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GUVERNUL ROMÂNIEI



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Instrumente Structurale
2007-2013



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UNIVERSITATEA DE MEDICINĂ ȘI
FARMACIE "CAROL DAVILA"
BUCUREȘTI

AD-COR Program inovativ de formare in domeniul cardiologiei pediatrice POSDRU/179/3.2/S/152012

Data: 12-11-2015

MODUL TEORETIC

Cardiopulmonary bypass circuit for temporary life support

Imputernicit: Prof. Dr. Tammam Youssef

Activitate prestata de I.R.C.C.S. POLICLINICO SAN DONATO – MILANO, ITALIA in
baza contractului nr. 18/22144/29.07.2015



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Acest material a fost documentat/ validat/ prezentat la sesiunile de formare în cadrul proiectului „AD-COR Program inovativ de formare în domeniul cardiologiei pediatrice” - POSDRU/179/3.2/S/152012, proiect cofinanțat din Fondul Social Operațional Sectorial Dezvoltarea Resurselor Umane 2007-2013.

Beneficiar: Universitatea de Medicină și Farmacie „Carol Davila” București

Conținutul acestui material nu reprezintă în mod obligatoriu poziția oficială a Uniunii Europene sau a Guvernului României

Artificial lung vs. native lung on Respiratory ECMO:

**Conflicting interest or
synergy?**

Cotza Mauro, CCP
ECMO Team
IRCCS PSD

ECMO:

ExtraCorporeal Membrane Oxygenation

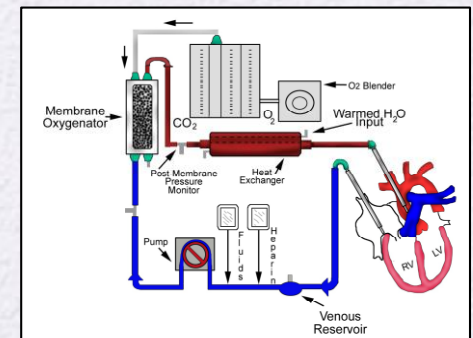
“Cardiopulmonary bypass circuit for temporary life support”

- for patients with potentially reversible cardiac and/or respiratory failure
- when no other form of treatment has been or is likely to be successful.

ECMO IS NOT A THERAPY:

IS A “BRIDGE” TO DECISION

- allows to “buy time”
 - for recovery from lung or cardiac disease
 - To optimize medical/surgical options



WHEN ECMO IS USEFULL?

Respiratory Indications

○ ACUTE/CHRONIC LUNG FAILURE

NEONATES

- Persistent Pulmonary Hypertension
- Meconium Aspiration Syndrome
- Respiratory Distress Syndrome
- Congenital Diaphragmatic Hernia (CHD)

PEDS and CHILDRENS

- Sepsis/pneumonia
- ARDS in pneumonia post chemio Therapy
- Chronic/acute lung failure in Cystic Fibrosys

ADULTS

- ARDS:
 - Viral/bacterial Pneumonia
 - Thoracic Trauma
- Primary graft failure following lung transplantation.

AND WHEN IT IS NOT?

Contraindications 1

- considerations must be weighed before planning an ECMO implant:
 - ACUTE ORGAN (heart and/or lungs) FAILURE irreversible (A)
 - Chronic end stage organ failure (kidney, liver, metabolic syndrome) (A)
 - Lethal congenital anomalies (A)
 - Gestational age < 34 weeks (R)
 - NO other option after ECMO (BRIDGE TO BRIDGE/TX)? (A)

AND WHEN IT IS NOT?

Contraindications 2

- PRE-ECMO clinical consideration:
 1. Active (disseminated) malignancy (A)
 2. Contraindications to anticoagulation therapies (A)
 3. Known severe brain injury (Severe irreversible brain damage, Grade III or IV Intra Ventricular Hemorrhage) (A)
 4. Graft vs. host disease (post organ transplantation) (A)
 5. Unwitnessed cardiac arrest or cardiac arrest of prolonged duration without effective CPR ($ET\ CO_2 < 18$) (A)

Advanced age and palliated CHD questionable contraindication (R). Evaluation on:

1. QOL pre-acute events
2. Life expectancy

AND WHEN IT IS NOT?

Contraindications 3

- Technical contraindications
- A-V ECMO
 - aortic disease (dissection, coartaction, severe vasculopathy) (A)
 - AOV regurgitation (blood “goes back” in to the left ventricle impairing heart recovery) (A)
 - Mechanical prosthetic valve (valve thrombosis, aortic root thrombosis despite aggressive anticoagulation therapy) (A/R)
- ALL ECMO
 - weight in neonates less than 1.6 kg (vessels cannulation) (A)

Respiratory ECMO: why yes...

- Indications codified
- Consolidated approach methodology
- Reliable technology
- Clinically and economically effective

VV ECMO inclusion criteria - **Murray score**
= average score of all 4 parameters

Parameter / Score	0	1	2	3	4
$\text{PaO}_2/\text{FiO}_2$ (On 100% Oxygen)	$\geq 300 \text{ mmHg}$ $\geq 40 \text{ kPa}$	225-299 30-40	175-224 23-30	100-174 13-23	<100 <13
CXR	normal	1 point per quadrant infiltrated			
PEEP (cmH ₂ O)	≤ 5	6-8	9-11	12-14	≥ 15
Compliance (ml/cmH ₂ O)	≥ 80	60-79	40-59	20-39	≤ 19



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

Giles JF, Park, Miranda Mugford, Ravindranath Tirunavali, Andrew Wilson, Elizabeth Allen, Mariamma M Thekenany, Clare J J Hibbert, Ann Truesdale, Felicity Oram, Nicola Cooper, Richard K Famin, Diana Elbourne, for the CESAR trial collaboration

Summary

Background Severe acute respiratory failure in adults causes high mortality despite improvements in ventilation techniques and other treatments (eg, steroids, prone positioning, bronchoscopy, and inhaled nitric oxide). We aimed to delineate the safety, clinical efficacy, and cost-effectiveness of extracorporeal membrane oxygenation (ECMO) compared with conventional ventilation support.

Lancet 2009; 374: 1361-63
Published Online
September 16, 2009
DOI:10.1016/S0140-6736(09)60092-2

ECLS Registry Report International Summary July, 2015



Extracorporeal Life Support Organization
2800 Plymouth Road
Building 300, Room 303
Ann Arbor, MI 48109

Overall Outcomes				
	Total Patients	Survived ECLS		Survived to DC or Transfer
Neonatal				
Respiratory	28,271	23,791	84%	20,978 74%
Cardiac	6,046	3,750	62%	2,497 41%
ECPR	1,188	766	64%	489 41%
Pediatric				
Respiratory	6,929	4,579	66%	3,979 57%
Cardiac	7,668	5,084	66%	3,878 51%
ECPR	2,583	1,432	55%	1,070 41%
Adult				
Respiratory	7,922	5,209	66%	4,576 58%
Cardiac	6,522	3,661	56%	2,708 42%
ECPR	1,985	791	40%	589 30%
Total	69,114	49,063	71%	40,764 59%
Centers				

... why not (or not enough “yes”)

ASAIO Journal 2013

Adult Circulatory Support

Extracorporeal Life Support Organization Registry Report 2012

MATTHEW L. PADEN,* STEVEN A. CONRAD,† PETER T. RYCUS,‡ AND RAVI R. THIAGARAJAN§, ON BEHALF OF THE ELSO REGISTRY

Complicated

or

"complicating?"

Table 6. Mechanical and Patient-related Complications for Respiratory ECLS

	Neonatal	Pediatric	Adult
Mechanical			
Oxygenator failure	5.9 (53)	12.6 (43)	16.1 (45)
Circuit rupture	0.3 (58)	0.7 (48)	0.3 (30)
Pump malfunction	1.7 (66)	2.4 (46)	2.1 (38)
Cannula problems	11.6 (67)	15.3 (52)	7.7 (43)
Patient-related			
ICH	7 (44)	6 (23)	3.9 (17)
Cannula site bleeding	7.3 (64)	16.6 (52)	17.2 (52)
Surgical site bleeding	6.3 (43)	14 (46)	16.7 (42)
Cardiac tamponade	0.6 (42)	1.9 (39)	2.6 (44)
Clinical seizures	9.3 (61)	5.7 (34)	1.1 (45)

Table entries are reported in percentage (% survival).

ECLS, extracorporeal life support; ICH, intracranial hemorrhage.

Potential Complications

Circuit

- Air embolism
- Circuit thrombosis -> Oxygenator Failure
- Thromboembolism
- Circuit rupture
- Pump failure
- Accidental decannulation
- Blocking /kinking of tubing

Patient

- Bleeding
- Haemolysis
- Desaturation
- Infection
- Cerebral injury
- Limb ischaemia - In VA-ECMO with return cannula in femoral artery
- Vessel damage during insertion.
- Unidentified heart failure.

“COMPLICATION ECMO RELATED”

- Of ECMO system?

- Of patient on ECMO?



- "associated" to the ECMO procedure?

ECMO AND RESPIRATORY DISTRESS

ECMO PARADIGM: “TO BUY TIME”

for what?

- Maximize recovery of lung function
 - Protective ventilation
 - Steroids/antibiotics therapy
 - Fluid balance
- Prevent and treat complication ECMO correlated

**DAYS
WEEKS
MONTHS**

“run away!!!”

as soon as conditions allow

1. Lung and “gentle” ventilation

- INADEQUATE FLOW OR ECMO GAS EXCHANGE?
 - PROTECTIVE VENTILATION UNENFORCEABLE

ECMO V-V PURPOSE

- $\text{PaCO}_2 > 45 \text{ mmHg}$
- Compensated Ph
- $\text{PaO}_2 > 40 \text{ mmHg}$
- $\text{SATAO}_2 > 80\%$
- $\text{O}_2 \text{ content} > 17 \text{ ml/Dl}$

• De-cap

- Low blood flow
- HI gas flow

• Oxygenation

- HI blood flow
- Gas flow according to PaCO_2

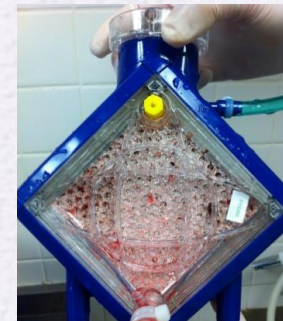
“ELSO G.L.”

DECAP: GAS flow

- Post membrane gas exchange are adequated?
 - Membrane size??
 - Sweep gas adequated?
 - FiO₂ (oxygenator P/F >150)?
 - Artificial lung failure (membrane thrombosis, plasma leakage, condensation)?



- Monitor
 - IN-OUT pressure gradient
 - IN-OUT BGA
 - VO₂ VCO₂
 - T° IN-OUT
 - PaCO₂: hyper-ventilation break down respiratory drive (CNS inhibition!!!)



ECMO is really a ventilatory support to lungs or viceversa???

OXYGENATION: Blood flow

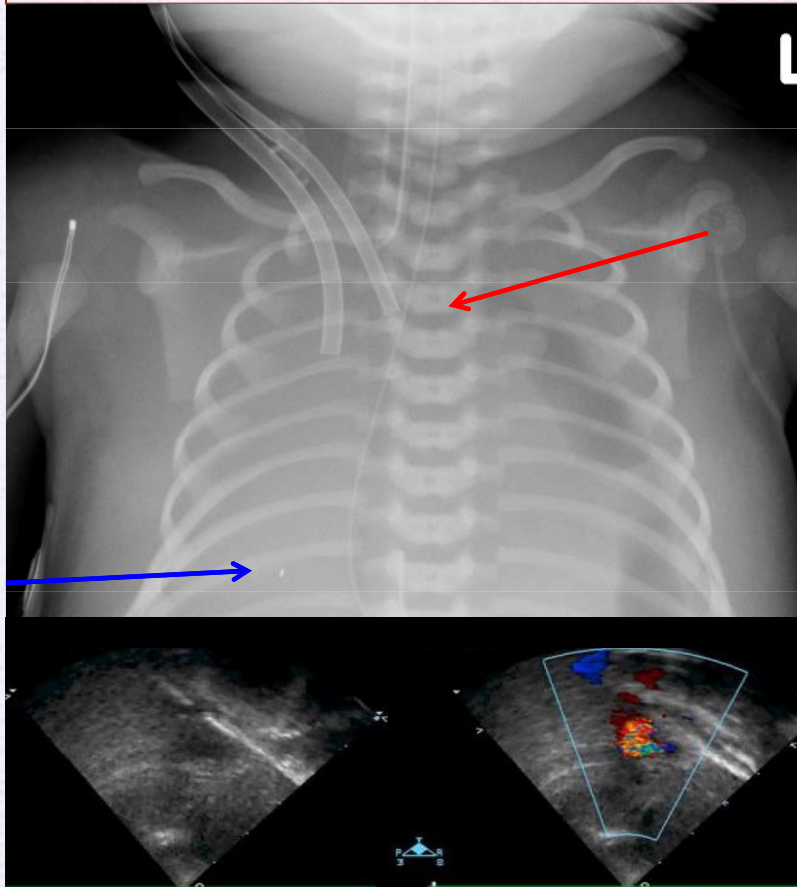
- What hinders the blood flow?
 - Cannulas size/shape?
 - Correct position (CA-JV, FA-FV, FV-FV, JV-FV, Double lumen,)?
 - Pre-load and after-load are adequated (chattering, trans-membrana A/O trans-cannula gradient, drainage aspiration pressure)?
 - **SYSTEM THROMBOSIS (PUMP, OXYGENATORS OR LINES)???**

Table 1. Causes, Symptoms, and Treatment of Low Circuit Flow

Cause	Symptoms	Treatment
Thrombus in the pump	Change in sound of pump Rising plasma hemoglobin Visible thrombus in pump	Change the pump or entire circuit Increase anticoagulation
Thrombus in the oxygenator	Increasing pressure drop across the oxygenator Low postoxygenator PO ₂ ; high postoxygenator PCO ₂ (for a given sweep gas flow) Visible thrombus in the oxygenator	Change the oxygenator or the entire circuit Increase anticoagulation
Obstruction of the drainage cannula	Increased chatter in drainage limb Echocardiographic signs of problems with drainage cannula (thrombus/malposition)	Reposition drainage cannula Place a second drainage cannula

Paradigm of Cannulation

V-A ECMO

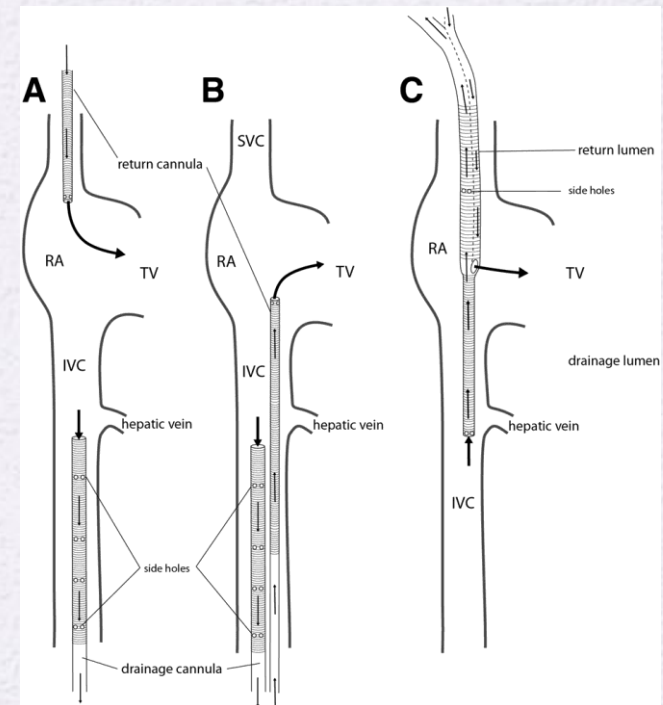


V-VDL ECMO



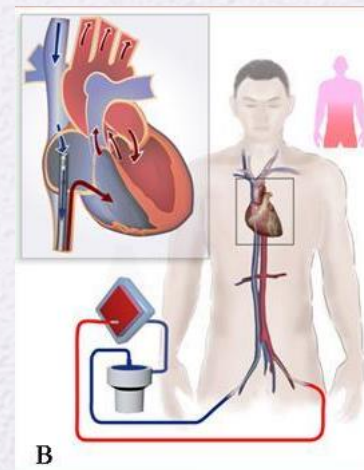
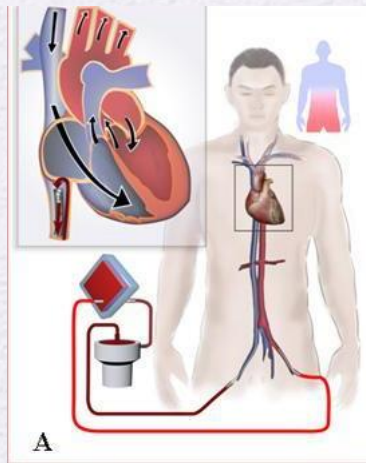
Affecting oxygenation: V-V ECMO recirculation

- Blood coming from ECMO is drained back to ECMO before been returned to patient
 - Average 30% recirculation with V-V ECMO
 - SaO_2 low as 80-85%
- Clinical signs:
 - decrease in arterial saturation
 - increase pre-membrane saturation
- Factors that increase recirculation:
 - Small distance between drainage and return cannula
 - Axial rotation in DLC (“Coanda effects”)
 - Excessive suction in hypovolemic patient
 - Increased cardiac output (INCREASED FLOW “ESCAPING” to the lungs)



Affecting oxygenation: Arlequin Syndrome in V-A ECMO

- V-A ECMO effective for cardiac failure
- Ineffective for respiratory failure
 - Fails to perfuse aortic arch if LV is ejecting
 - Poorly oxygenated blood delivered to brain and coronaries (Arlequin Syndrome)
- **VA-V ECMO**
 - **Addition of arterialized IJ cannula improved oxygenation to coronaries and brain**



WHICH IS THE “RIGHT” TARGET FLOW?

- hemodynamics before ECMO (Swan-Ganz A/O ETT/ETE)
 - REAL CO QUANTIFICATION (consider volemia, inotropic agents)
 - cardiac function
 - Vaso-active response
- PARTIAL SUPPORT VS TOTAL SUPPORT
 - Drainage and return ECMO pressure
 - Prevent hemolytic trauma due to ECMO component (ANEMIA, TRASFUSIONs, **TRALI**)

2. Lung and pharmacological therapy

- PROPHYLAXIS E/O GOAL ORIENTED ANTIBIOTIC THERAPY

- ARDS: multifactorial etiology,
 - Bacteric
 - Viral
- Increased risk of infection
 - Immunodepression
 - Vascular accesses
 - Oro-Tracheal Intubation
 - CVP
 - Nosocomial infections (ICU)

- SEDATION/ANALGESIA

- Pre-existing
- During cannulation and till stabilize the patient
- Maintaining sedation and analgesia
 - Patient collaborative?
 - Ventilatory support with independent respiratory drive (PS, PC, c-pap)
 - Not collaborative
 - Paralyze, sedation
 - Total ventilators dependancy (VC)

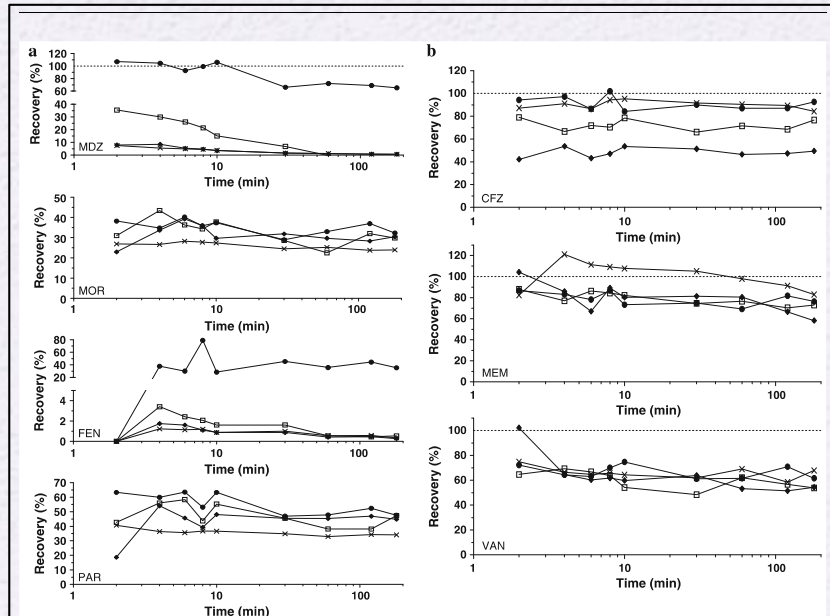
E. D. Wildschut
M. J. Ahsman
K. Allegaert
R. A. A. Mathot
D. Tibboel

Determinants of drug absorption in different ECMO circuits

- ECMO circuit tested
 - 3 NEONATAL CIRCUITS (ROLLER+SILICONIC MEMBRANE)
 - 2 PEDIATRICS CIRCUITS (ROLLER+SILICONIC MEMBRANE)
 - 2 NEONATAL USED CIRCUITS(ROLLER+ SILICONIC MEMBRANE)
 - 2 NEONATAL CIRCUITS (CENTRIFUGAL +HOLLOW FIBER OXYGENATOR)
- DRUGS INVESTIGATED
 - MIDAZOLAM
 - MORPHINE, FENTANYL, PARACETAMOL
 - CEFAZOLIN, MERROPENEM, VANCOMICYN

E. D. Wildschut
M. J. Ahsman
K. Allegaert
R. A. A. Mathot
D. Tibboel

Determinants of drug absorption in different ECMO circuits



LEGEND:

Neonatal roller pump circuits (x),
neonatal centrifugal pump circuits (filled circles),
paediatric roller pump circuits (filled diamonds)
neonatal used roller pump circuits (open squares)

- Significant absorption of drugs occurs in the ECMO circuit, correlating with increased lipophilicity of the drug.
- Centrifugal pump circuits with hollow-fibre membrane oxygenators show less absorption for all drugs, most pronounced for lipophilic drugs.
- **Results suggest that pharmaco- kinetics and hence optimal doses of these drugs may be altered during ECMO.**

RESEARCH

Open Access

Sequestration of drugs in the circuit may lead to therapeutic failure during extracorporeal membrane oxygenation

Kiran Shekar^{1*}, Jason A Roberts², Charles I McDonald¹, Stephanie Fisquet¹, Adrian G Barnett³, Daniel V Mullany¹, Sussan Ghassabian⁴, Steven C Wallis², Yoke L Fung¹, Maree T Smith⁴ and John F Fraser¹

- 4 IDENTICAL CIRCUITS
 - PRIMING AS FOR ADULT ECMO (CRISTALLOID+ALBUMIN, THEN DONOR WHOLE BLOOD)
 - PHYSIOLOGICAL HOMEOSTASIS 24 HRS
 - BASELINE
 - FENTANYL, MORPHINE, MIDAZOLAM, MERROPENEM, VANCOMICYN (THERAPEUTIC CONCENTRATION)
- 4 FURTHER SAMPLES TO ACHIEVE STABILITY TEST

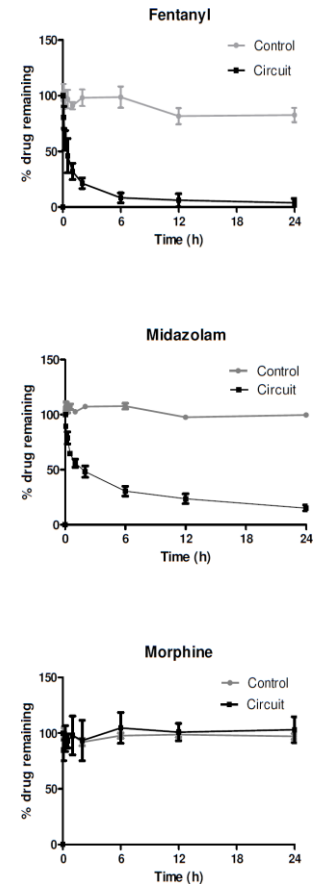
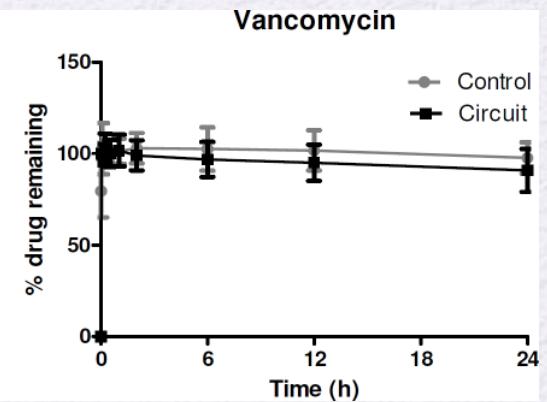
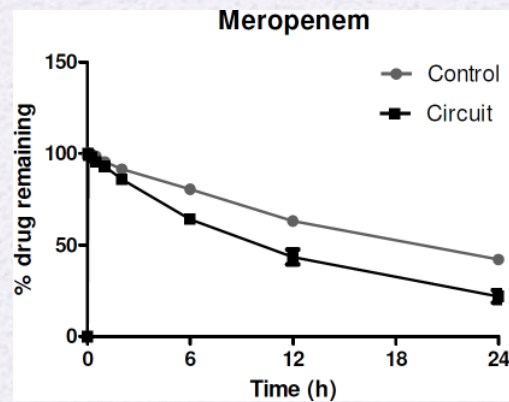
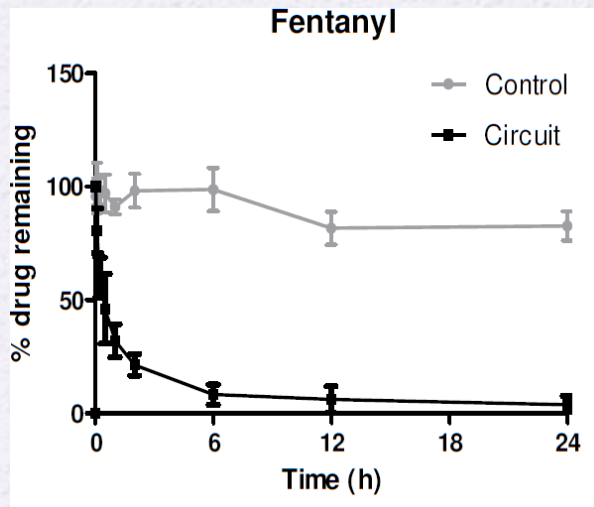
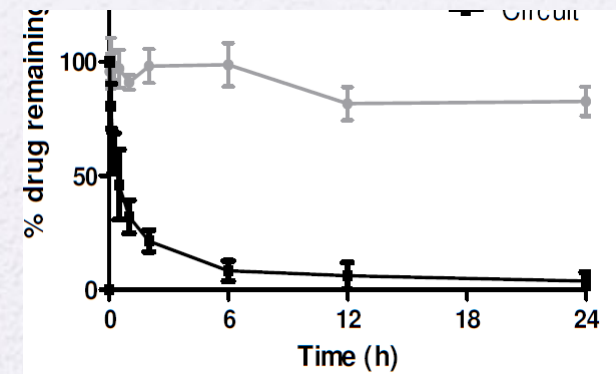
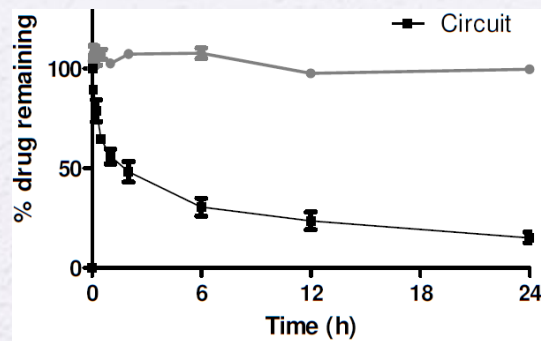


Figure 1 Percentage of drug remaining in extracorporeal membrane oxygenation circuits and the controls plotted against time. Lipophilic drugs such as fentanyl and midazolam were significantly sequestered in the circuit despite being stable in the controls. Morphine was relatively stable in both controls and the circuits.



Lipophilic drugs appear to be more significantly sequestered in the ECMO circuit:

- Fentanyl and midazolam are more significantly sequestered than morphine.
- Meropenem may have to be administered more frequently during ECMO.
- Physical instability of meropenem may affect its delivery by a continuous infusion.
- Sequestration of drugs in the circuit may have implications on both the choice and dosing of a particular drug prescribed during ECMO.

3. Lung and Transfusions

Blood components transfusion associated to worse outcome on ECMO

Lungs are particularly affected

- Leucocytes infarction (neutrophilic activation)
- Fluid overload

WHY I TRANSFUSE?

- Anemia (RBC)
- Coagulation factors depletion (FFP)
- Platelets depletion (PLTs)



Peripheral Extracorporeal Membrane Oxygenation System as Salvage Treatment of Patients With Refractory Cardiogenic Shock: Preliminary Outcome Evaluation

Antonio Loforte, Andrea Montalto, Federico Ranocchi, Paola Lilla Della Monica, Giovanni Casali, Angela Lappa, Antonio Menichetti, Carlo Contento, and Francesco Musumeci

Department of Cardiac Surgery and Transplantation, San Camillo Hospital, Rome, Italy

Abstract: The novel Permanent Life Support (PLS; Maquet, Jostra Medizintechnik AG, Hirrlingen, Germany) as peripheral veno-arterial extracorporeal membrane oxygenation (ECMO) support system has been investigated as treatment for patients with refractory cardiogenic shock (CS). Between January 2007 and July 2011, 73 consecutive adult patients were supported on peripheral PLS ECMO system at our institution (55 men; age 60.3 ± 11.6 years, range: 23–84 years). Indications for support were failure to wean from cardiopulmonary bypass in the setting of postcardiotomy ($n=50$) and primary donor graft failure ($n=8$), post-acute myocardial infarction CS ($n=12$), and CS on chronic heart failure ($n=3$). Mean support time was 10.9 ± 7.6 days (range: 2–34 days). Overall, 26 (35.6%) patients died on ECMO. Among survivors on ECMO, 44 (60.2%) patients were successfully weaned from support, and three (4.1%) were switched to a mid-long-term ventricular assist device. Thirty-three (45.2%) were successfully discharged. The following variables were significantly different if survivors and nonsurvivors on ECMO were compared: age ($P=0.04$), female gender ($P<0.01$), cardiopulmonary

resuscitation before ECMO ($P<0.01$), lactate level before ECMO ($P=0.01$), number of platelets, fresh frozen plasma units, and packed red blood cells (PRBCs) transfused during ECMO support ($P=0.03$, $P=0.02$, and $P<0.01$), blood lactate level ($P=0.01$), and creatine kinase isoenzyme MB (CK-MB) relative index 72 h after ECMO initiation ($P<0.001$), and multiple organ failure on ECMO ($P<0.01$). Stepwise logistic regression identified blood lactate level and CK-MB relative index at 72 h after ECMO initiation, and number of PRBCs transfused on ECMO as significant predictors of mortality on ECMO ($P=0.011$, odds ratio [OR]=2.48; 95% confidence interval [CI]=1.11–3.12; $P=0.012$, OR=2.81, 95% CI=1.026–2.531; and $P=0.012$, OR=1.94, 95% CI=1.02–5.21; respectively). Patients with an initial poor hemodynamic status could benefit by rapid peripheral installation of PLS ECMO. The blood lactate level, CK-MB relative index, and PRBCs transfused should be strictly monitored during ECMO support.

Key Words: Cardiogenic shock—Mechanical circulatory support—Extracorporeal membrane oxygenation.

3. Lung and Transfusions

COAGULATION FACTORS AND PLATELETS ADMINISTRATION:

- Pre-existing hemostatic disorders
 - Immature coagulation system
 - Hepatic dysfunction (acute/chronic)
 - Infection/sepsis
 - Previous cardiac surgery on CPB
 - Extrinsic activation (“Tissue factor”) pathway
- BLEEDING
 - TRAUMA
 - ANTICOAGULATION

ANTICOAGULATION

on ECMO:

- Hemostatic activation by material dependent stimulus (“Contact Activation Pathway”)
 - coagulation factors consumption
 - Increased thrombin generation
 - Platelets adhesion and aggregation, fibrinogen adsorption)
 - Endogen anticoagulation consumption
 - AT₃
 - fibrinolysis
- Red blood cells lesion (hemolysis)



ANTICOAGULATION IS MANDATORY IN PRESENCE OF
EXTRA-CORPOREAL CIRCULATION

Anticoagulation paradigm: eternal conflict?!?

- Prevent thrombosis
- Inhibit thrombin
- Inhibit platelets

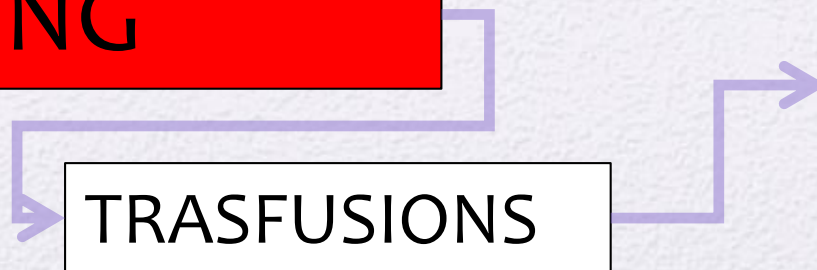
- Prevent bleeding
- Protect thrombin
- Protect platelets

- Bleeding and thrombosis: 2 sides of the same coin
 - Excessive Anticoagulation : **Hemorrhagic risk**
 - Inadequate anticoagulation: **coagulopathy (factors consumption)**

BLEEDING

TRASFUSIONS

TRALI



Bleeding sites

- Bleeding reported in 2-18% in nwb and peds respiratory ECMO
- GI bleeding and DIC complications not frequent but associated to poor survival

Neonatal Respiratory Complications

	<i>No. Reported</i>	<i>% Reported</i>	<i>No. Survived</i>	<i>% Survived</i>
Hemorrhagic: GI hemorrhage	472	1.6%	205	43%
Hemorrhagic: Cannulation site bleeding	2,216	7.7%	1,408	64%
Hemorrhagic: Surgical site bleeding	1,804	6.3%	770	43%
Hemorrhagic: Hemolysis (hgb > 50 mg/dl)	3,074	10.7%	1,936	63%
Hemorrhagic: Disseminated intravascular coagulation (DIC)	835	2.9%	322	39%

Pediatric Respiratory Complications

	<i>No. Reported</i>	<i>% Reported</i>	<i>No. Survived</i>	<i>% Survived</i>
Hemorrhagic: GI hemorrhage	285	4.0%	82	29%
Hemorrhagic: Cannulation site bleeding	1,285	18.2%	695	54%
Hemorrhagic: Surgical site bleeding	914	12.9%	430	47%
Hemorrhagic: Hemolysis (hgb > 50 mg/dl)	698	9.9%	310	44%
Hemorrhagic: Disseminated intravascular coagulation (DIC)	390	5.5%	104	27%

ANTICOAGULATION PROTOCOLS

- **UNFRACTIONED HEPARIN (UFH)**
- Thrombin generation inhibition
 - Counteract coagulation factors consumption
 - Prevent thrombo-embolic complication
- “side effects”:
 - Type 1 thrombocytopenia (heparin)
 - HIT2 (immuno mediated)
 - multi-site bleeding

	ACT (sec)	TEG K (R TIME, min)	FibTEM (mm)	LAB (A- PTT, PTT ratio)	INR	PIASTRINE (10 ³ /nanol)	AT3 (%)	D-Dimero (nanog/L)	FIBRINOGENO (mg/L)
L-VAD	>150	10-12	>10	45-60, 1.5-1.8	1.3- 1.5	>80000 (sang attivo/ad alto rischio) >45000 (non sanguinamento, basso rischio	70-80	<300	<100
R-VAD	>150	10-12	>10	45-60, 1.5-1.8	1.3- 1.5	>80000 (sang attivo/ad alto rischio) >45000 (non sanguinamento, basso rischio	70-80	<300	>100
BI-VAD	>150	10-12	>10	45-60, 1.5-1.8	1.3- 1.5	>80000 (sang attivo/ad alto rischio) >45000 (non sanguinamento, basso rischio	70-80	<300	>100
ECMO V-A	180- 220	16-25	>10	50-80, 1.5-2.0	1.3- 1.5	>80000 (sang attivo/ad alto rischio) >45000 (non sanguinamento, basso rischio	70-80	<300	>100
ECMO V-V-	180- 220	16-25	>10	50-80, 1.5-2.0	1.3- 1.5	>80000 (sang attivo/ad alto rischio) >45000 (non sanguinamento, basso rischio	70-80	<300	>100

DTI to prevent bleeding and transfusion

Ranucci *et al. Critical Care* 2011, **15**:R275
<http://ccforum.com/content/15/6/R275>



RESEARCH

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Bivalirudin-based versus conventional heparin anticoagulation for postcardiotomy extracorporeal membrane oxygenation

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Ranucci *Critical Care* 2012, **16**:427
<http://ccforum.com/content/16/3/427>

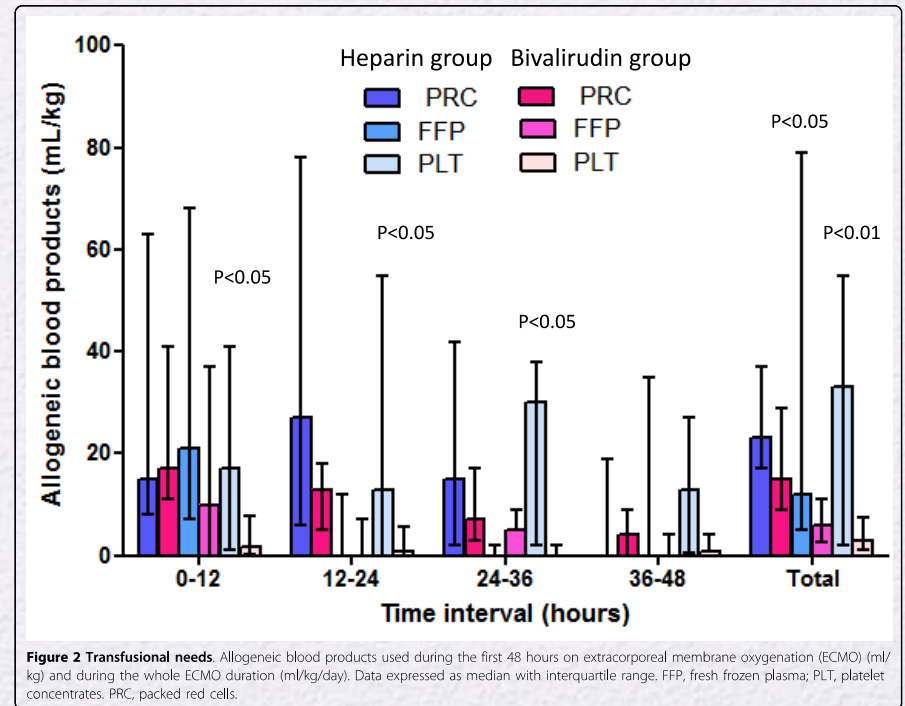
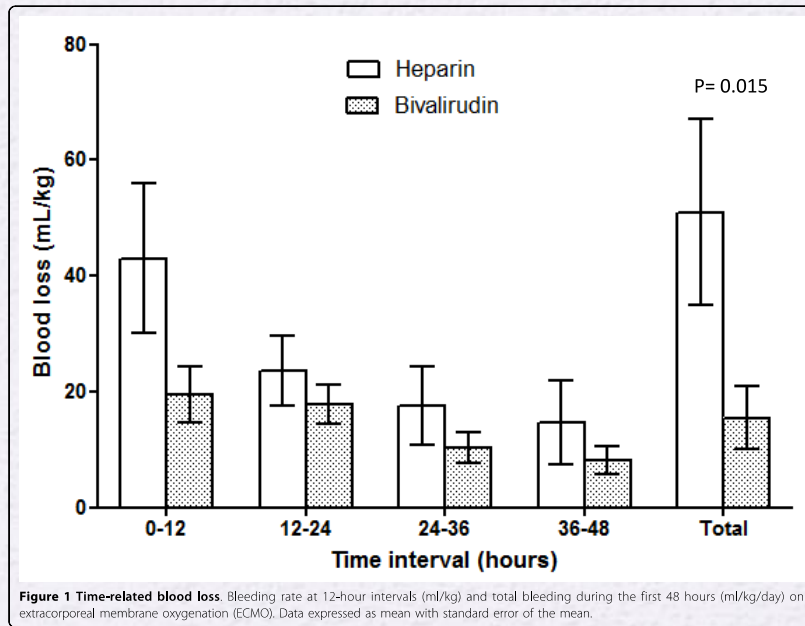


LETTER

Bivalirudin and post-cardiotomy ECMO: a word of caution

Marco Ranucci*

DTI to prevent bleeding and transfusion



DTI to prevent bleeding and transfusion

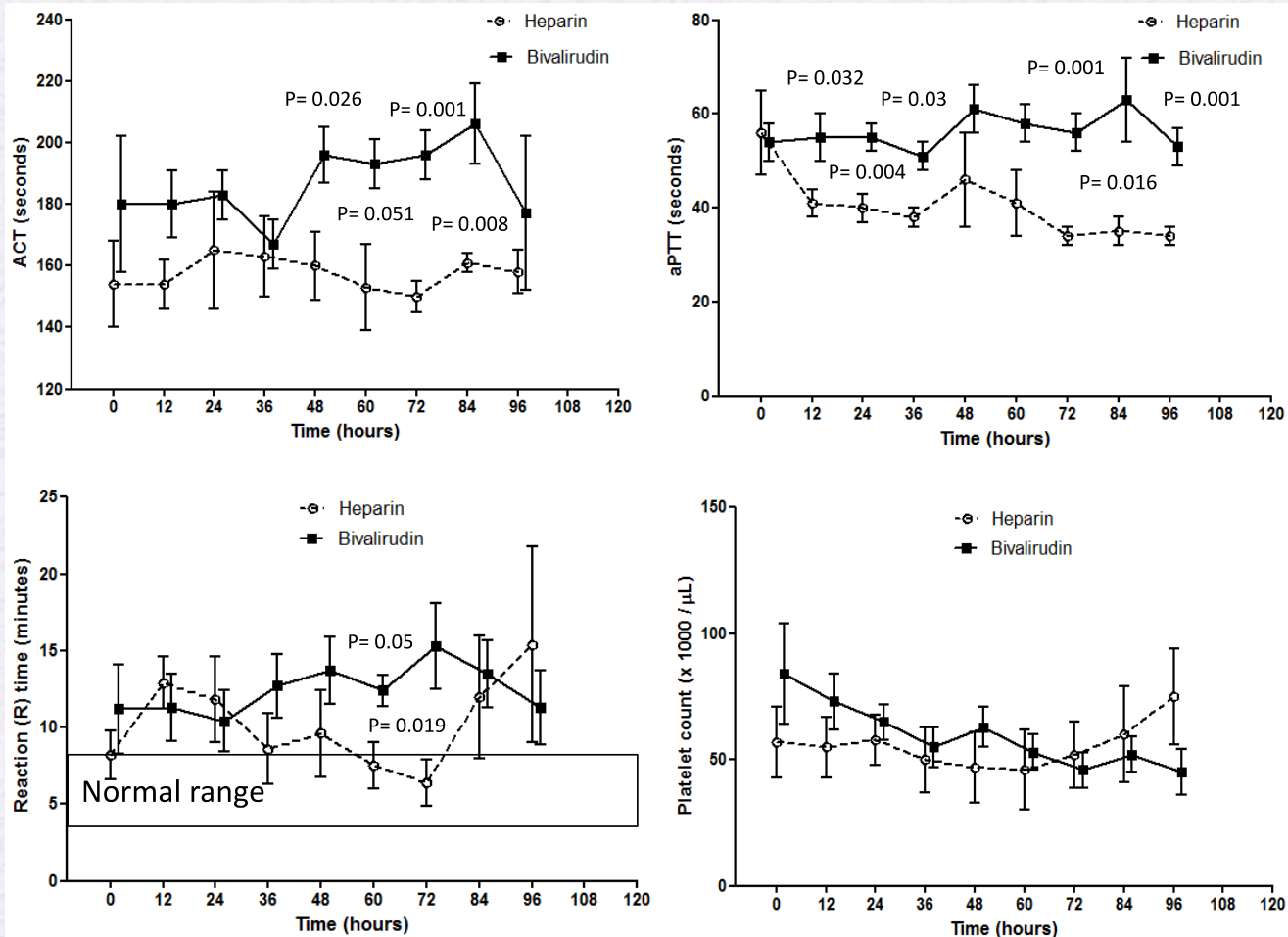


Figure 3 Coagulation parameters. Activated clotting time (ACT), activated partial thromboplastin time (aPTT), reaction (R) time at thromboelastography, and platelet count during the first 96 hours on extracorporeal membrane oxygenation. Data expressed as mean with standard error of the mean.

Acquired Von Willebrand disease

Advance Publication

Journal of Atherosclerosis and Thrombosis, Vol 21, No. ●

Journal of Atherosclerosis and Thrombosis

Original Article

Accepted for publication: August 21, 2014

Published online: September 4, 2014

Early Diagnosis of Acquired von Willebrand Syndrome (AVWS) is Elementary for Clinical Practice in Patients Treated with ECMO Therapy

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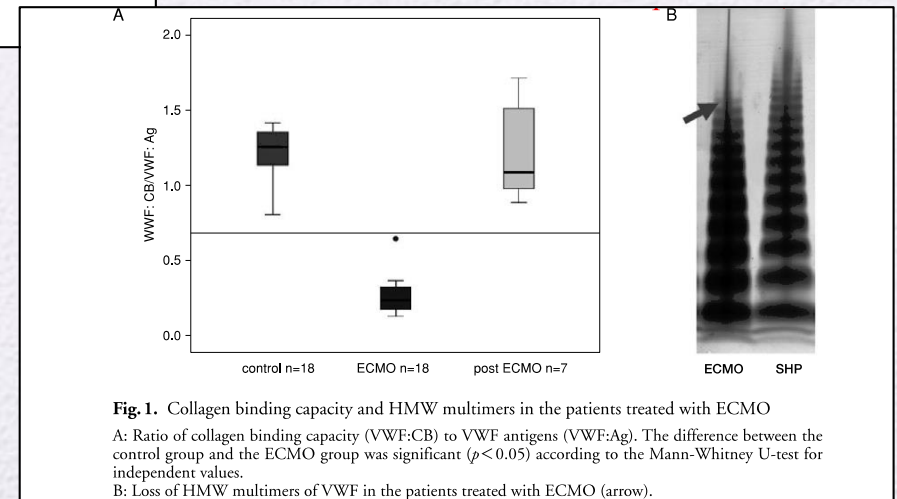
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From VAD experience

Table 2. Number of patients with a decreased ratio of collagen binding capacity (VWF:CB) to VWF antigens (VWF:Ag) or missing VWF HMW multimers

	VWF:CB/VWF:Ag ratio reduced (<0.7)	VWF HMW missing
Before ECMO implantation	0/2	0/2
After ECMO implantation	8/8	17/18 (1 borderline)
During ECMO therapy	8/8	8/8
After ECMO explantation	0/7	0/7
Control group	0/18	0/18

Reversible after ECMO



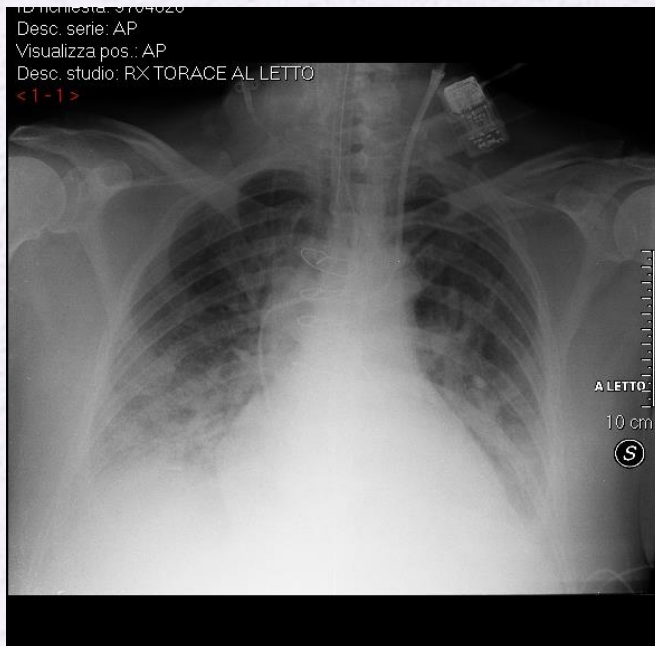
M.V

- Male, 64 aa
- Hypertension, NIDDM, former smokeer
- ECO: EF 53%, no other anomalies
- ECO aortic arch vessels:
 - dx diffused ateromasia w/o stenosis
 - Sx common and ext carot art without lesions, fibrocalcific plaque 25-30% ICA
 - Vertebral and subclavian aa w/o lesions and normal flowmetry
- CAD post STEMI (PTCA+DES)
- CGR: 3 vessel disease
- CABGx4 and TEA of MO

- O.R.
 - IABP, open chest
 - Amine ad alto dosaggio (ADH, NORA, Glipressina)
 - Vasoplegia in the postop course
- I.C.U.
 - Swan-Ganz: C.I. 4.0 l/m²/min
 - NO 30 PPM
 - No other problems in the PO course: progressive reduction of inotropic support, good gas exchange, empiric antibiotic tp
 - In 5° PO day: chest closure; respiratory weaning
 - In 6° PO day IABP weaning ; C.I. 2.5 l/m²/min; fever: culture tests.
 - In 7° PO day: culture test positive for Klebsiella Pneumoniae MDRO in the bronco aspired

10 P.O. day

14.12

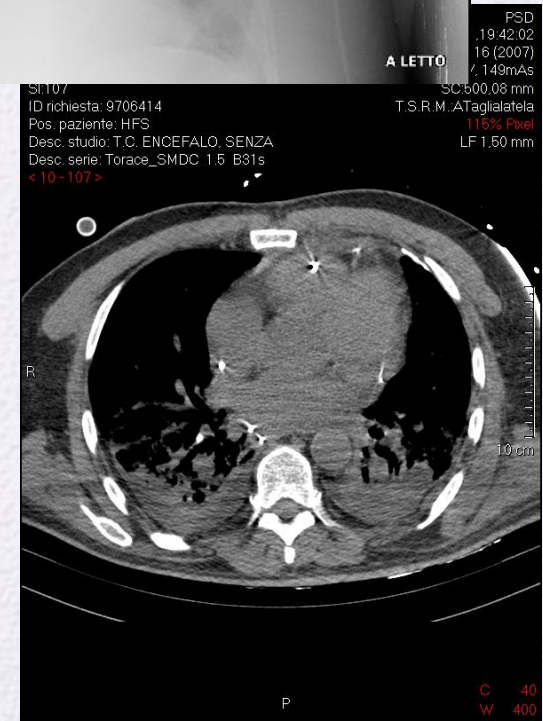
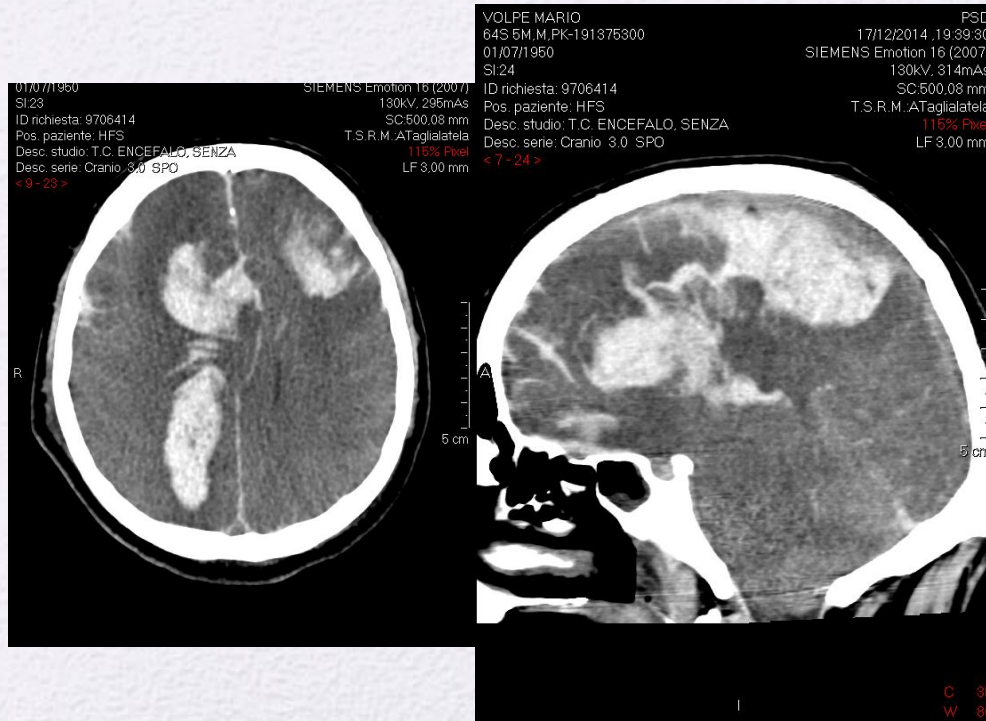
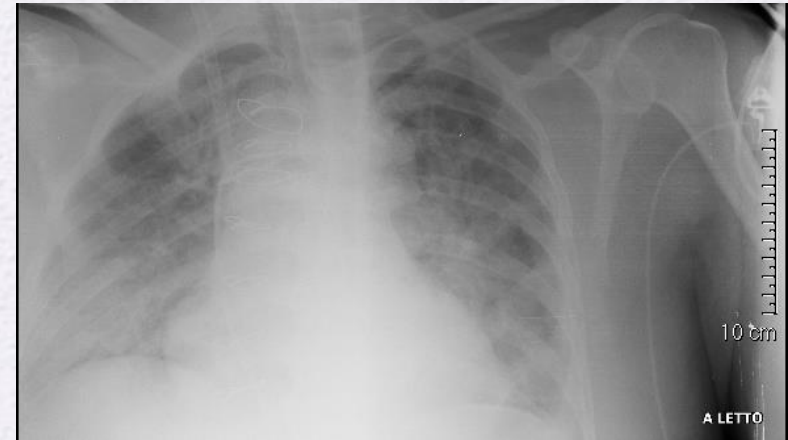


- Maximal ventilation settings
- P/F 70, $\text{PaCO}_2 > 50 \text{ mmHg}$
- Lungs Compliance 36 ml/cm H₂O
- FA, hypotension
- Hi dose inotropic support
- Oligoanuria
- Cvvh-df

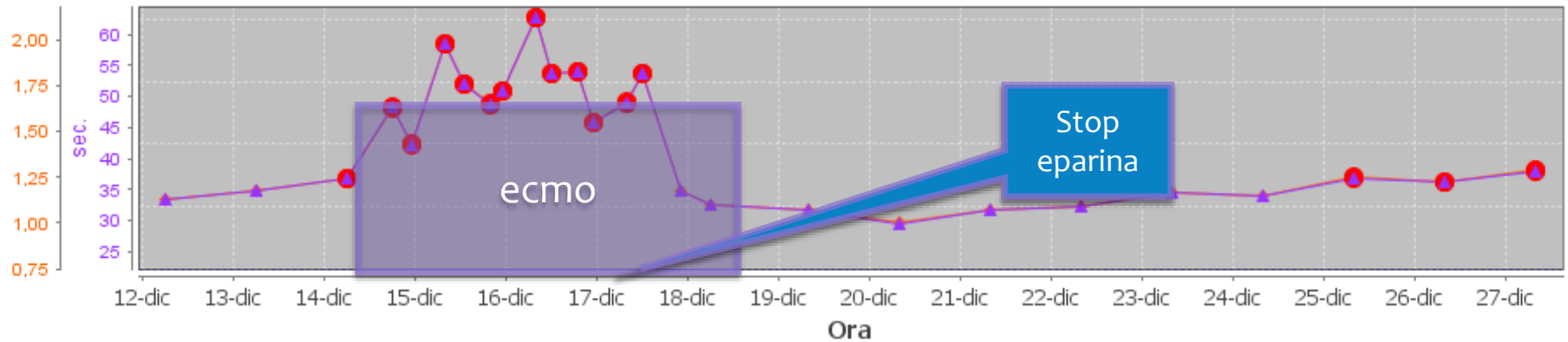
ECMO V-V

13 P.O. day

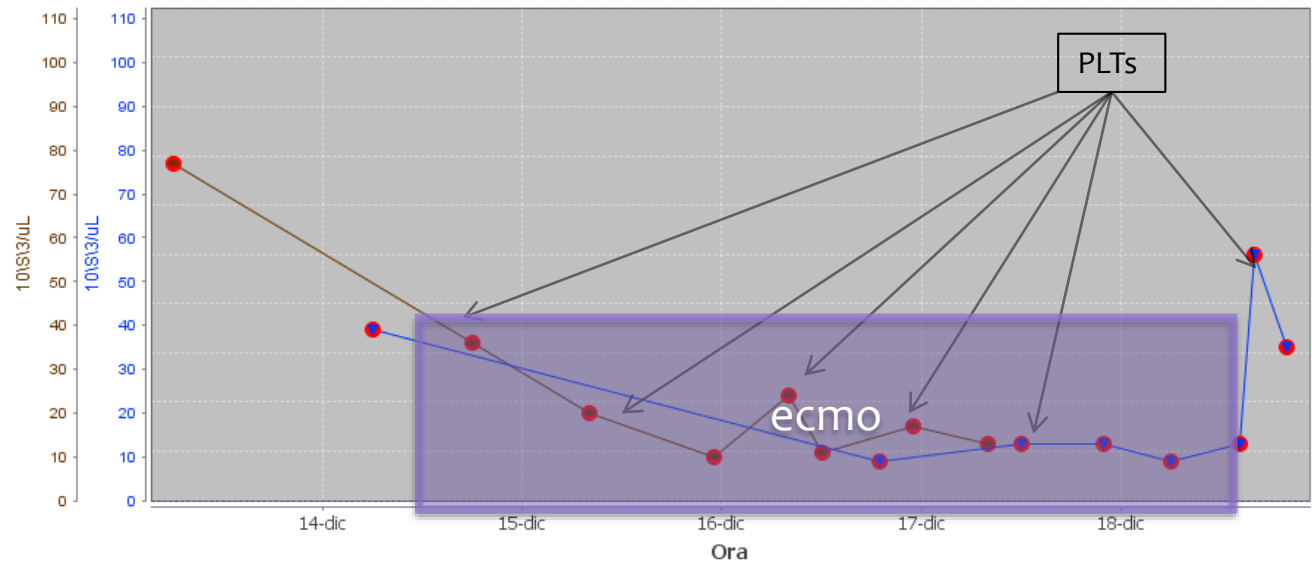
- neuro cognitive decline
- Progressive inhibition of respiratory drive
- Neurologic evaluation: Glasgow 3
- Head and thoracic CT scan on V-V ECMO



What happened? PTT, Platelets

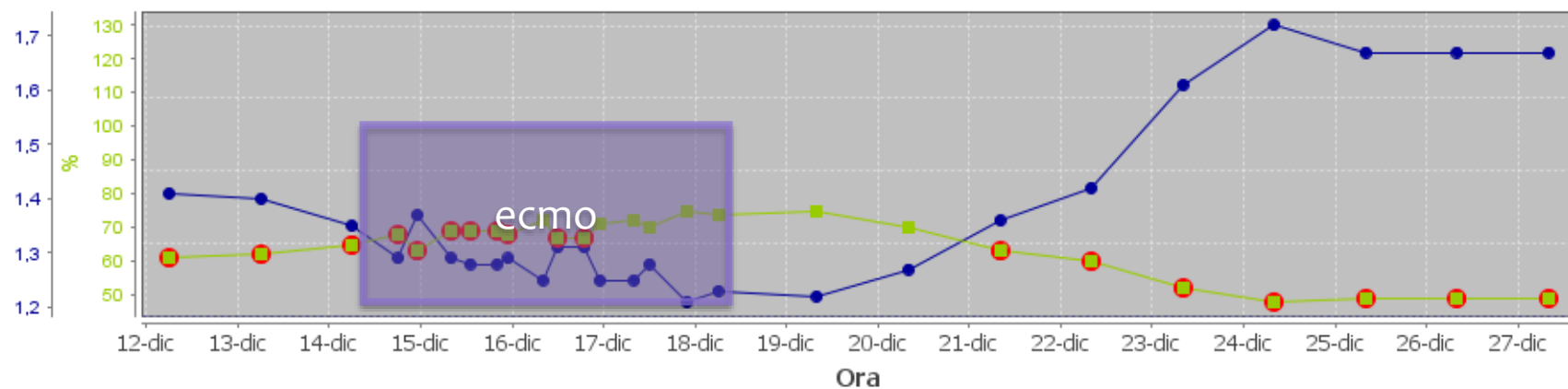


▲ P-TEMPO TROMBOPLASTINA PARZIALE (aPTT) - Tempo di Tromboplastina Parziale Attivato - Plasma
 ◆ P-TEMPO TROMBOPLASTINA PARZIALE (aPTT) - Ratio - Plasma

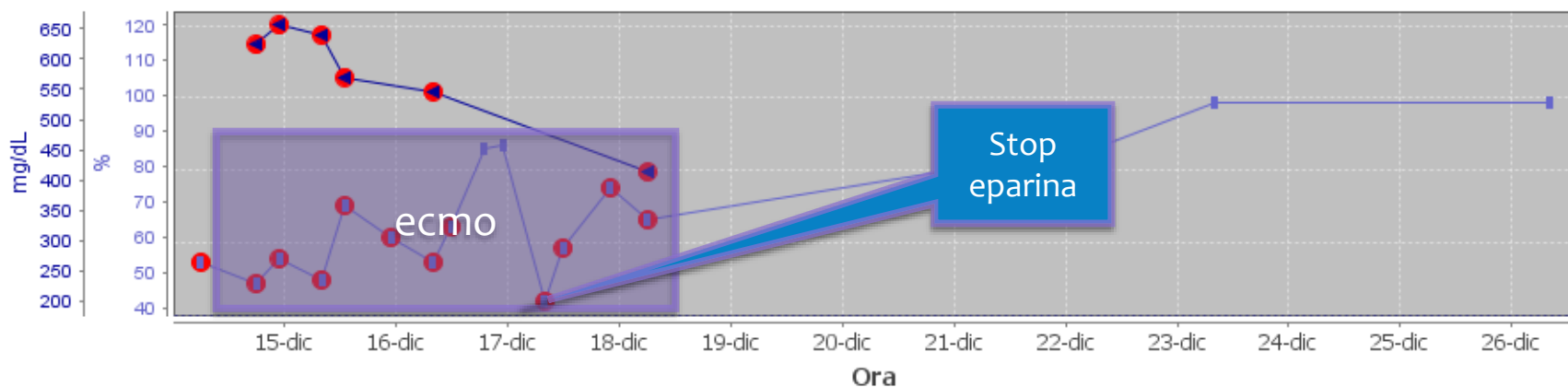


▲ Sg-EMOCROMO E FORMULA LEUCOCITARIA - Piastrine - Sangue intero
 ◆ Sg-EMOCROMO - Piastrine - Sangue intero

PT, INR, AT3

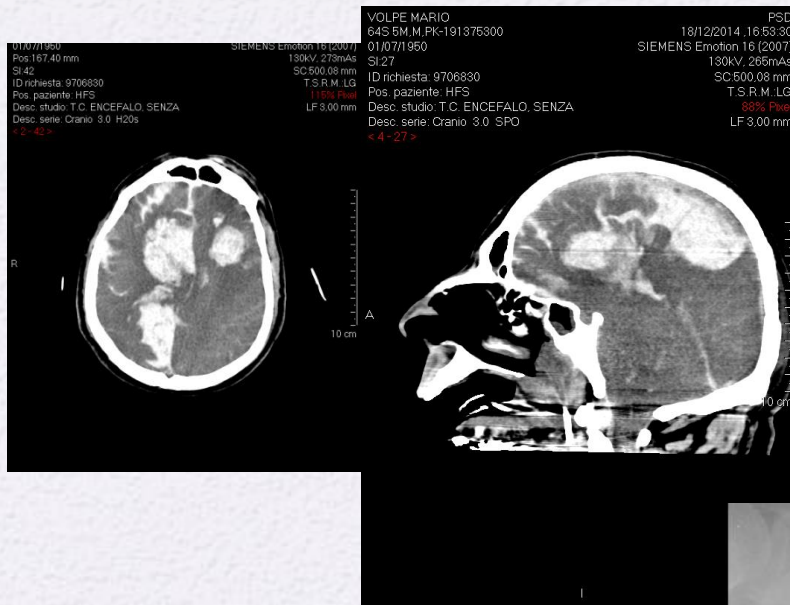


■ P-TEMPO DI PROTROMBINA (PT) - Attività Protrombinica - Plasma ● P-TEMPO DI PROTROMBINA (PT) - Rapporto Normalizzato Internazionale (INR) - Plasma



■ P-ANTITROMBINA III - Plasma ● P-FIBRINOGENO - Plasma

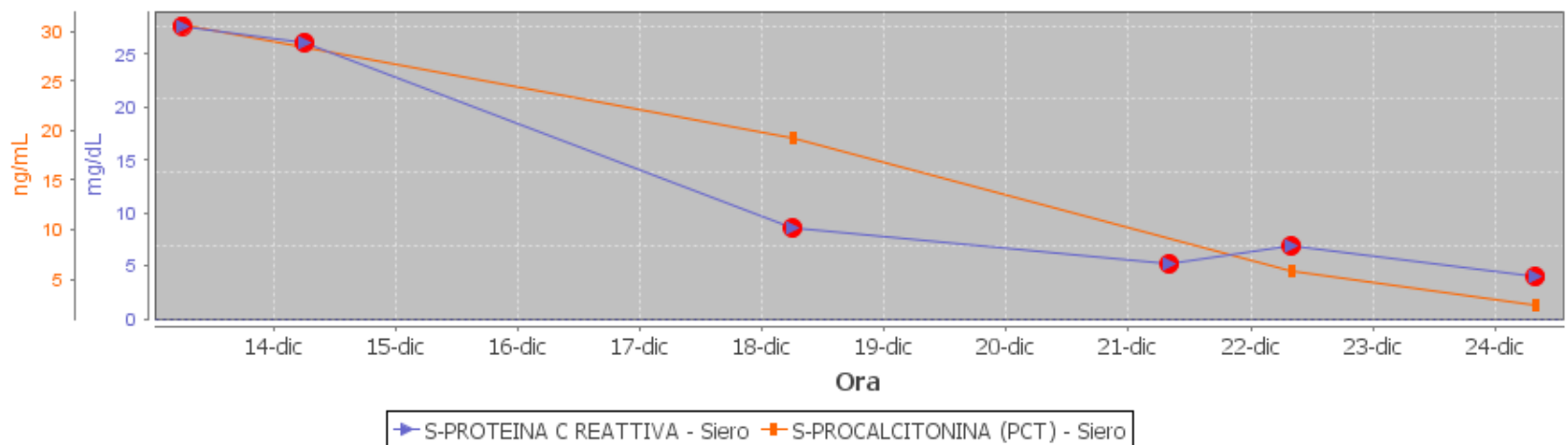
14 P.O. day



- Trial off for weaning successful
- Protective ventilation
- P/F > 150
- Lung compliance 77 ml/cm H₂O



16 P.O. day



Looking back...

- NOT INTRA DEVICE SIGNS OF THROMBOSIS (96 HRS OF SUPPORT)
- Tipo 1 HIT?
- Acquired Von Willebrand?
- Modify anticoagulation therapy towards DTI once FA reversal (HIT 2 tests negative)

Neurologic Injuries on ECMO

- CNS Hemorrhage incidence: 6-7%
- Associated to poor survival (21% in peds)
- Worsening parallel to age increase

Neonatal Respiratory Complications

	<i>No. Reported</i>	<i>% Reported</i>	<i>No. Survived</i>	<i>% Survived</i>
Neurologic: Brain death clinically determined	246	0.9%	0	0%
Neurologic: Seizures: clinically determined	2,539	8.9%	1,534	60%
Neurologic: Seizures: EEG determined	356	1.2%	175	49%
Neurologic: CNS infarction by US/CT	2,000	7.0%	1,067	53%
Neurologic: CNS hemorrhage by US/CT	2,128	7.4%	922	43%

Pediatric Respiratory Complications

	<i>No. Reported</i>	<i>% Reported</i>	<i>No. Survived</i>	<i>% Survived</i>
Neurologic: Brain death clinically determined	335	4.7%	0	0%
Neurologic: Seizures: clinically determined	356	5.0%	122	34%
Neurologic: Seizures: EEG determined	110	1.6%	38	35%
Neurologic: CNS infarction by US/CT	297	4.2%	99	33%
Neurologic: CNS hemorrhage by US/CT	449	6.3%	95	21%

F.P., male, 52 yrs

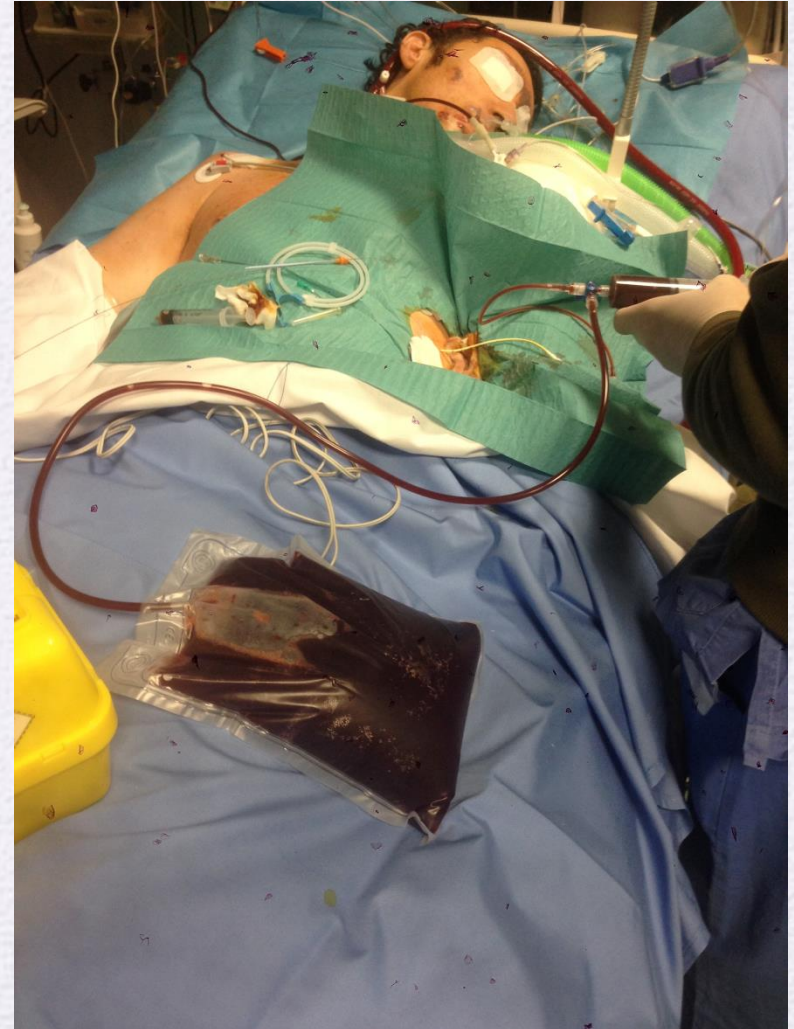
- Mitr Reg x acute papil musc rupture
- Pulm edema
- OR: mitr valv replac (mech)
- ADH>IABP>V-A ECMO
 - Arlequin Syndrome
- Weaned after 7 days support
- After 10 days
 - Progressive decline in gas exchange
 - C-PAP>re-intubation>NO>inotropes
 - V-V ECMO

RIGHT CHOICE?



Let's have a look...

What we missed?



- Peripheral septic embolization
- Bilateral massive pleural effusion (ECO diagnosed post ecmo implant)
- Bronchial culture + Klebsiella
 - PCT+++ NOT REPORTED
 - Culture results after patient death

Which was ECMO indication?

- compassionate “evening” ECMO
 - Compassionate for the patient or for the ICU clinicians? Or both?
- WE TREATED NUMBERS, NOT PATIENT LUNG DYSFUNCTION!!!
 - Patient was not on antibiotic therapy
 - Pleural effusion was misconfused
 - Not CT scan was performed

ECMO WAS NOT THE SOLUTION

Pulmonary and infectious complications

Adult Respiratory Complications	<i>No. Reported</i>	<i>% Reported</i>	<i>No. Survived</i>	<i>% Survived</i>
Pulmonary: Pneumothorax requiring treatment	785	9.7%	367	47%
Pulmonary: Pulmonary hemorrhage	527	6.5%	209	40%
Infectious: Culture proven infection (see Infections)	1,463	18.0%	707	48%
Infectious: WBC < 1,500	162	2.0%	55	34%

Conclusion

- Maximize ECMO performance to allow ultra protective ventilation
- Consider sedatives, analgesics e antibiotics with low grade adsorption
- Consider alternatives anticoagulation drugs to minimize coagulation factors consumption