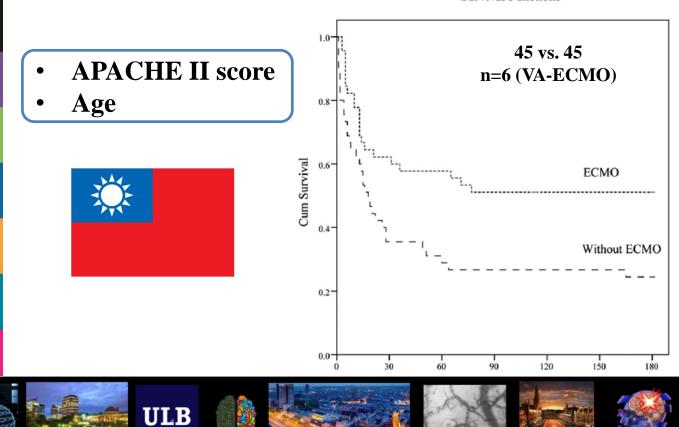
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2017 Annals of Cardiac Anaesthesia



Acute Respiratory Distress Syndrome With and Without Extracorporeal Membrane Oxygenation: A Score Matched Study

Hsiao-Chi Tsai, MD,* Chih-Hsiang Chang, MD,* Feng-Chun Tsai, MD, Pei-Chun Fan, MD, Kuo-Chang Juan, MD, Chan-Yu Lin, MD, Huang-Yu Yang, MD, Kuo-Chin Kao, MD, Ji-Tseng Fang, MD, Chih-Wei Yang, MD, Su-Wei Chang, PhD, and Yung-Chang Chen, MD



Ann Thorac Surg 2015



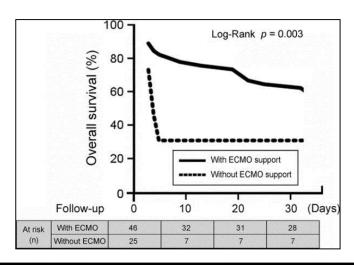


Extracorporeal Life Support for Cardiogenic Shock or Cardiac Arrest Due to Acute Coronary Syndrome

Shingo Sakamoto, MD, Norimasa Taniguchi, MD, Shunsuke Nakajima, MD, and Akihiko Takahashi, MD

Departments of Cardiology and Cardiac Surgery, Sakurakai Takahashi Hospital, Hyogo, Japan

- N=98 (34% cardiogenic shock)
- 55% were weaned from ECLS
- ECLS-related complications occurred in 36%
- All-cause in-hospital mortality rate was 67%



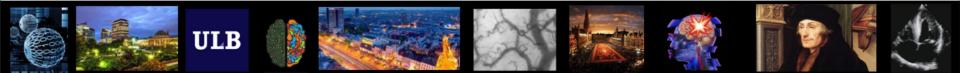
Sheu, CCM 2010

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- Cardiac arrest (in- and out-of hospital)
- Refractory cardiogenic shock due to acute myocardial infarction (AMI)
- AMI mechanical complications (VSD, LVFWR)
- Post-cardiotomy syndrome
- Massive pulmonary embolism
- Decompression of decompensated end-stage dilated cardiomyopathy
- Acute myocarditis
- <u>Support for interventional procedures</u>

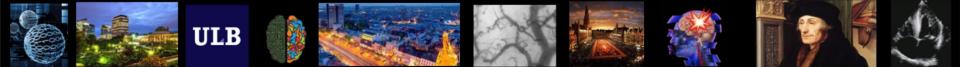




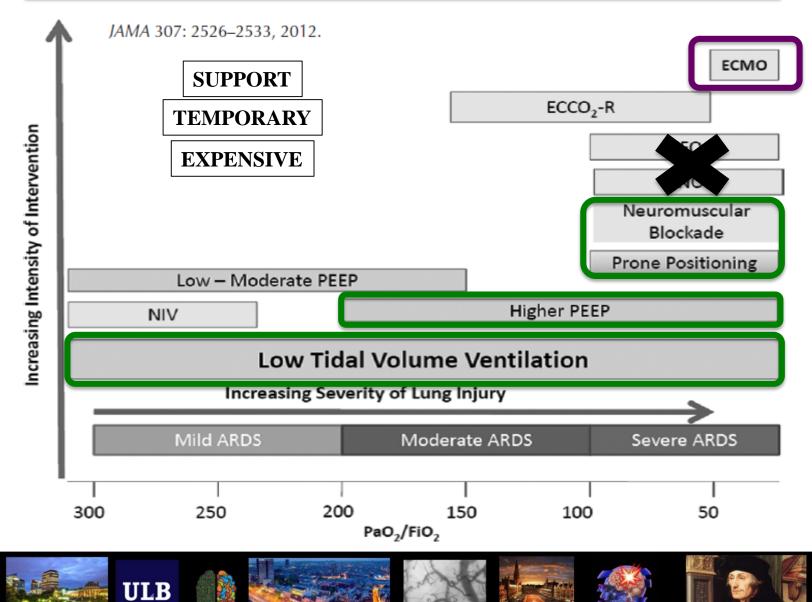
The ELSO's suggestion:



".....ECMO initiation should be considered in hypoxic respiratory failure when the risk of mortality is 50% or greater....."









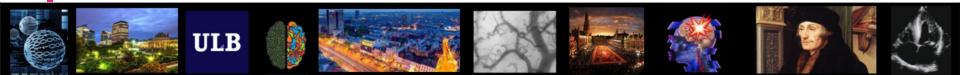


B. Contraindications

There are no absolute contraindications to ECLS, as each patient is considered individually with respect to risks and benefits. There are conditions, however, that are known to be associated with a poor outcome despite ECLS, and can be considered relative contraindications.

- Mechanical ventilation at high settings (FiO2 > .9, P-plat > 30) for 7 days or more
- 2. Major pharmacologic immunosuppression (absolute neutrophil count <400/ml3
- 3. CNS hemorrhage that is recent or expanding





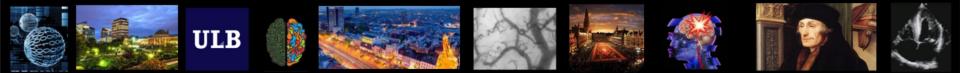


VV-ECMO: HRF - Selection





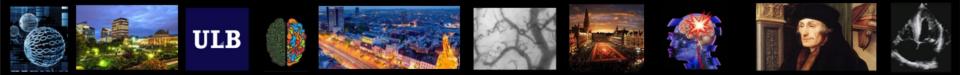
- $PaO_2/FiO_2 < 80$ and $FiO_2 > 80\%$ with PEEP > 10-15 cmH₂O and Pplat > 30 cmH₂O
- $\mathbf{pH} < 7.25$ and $\mathbf{PaCO}_2 > 55$ mmHg for 2 hours together with severe hypoxemia
- No response to **recruitment** manoeuvres or **PP**
- Reversible or potentially treatable **cause**
- Duration of $\mathbf{MV} < 10$ days
- Absence of **CIs**
- **Age** < 75 years







- Irreversible disease
- More than **two chronic organ dysfunctions** (lungs excluded)
- Malignant and/or **terminal illness**
- **Refusal** of blood products
- Chronic severe pathologies
- Intracranial bleeding *
- Major contra-indications for anti-coagulation *
- ETI and MV > 7 (10) days *
- Low platelets count (<50,000/mm³) *
- Age > 80 years*



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VV-ECMO: Immunocompromised Pts



De Rosa et al. BMC Anesthesiology 2014, 14:37 http://www.biomedcentral.com/1471-2253/14/37

CASE REPORT



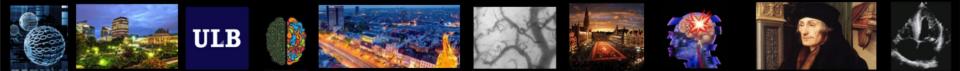
Anesthesiology

BMC

Extra Corporeal Membrane Oxygenation (ECMO) in three HIV-positive patients with acute respiratory distress syndrome

Francesco Giuseppe De Rosa^{1*†}, Vito Fanelli^{2†}, Silvia Corcione¹, Rosario Urbino², Chiara Bonetto², Davide Ricci³, Mauro Rinaldi³, Giovanni Di Perri¹, Stefano Bonora¹ and Marco V Ranieri²

- Several case reports in HIV patients (PCP)
- Diffuse Alveolar Hemorrhage
 - Wegener's granulomatosis
 - SLE vasculitis
 - Polyarteriitis nodosa, Microscopic polyangitis
 - Thrombocytopenia

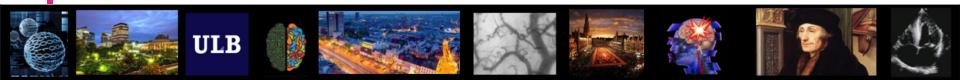






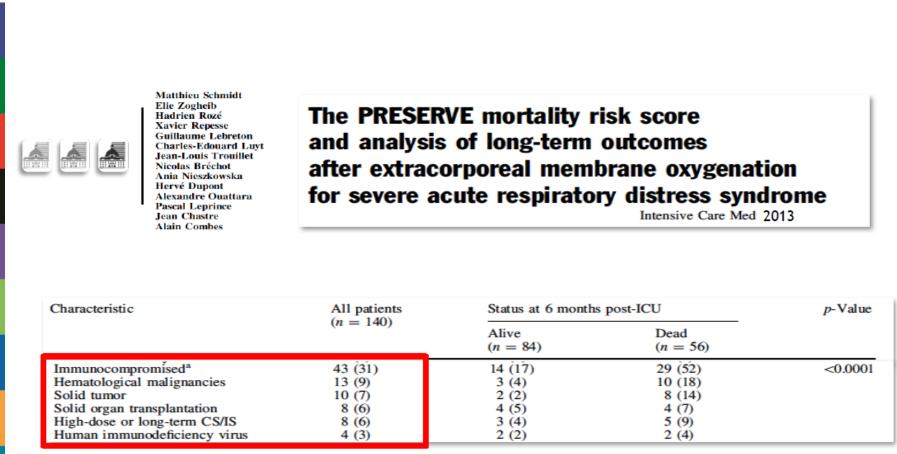
- Endotracheal Tumor resection / Brocho-oesophageal fistula
- Pneumectomy
- Bleomycin lung toxicity
- Bridge to chemotherapy (teratoma; B- or T-lymphoma)
- Bridge to airway stenting and Rx-therapy
- Severe Tumor Lysis and ARDS
- Post major **lung resection** (7/63 pts) *

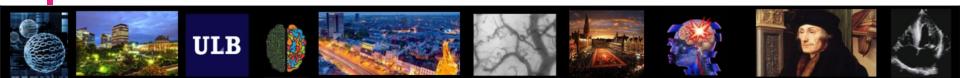
Dunkman, A A Case Rep 2017 Shah, Innovations 2017 Chung, Cancer Res Treat 2017 McLenon, Ann Thorac Surg 2016 Sanford, Pediatric Blood Cancer 2016 Jung, Thorac Cancer 2017 *



VV-ECMO: Cancer patients





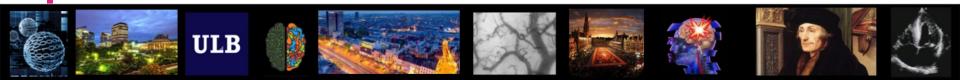






- Cardiogenic shock for pheocromocytoma
- Bridge-to-decision in systemic light-chain amyloidosis
- Cardiac Lymphoma
- Toxoplasma myocarditis < BMT
- Fulminant myocarditis < 5-FU
- Massive pulmonary embolism

Bouabdallaoui, Asian Cardiovasc Thorac Ann 2017 Amraotkar, Tex Heart Inst J, 2016 Allain, Eur J Cardiothorac Surg 2015 Hadem, Clin Res Cardiol 2006





Extracorporeal life support for adults with malignancy and respiratory or cardiac failure: The Extracorporeal Life Support experience American Journal of Surgery (2010)

• 72 adult (>21 yrs) patients

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- **Solid**, n= 47 (65%); **Hematologic**, n=21 (29%)
- Respiratory ECMO, n=54 (75%), 18 Cardiac ECMO (n=8 ECPR)

ECLS Indication	Cancer Patier (Survival † Discharr	Other Adults [†] (Survival to Discharge)	Р
Respiratory support Cardiac support ECPR	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	51% (n = 798/1,558) 34% (n = 333/979) 27% (n = 91/340)	.0003 .0579 1.0
All	3. √₀ (n = 23 / 72)		



ECMO: Cancer patients



Patient no.	Disease	Therapy status (days posttherapy)	Etiology of ARF	APACHE II score	LIS	ECMO days	Bleeding	Out- come	Cause of death
1	PHG	-	Pneumonia	8	2.5		Minor	Died	Sepsis
2	MDS	Danazol	PAP	11	2.7		Major	Died	Pneumonia
3	HLH	Induction on ECMO	Pneumonia	14	3	0 3	-	Died	Pneumonia
4	AML	Allo SCT (30)	Pneumonia	11 14 31 101		5	Major	Died	Pulmonary hemorrhage
5	AML	Allo SCT (420)	Pneumonia		2.25	28	-	Died	Pneumonia
6	PMF	Allo SCT (84)	Pneumonia	Lev /	2	13	-	Died	RV failure
7	MM	Chemotherapy (55)	Pneumoni		3	27	-	Died	Sepsis
8	HD	Chemotherapy (22)	Pneum	2 16	2.5	8	-	Died	Sepsis
9	AML	Induction (10)	Pneum RAS S	13	2	2	Major	Died	Pulmonary hemorrhage
10	AML	Allo SCT (2,190)		17	2.5	3	-	Died	Pneumonia
11	AML	Allo SCT (1,735)	nonia	22	3	9	-	Died	Sepsis
12	AML	Allo SCT (417)	Pheumonia	13	2	1		Died	MOF
13	AML	Induction (22)	Pneumonia	16	2.25	8	Major	Died	Pulmonary hemorrhage
14	AML	Allo SCT (73)	Pneumonia	13	2.5	5	-	Died	MOF
15	ALL	Induction (27)	Pneumonia	32	2.25	7	-	Died	Sepsis

Kang, Korean J Internal Med 2015











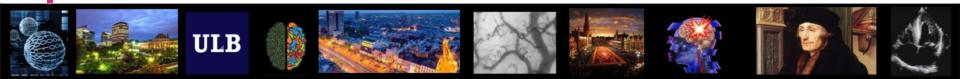




Extracorporeal membrane oxygenation in adult patients with hematologic malignancies and severe acute respiratory failure Critical Care 2014, 18:R20

Philipp Wohlfarth¹, Roman Ullrich², Thomas Staudinger¹, Andja Bojic¹, Oliver Robak¹, Alexander Hermann¹, Barbara Lubsczyk², Nina Worel³, Valentin Fuhrmann⁴, Maria Schoder⁵, Martin Funovics⁵, Werner Rabitsch¹, Paul Knoebl¹, Klaus Laczika¹, Gottfried J Locker¹, Wolfgang R Sperr¹, Peter Schellongowski^{1*} and Arbeitsgruppe für hämato-onkologische Intensivmedizin der Österreichischen Gesellschaft für Internistische und Allgemeine Intensivmedizin und Notfallmedizin (ÖGIAIN)

- 2000-2013; 541 pts with hematological malignancies
- 368 (68%) on mechanical ventilation 14 treated with ECMO (3.8%)
- Median age = 32 (22-51) years
- VV-ECMO 11 (79%)
 Vasopressors 14 (100%)
 RRT 5 (36%)
 Thrombocytopenia 11 (79%)





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ECMO: Cancer patients



Wohlfa	Wohlfarth, Crit Care 2014		P/F: 60 (53 – 65)			Plt: 35 G/L (2		
atient number	Malignancy	Therapy status (days since therapy)	Etiology of ARF	SAPS II	LIS	ECMO days	Bleeding	ICU and hospita outcome
1	CNS NHL	Chemotherapy (51)	Pneumonia	45	3.7	9	Minor	Died
2	Hodgkin lymphoma	Allo SCT (111)	Pneumonia	34	3.3	28 ^b	Major	Died
3	ALL	Consolidation (13)	Abdominal sepsis	78	2.3	4 ^c VA	-	Alive
4	ALL ^a	Induction on ECMO	TRALI	62	3.3	3	-	Alive
5	Burkitt lymphoma	Induction (16)	Pneumonia	63	3.8	Follow-	un (36.)	nonths):
6	ALL	Allo SCT (31)	Pneumonia	39	3.5		- `	ors alive
7	Hodgkin lymphoma	Allo SCT (33)	Pneumonia	65	3.3		mission	
8	ALL	Allo SCT (203)	Pneumonia	68	3.3			
9	DLBCL	Induction on ECMO	Pneumonia	102	4.0		apse	Dico
10	Multiple myeloma	Auto SCT (789)	Pneumonia	43	3.7	9	Major	Alive
11	Anaplastic T-cell NHL ^a	Induction on ECMO	Pneumonia	46	3.0	25 ^d	Major	Alive
12	DLBCL ^a	Induction on ECMO	NHL	36	3.3	3 ^c VA	-	Alive
13	AML	Consolidation (34)	Pneumonia	48	3.3	34	Major	Died
14	DLBCL ^a	Induction on ECMO	NHL	56	2.3	4 ^d VA	-	Alive
Chemo	therapy on EC	MO		51 (42-65)		.3 -3.7)		7/14 (50%

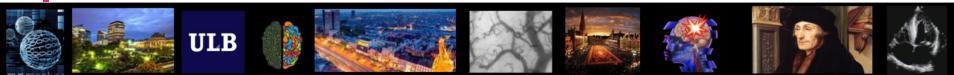


Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*

Philipp Wohlfarth, MD¹; Gernot Beutel, MD²; Pia Lebiedz, MD³; Hans-Joachim Stemmler, PhD⁴; Thomas Staudinger, MD¹; Matthieu Schmidt, PhD⁵; Matthias Kochanek, MD⁶; Tobias Liebregts, MD⁷; Fabio Silvio Taccone, PhD⁸; Elie Azoulay, PhD⁹; Alexandre Demoule, PhD^{10,11}; Stefan Kluge, MD¹²; Morten Svalebjørg, MD¹³; Catherina Lueck, MD²; Johanna Tischer, MD⁴; Alain Combes, PhD⁵; Boris Böll, MD⁶; Werner Rabitsch, MD¹; Peter Schellongowski, MD¹ on behalf of Intensive Care in Hematologic and Oncologic Patients (iCHOP) and the Caring for Critically Ill Immunocompromised Patients Multinational Network (NINE-I)



Crit Care Med 2017





Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*

Variable	All Patients (<i>n</i> = 37)	Nonsurvivors ($n = 30$)	Survivors $(n = 7)$	р
Underlying condition				0.000947
Acute leukemia	22 (59)	21 (70)	1 (14)	
Lymphoma	5 (14)	5 (17)	0	
Myelodysplastic syndrome	3 (8)	0	3 (43)	
Other malignant condition	4 (11)	2 (7)	2 (29)	
Nonmalignant disease	3 (8)	2 (7)	1 (14)	
Remission status at ICU admission ^b				1.0
Complete remission	27 (79)	22 (79)	5 (83)	
No remission, after engraftment	2 (6)	2 (7)	0	
No remission, prior engraftment	5 (15)	4 (14)	1 (17)	

Pneumonia 80%; 85% more than 1 OD; 50% Neutropenia

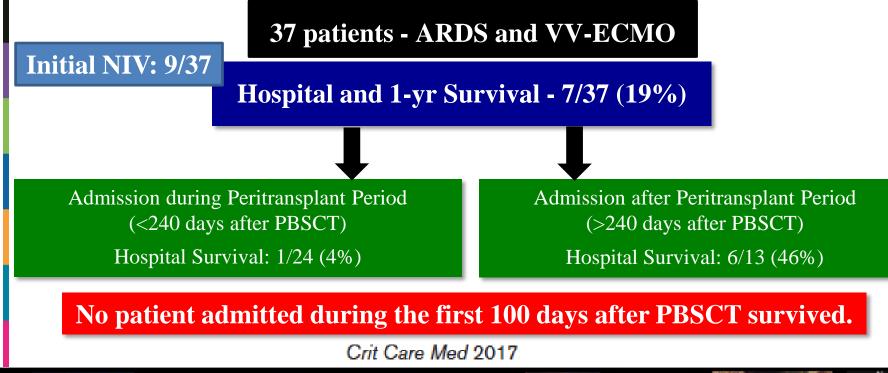


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Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*









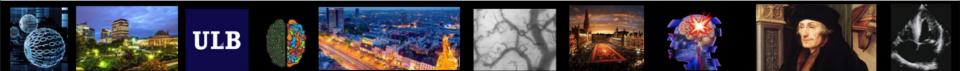
Extracorporeal Life Support for acute Respiratory Failure in Immunocompromised Patients - An international multicenter retrospective study (The IDEA study)



Matthieu Schmidt, Peter Schellongowski, Amandine Dorget, Nicolo Patroniti, Fabio Silvio Taccone, Dinis Reis Miranda, Jean Reuter, Hélène Prodanovic, Romain Sonneville, Marc Pierrot, Martin Balik, Sunghoon Park, Alain Combes.



Réseau européen de recherche en Ventilation Artificielle

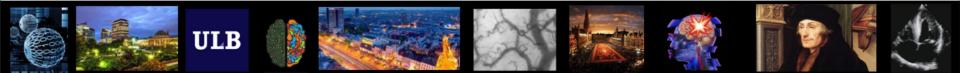






The IDEA study

- International, **multicenter** (n=10), retrospective cohort study (2008-2015)
- Immunocompromised status was defined as either:
 - 1. hematological malignancies
 - 2. active solid tumor
 - 3. solid organ transplant
 - 4. HIV
 - 5. long-term or high dose CS or immunosuppressive agents
- Acute Respiratory Failure
- VV-ECMO (88%) or ECCO₂R (7%)

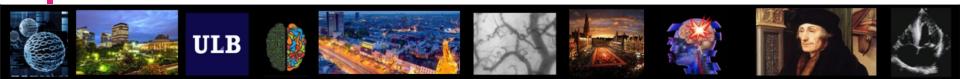






The IDEA study

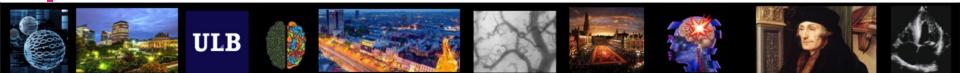
Characteristics	All patients
	(n=203)
Gender male	127 (62)
Age, years	51 (38-59)
APACHE II	28 (20-33)
SOFA ICU admission	12 (8-15)
Body mass index, kg/m ²	24.7 (21.7-28.2)
Charlson comorbidity score	3 (2-4)
Newly diagnosed IC status*	51 (25)





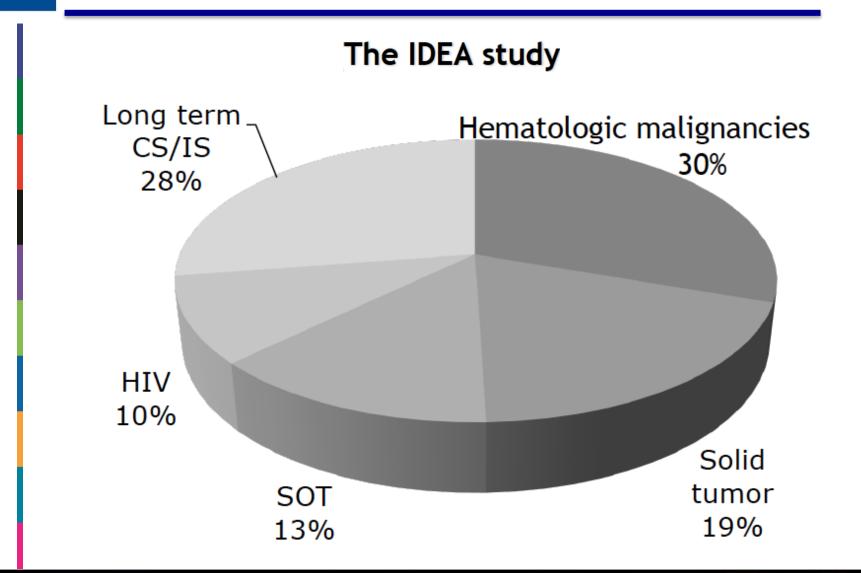
The IDEA study

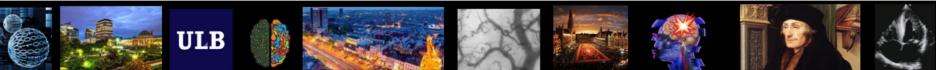
Bacterial pneumonia	63 (31)
Viral pneumonia [£]	38 (19)
Specific lung involvement	26 (12)
Pneumocystis jirovecii pneumonia	9 (4)
Post lung transplantation	6 (3)
Aspiration pneumonia	9 (4)
No definite diagnosis	21 (10)
Miscellaneous	41 (20)







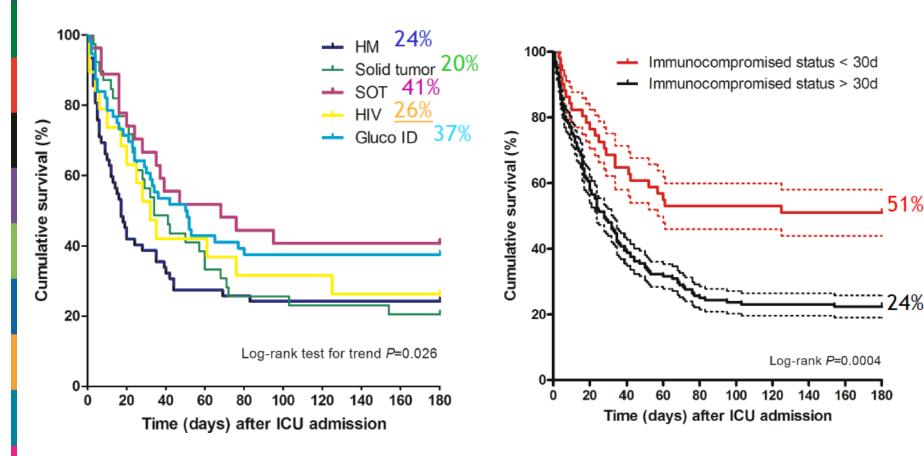


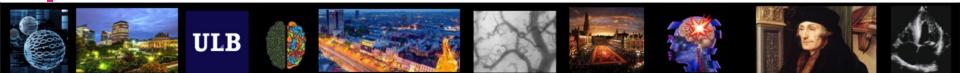








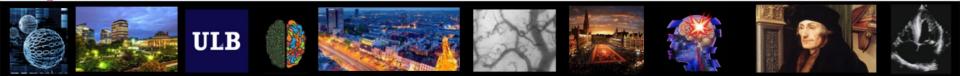






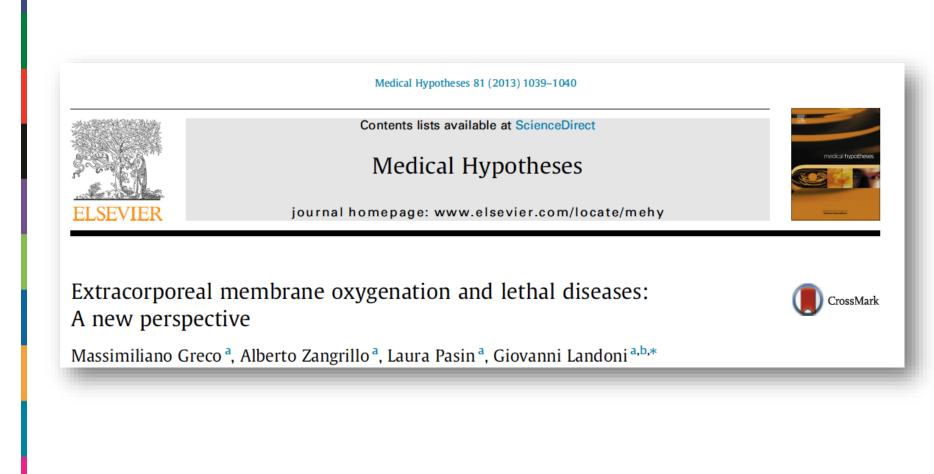


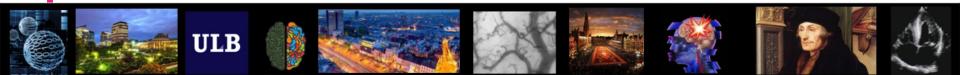
- The use of VV- or VA-ECMO in critically ill cancer adult patients is feasible - benefits on outcome ?
- ECMO has more complications than other therapies = **<u>SELECTION</u>**
- ECMO may be **a bridging tool** in carefully selected patients
- ECMO discouraged during the peri-transplant period after allogeneic
 PBSCT
- The role of ECMO centers on the benefits shown in different studies need to be determined













S.







THANKS

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