UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

Tuscany Keynote Lecture:

ECMO

Fabio Sangalli, MD, FASE

Department of Anaesthesia and Intensive Care Medicine
ASST Monza – Ospedale San Gerardo – Monza – Italy

Firenze, 26 Settembre 2019

22° Meeting
TUSCANY
Critical Care Group

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

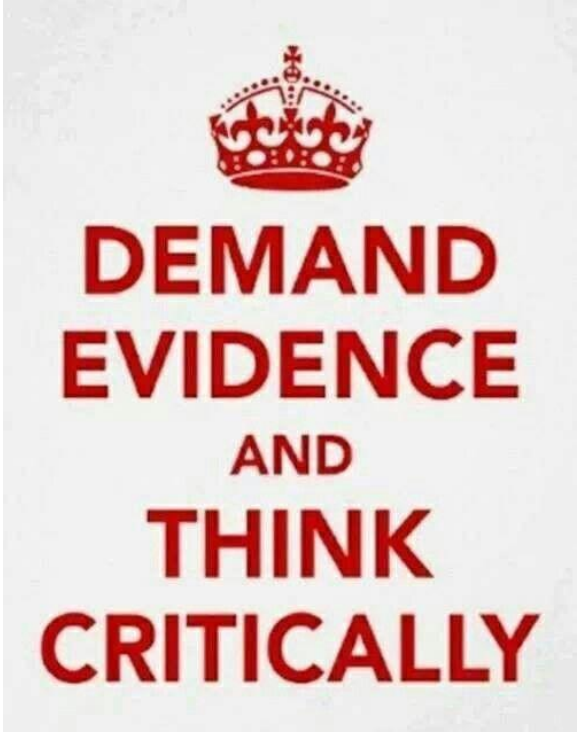
Sistema Socio Sanitario
Regione Lombardia
ASST Monza

Disclosure

✓No disclosures

To be covered

- ✓Some numbers
- ✓Three burning questions and four open issues

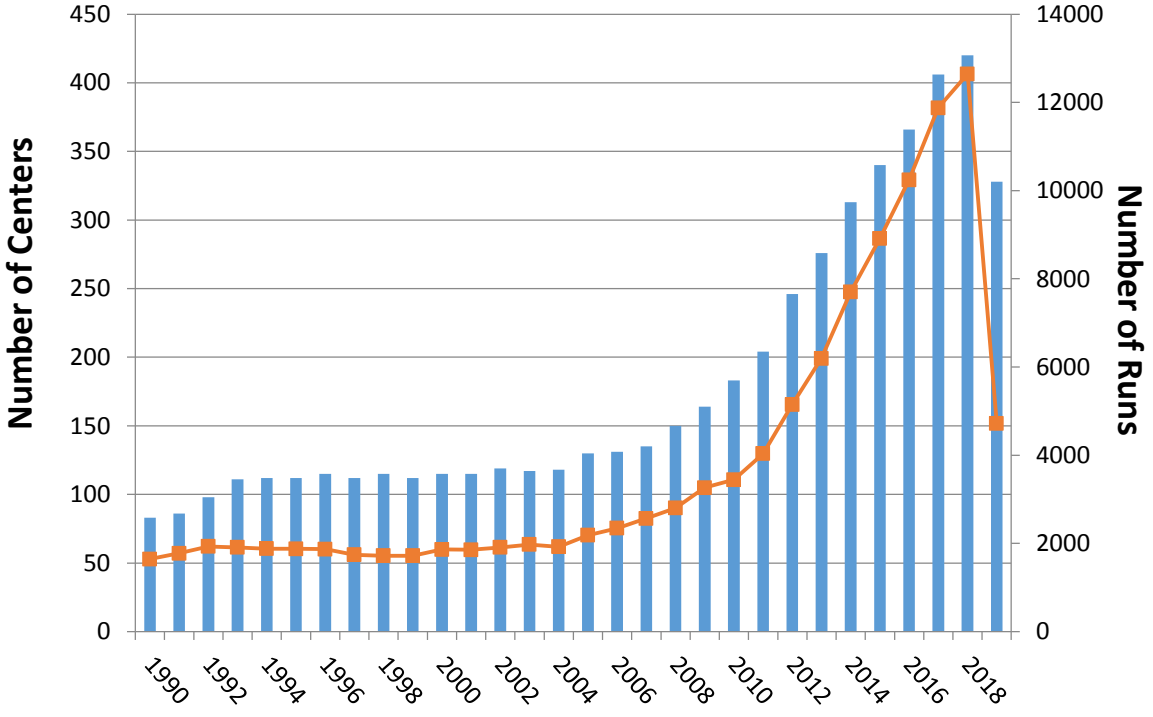


Active ECLS Centers and runs

ELSO Registry July 2019

@docsanga

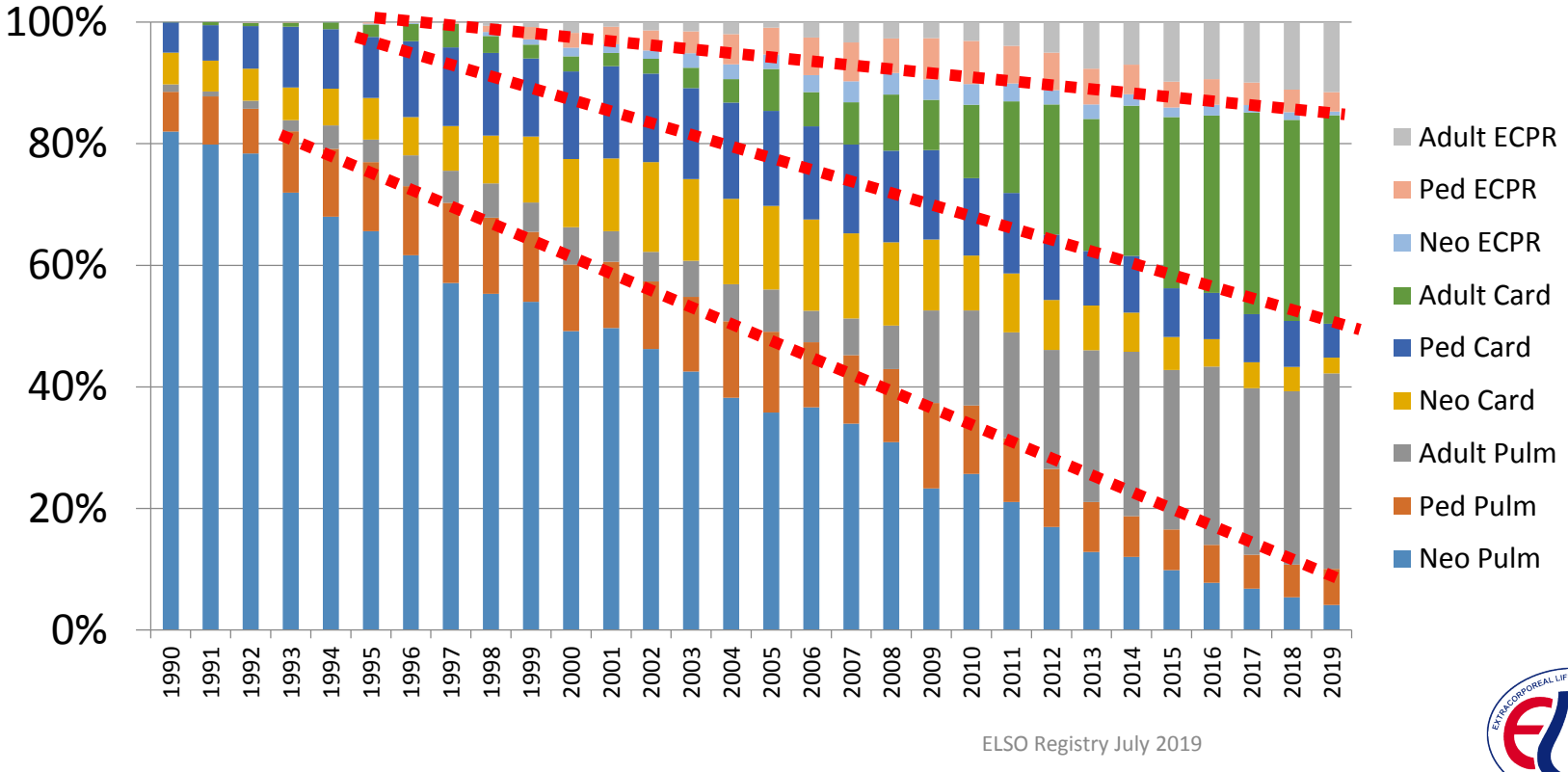
Active ECLS Centers and runs



	Total Runs	Survived ECLS		Survived to DC	
Neonatal					
Pulm	31.923	28.050	87%	23.360	73%
Card	8.498	5.874	69%	3.665	43%
ECPR	1.923	1.359	70%	812	42%
Pediatric					
Pulm	9.902	7.126	71%	5.879	59%
Card	11.839	8.512	71%	6.251	52%
ECPR	4.608	2.760	59%	1.957	42%
Adult					
Pulm	21.874	15.159	69%	13.088	59%
Card	22.193	13.177	59%	9.585	43%
ECPR	6.994	2.923	41%	2.074	29%
Total	**119.754**	**84.940**	**71%**	**66.671**	**55%**

ELSO Registry July 2019

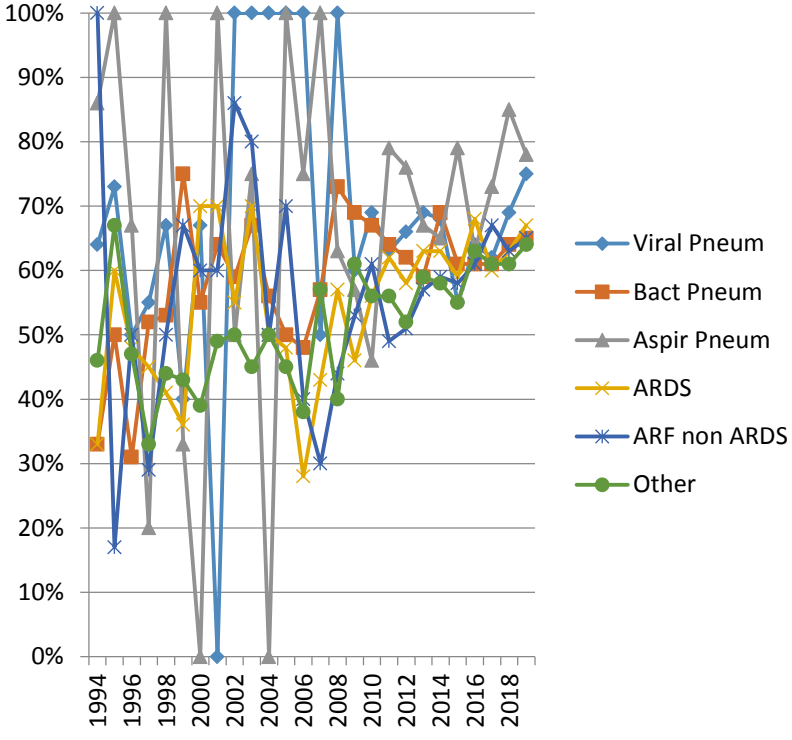
Runs by Year



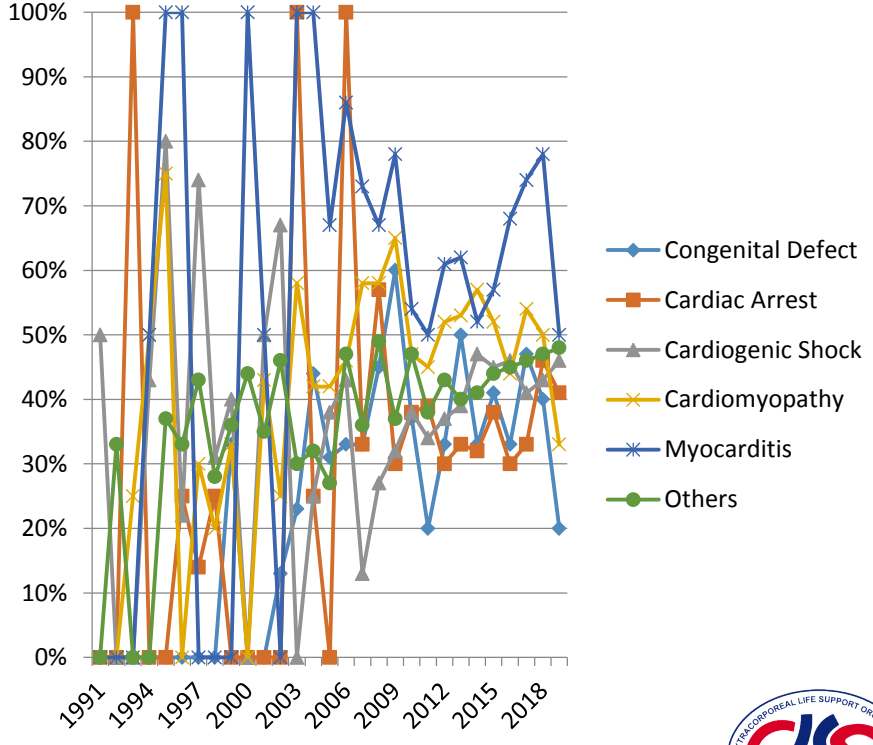
ELSO Registry July 2019

Adult Survival by Diagnosis and Year

Respiratory



Cardiac



ELSO Registry July 2019

Traditional Indications

Cardiac indications

- ✓ Refractory Cardiogenic Shock
  - Acute myocardial infarction
  - Fulminant myocarditis
  - After complicated cardiac surgery
  - Heart Transplantation
- ✓ Massive pulmonary embolism
- ✓ Septic shock with severe LV failure
- ✓ After Cardiac Arrest
- ✓ Refractory Cardiac Arrest

VA-ECMO

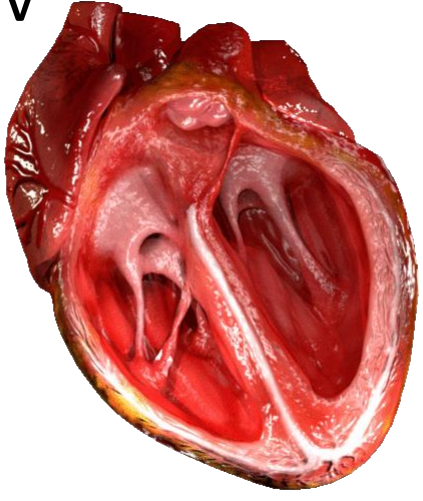
VV-ECMO?

Respiratory indications

- ✓ Rescue of severe hypoxaemia
  - ARDS, hypoxaemic ARF
- ✓ Hyper-protective ventilation
  - ARDS
- ✓ Alternative to invasive ventilation
  - ARDS, COPD
- ✓ Others (bridge to Tx, air leaks etc)

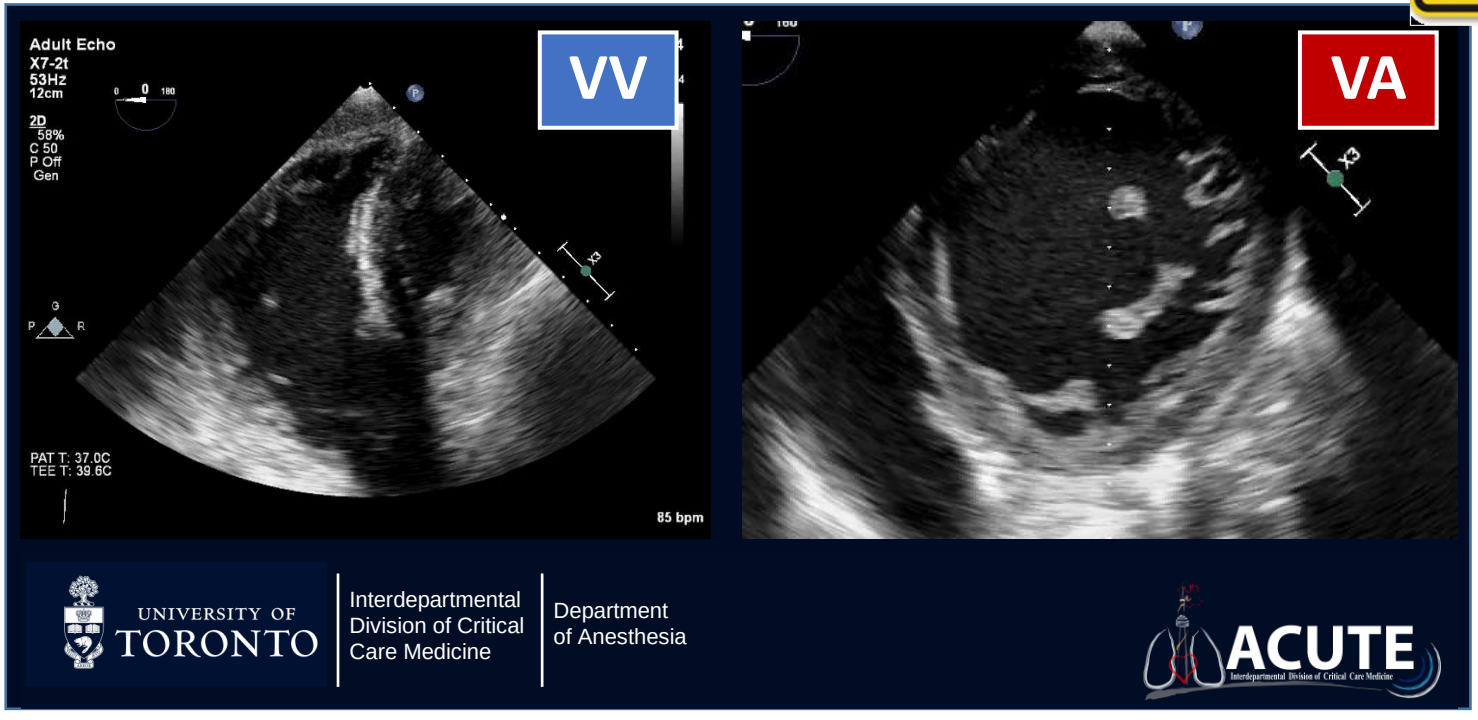
Traditional indications in ARF

If the heart is not compromised go for VV



If you need hemodynamic support go for VA

Tricky Indications in ARF



Courtesy: G. Doufle, TGH (modified)

Q #1: Is E-CPR a life saver or a costly toy?

Have we averted deaths using venoarterial ECMO?

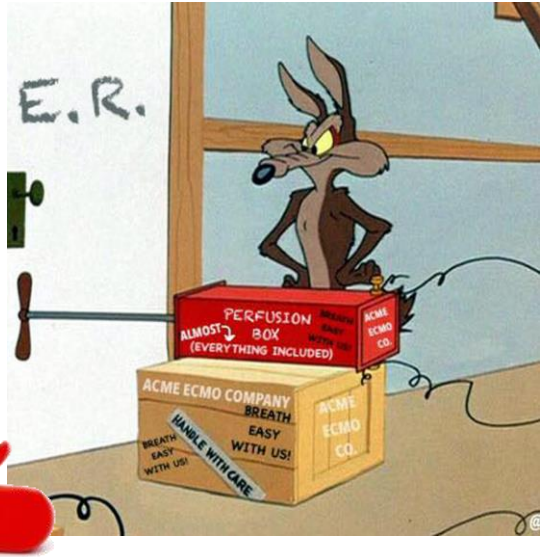
Matthieu Schmidt[1,2], Hannah Wunsch[3,4,5,6] and Daniel Brodie[7*]

- ✓Currently, the highest level of evidence is limited to small, single-center cohort studies with propensity analyses
- ✓The potential benefit of this intervention is highly dependent on the indication, and may range from great benefit (many deaths averted) to great harm (additional deaths due to VA-ECMO)
- ✓VA-ECMO might be expected to have the greatest benefit to mortality when it is initiated in patients during refractory cardiac arrest
- ✓The timing of initiation may be crucial to any potential for averting deaths with VA-ECMO

Intensive Care Med 2018

Q #1: Is E-CPR a life saver or a costly toy?

✓No direct comparison between conventional ALS and E-CPR



Q #1: Is E-CPR a life saver or a costly toy?

What we know is important:

- ✓No-flow and CA time (witnessed CA)
- ✓Quality of CPR
- ✓Signs of life
- ✓Transitory ROSC
- ✓(Rhythm?)
- ✓LOGISTICS

Q #1: Is E-CPR a life saver or a costly toy?

E-CPR is just a ring in the chain of survival

Consider:
- Ultrasound imaging
- Mechanical chest compressions
- Coronary angiography and PCI
- Extracorporeal CPR

Availability 24/7:
- Cath Lab
- Theatre
- Diagnostic facilities
- Advanced neurological monitoring
- Dedicated teams (ICU-neuro)

Laypeople education
- CPR
- AEDs

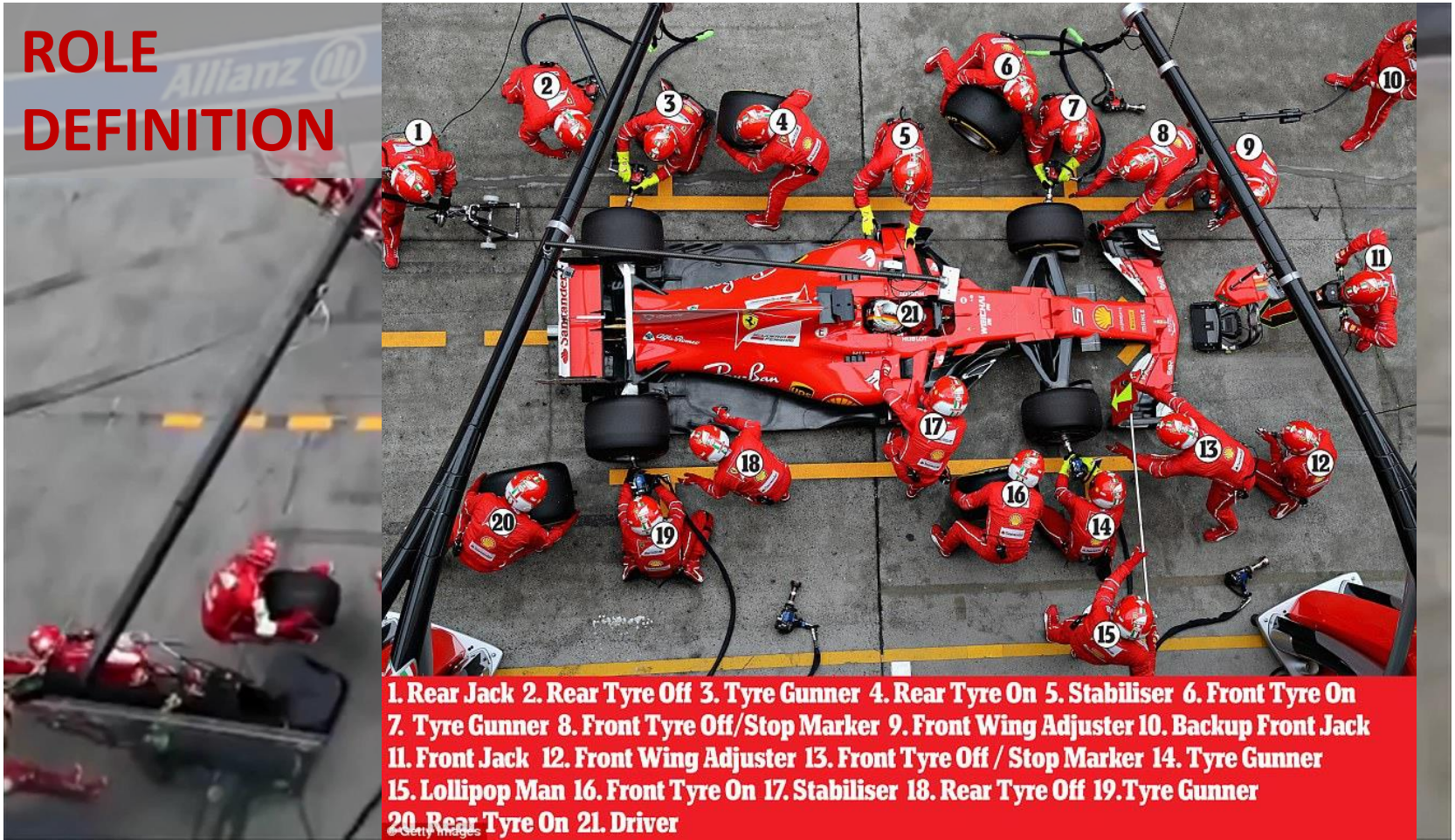
PAD Programmes

Bystander CPR
Dispatcer-assisted CPR
(hands-only CPR)

Widespread PADs
"Institutional" PADs
(Police, Firefighters…)
"Proximity rescuers"

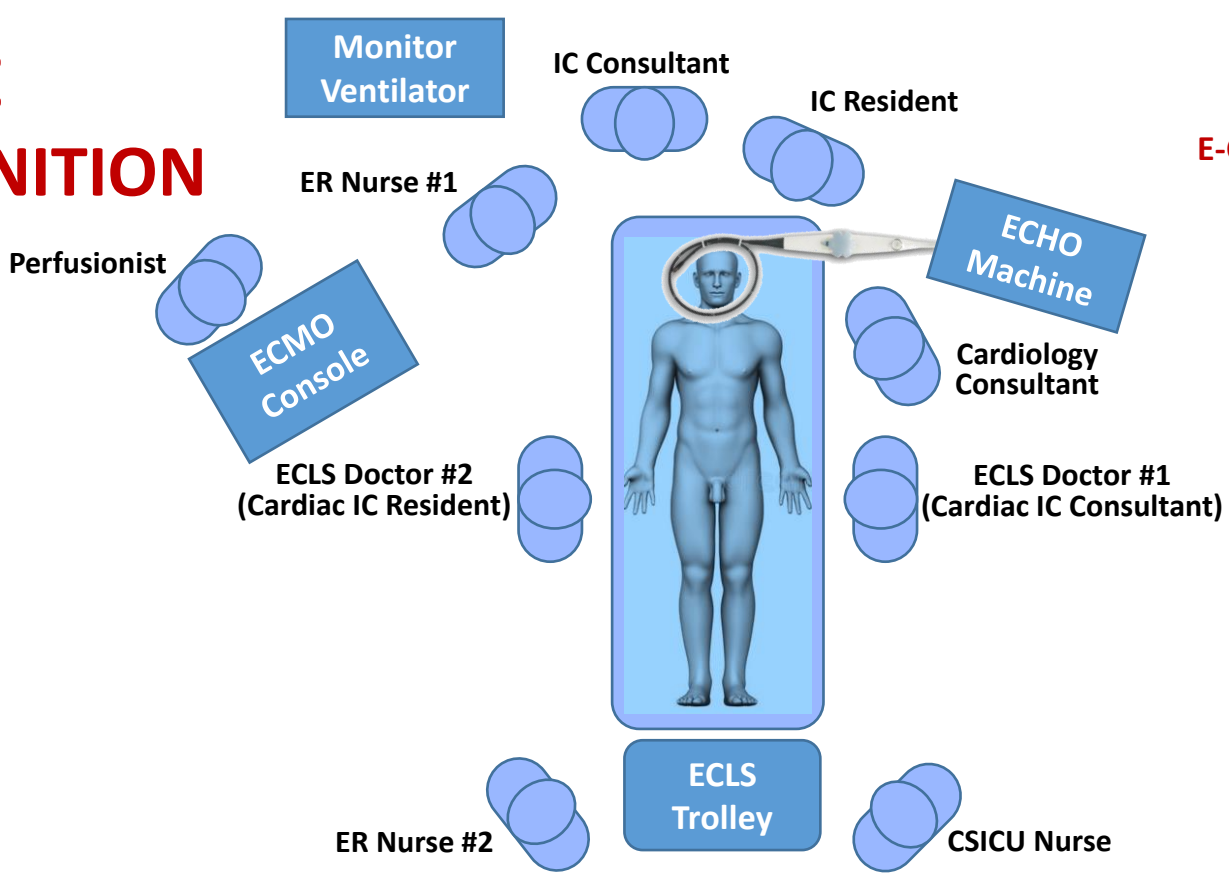
Advanced pre-H care
Pre-H/H networking
Minimise time on scene
Accurate communication

Q #1: Is E-CPR a life saver or a costly toy?



Q #1: Is E-CPR a life saver or a costly toy?

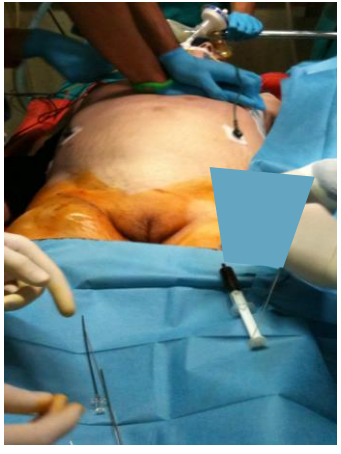
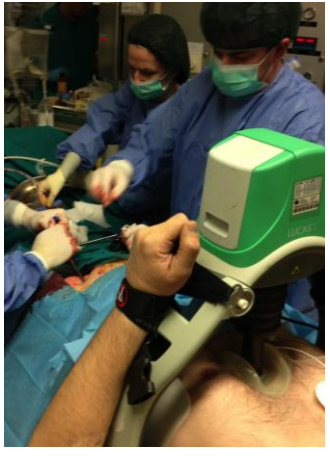
ROLE DEFINITION



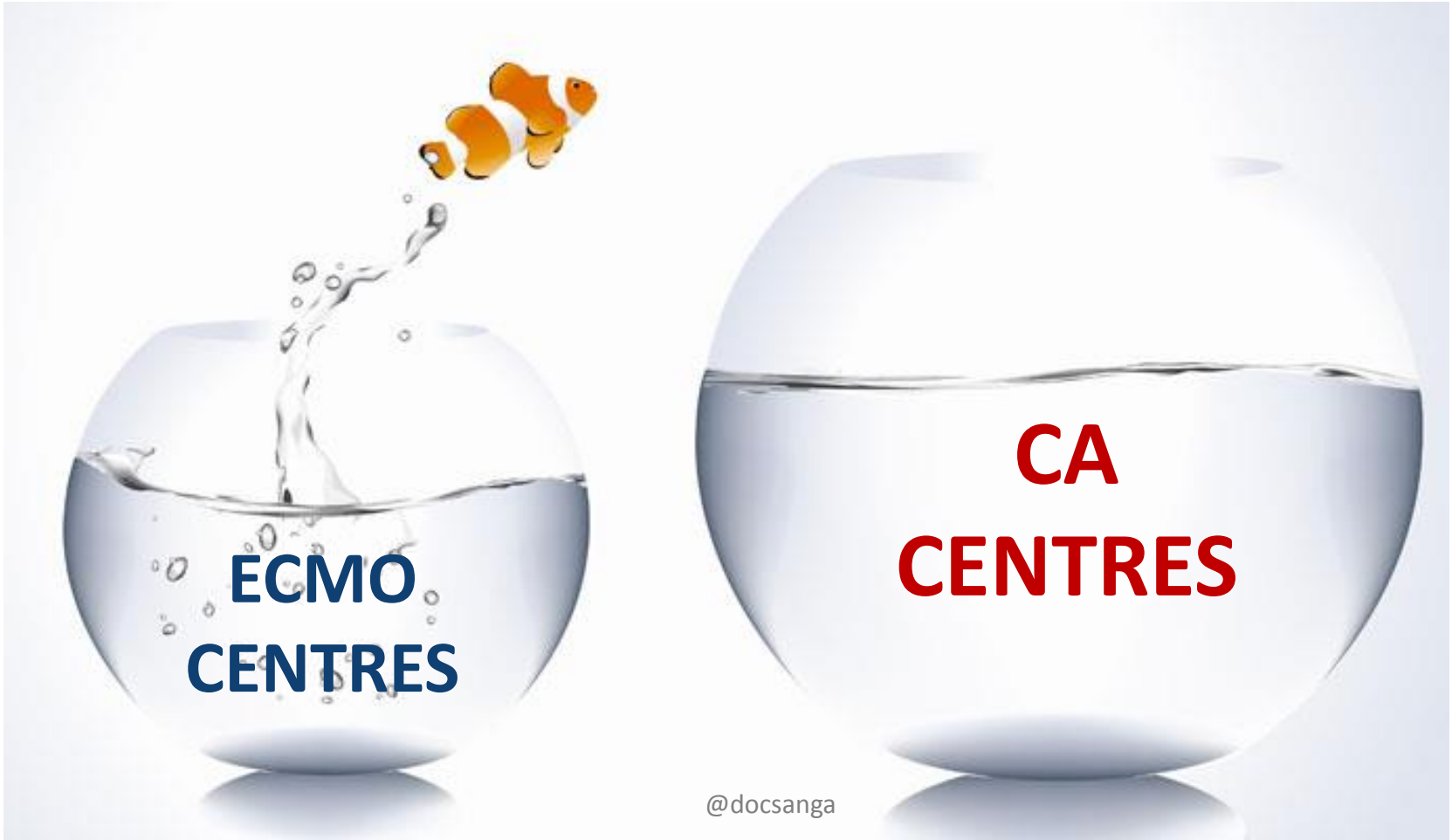
E-CPR ED Setup

Q #1: Is E-CPR a life saver or a costly toy?

E-CPR for OHCA

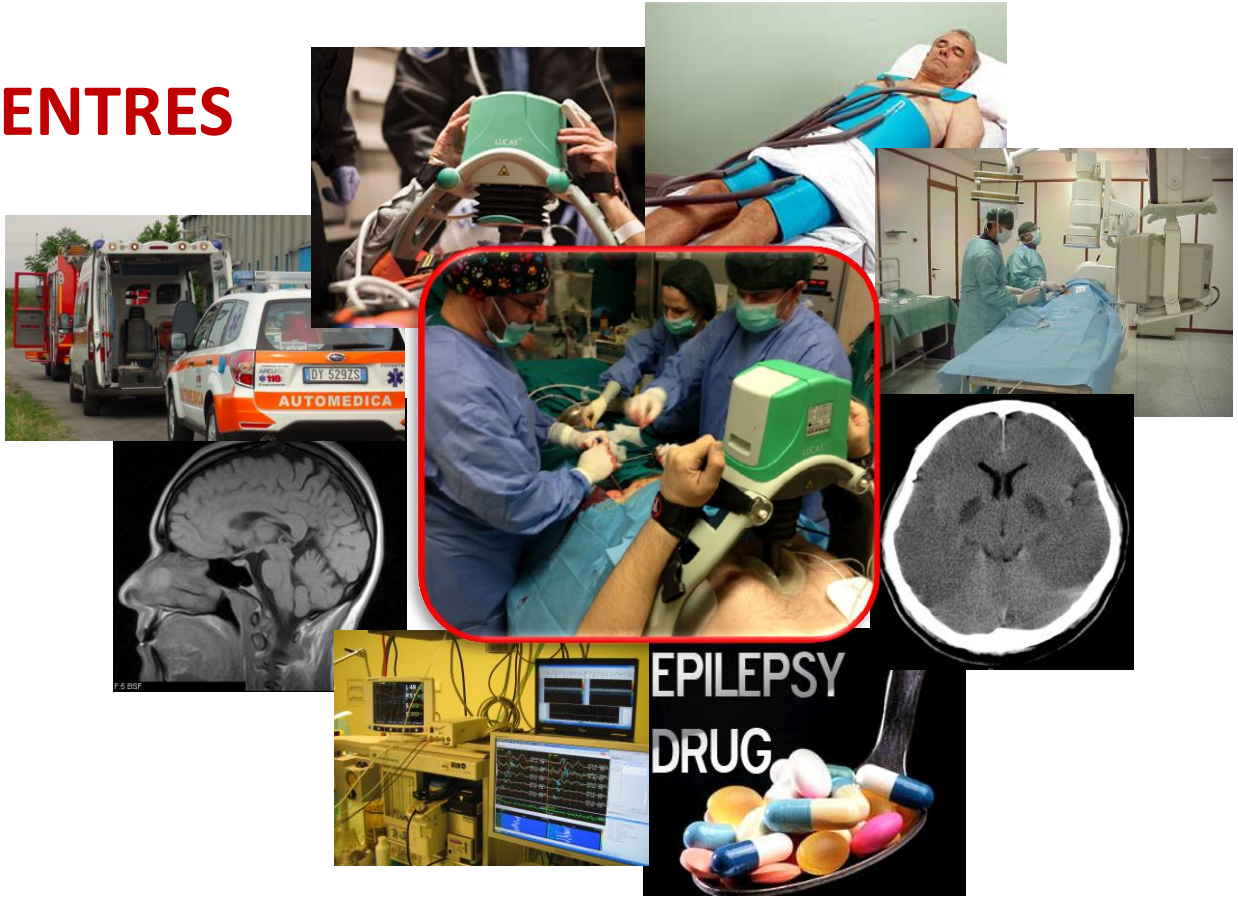
	2006-2010	2011-2012	2013-2017	2018-2019
				
Door-to-ECPR time (mins, median)	**43.8’** .	**30.8’** .	**22.7’** .	**15.6’** .
Survival to D/C (CPC 1-2)	**9%** .	**19%** .	**28%** .	**29%** .

Q #1: Is E-CPR a life saver or a costly toy?

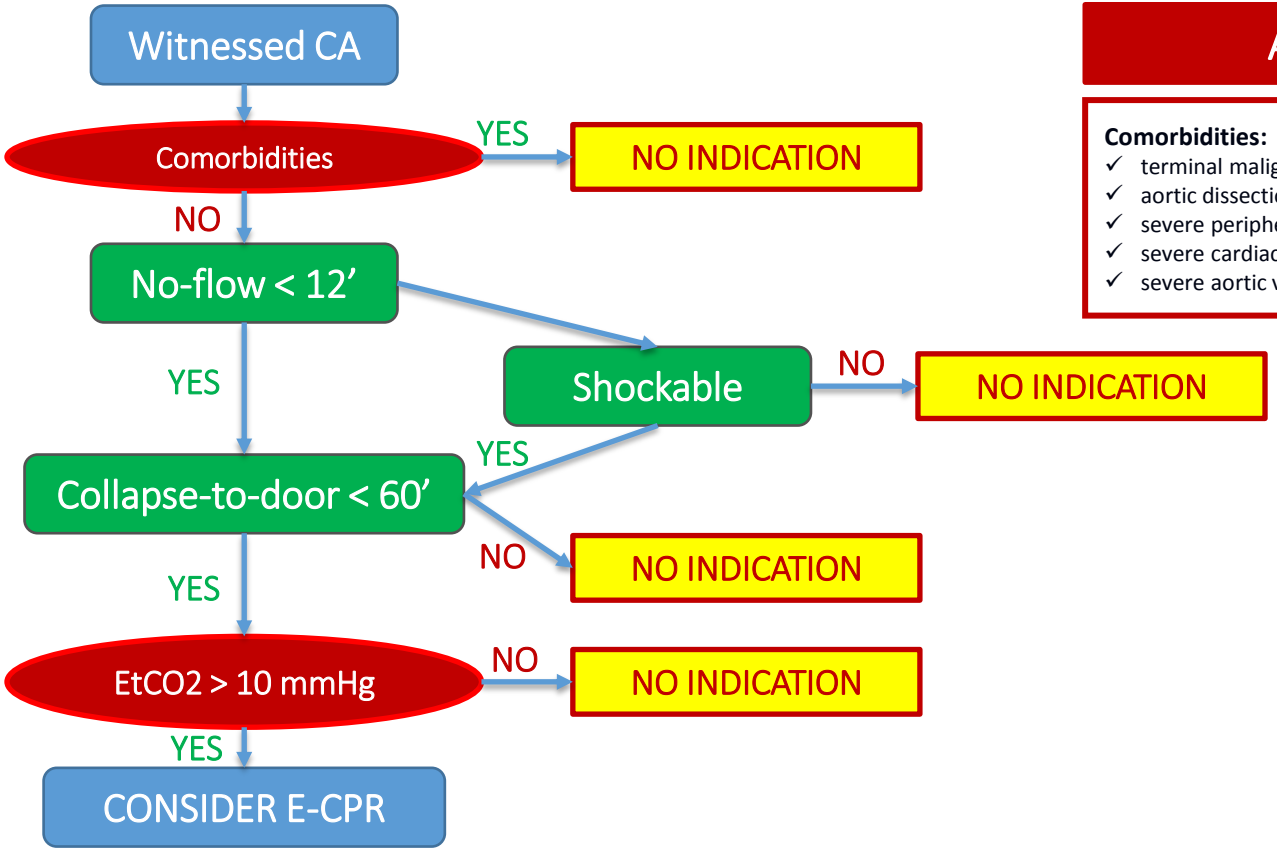


Q #1: Is E-CPR a life saver or a costly toy?

CA CENTRES



Q #1: Is E-CPR a life saver or a costly toy?



AGE: 12-70

Comorbidities:
- ✓ terminal malignancy
- ✓ aortic dissection
- ✓ severe peripheral arteriopathy
- ✓ severe cardiac failure without transplant indication
- ✓ severe aortic valve failure

Lombardia E-CPR Protocol

AREU
AZIENDA REGIONALE EMERGENZA URGENZA
Regione Lombardia

Q #1: Is E-CPR a life saver or a costly toy?

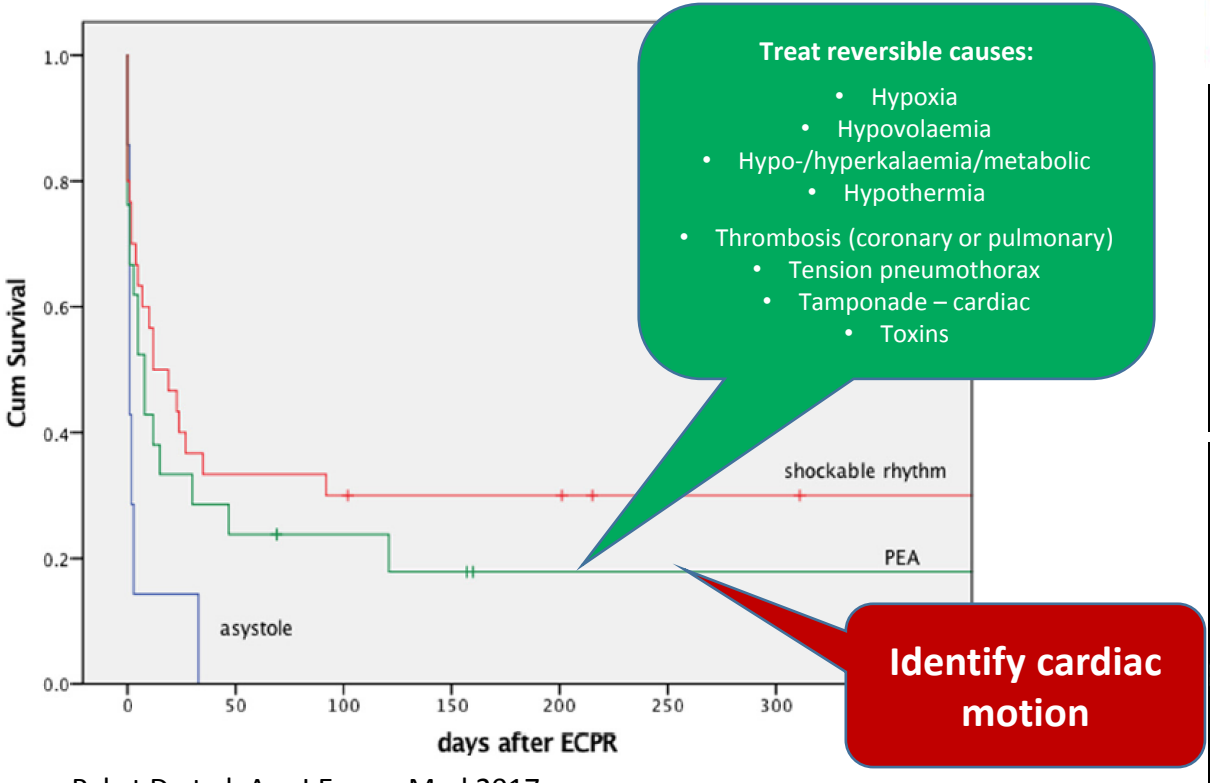
Lombardia ECMO activity 01/2016-03/2018

	2016	2017	2018	n. survived
E-CPR Patients	101	125	46	**98/272**
ECMO for CS	58	103	30	134/191
ECMO for ARDS	39	33	33	75/105
ECMO PE	4	2	5	3/11
ECMO for Hypothermia	4	5	0	4/9
ECMO < 16 aa	33	43	24	57/100
Total ECMO pts	236	312	147	**366/695**

36%

Q #1: Is E-CPR a life saver or a costly toy?

Is PEA a contraindication to E-CPR?

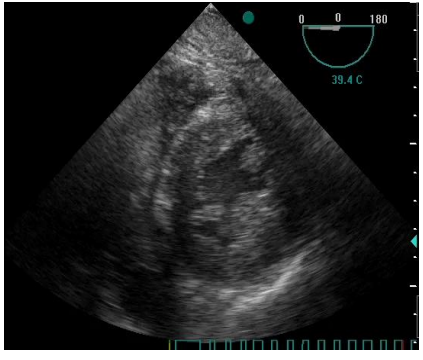


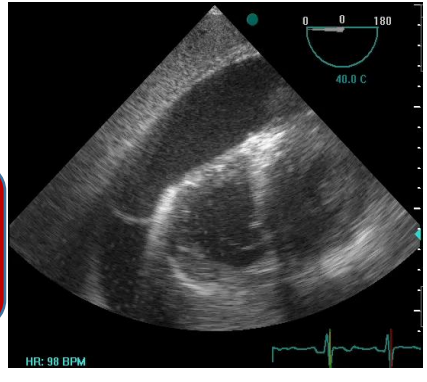
Treat reversible causes:

- Hypoxia
- Hypovolaemia
- Hypo-/hyperkalaemia/metabolic
- Hypothermia
- Thrombosis (coronary or pulmonary)
- Tension pneumothorax
- Tamponade – cardiac
- Toxins

Identify cardiac motion

CUORE
Cardiac Ultrasound Optimized REsuscitation

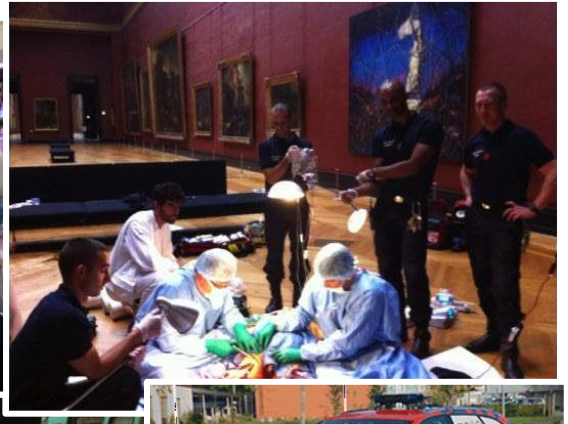




Pabst D et al. Am J Emerg Med 2017

Q #1: Is E-CPR a life saver or a costly toy?

Is it better to take the patient to ECMO or ECMO to the patient?



Q #1: Is E-CPR a life saver or a costly toy?

Q #1: Is E-CPR a life saver or a costly toy?

HORIZONTAL LIMITS

Q #2: Is trauma a contraindication to ECMO?

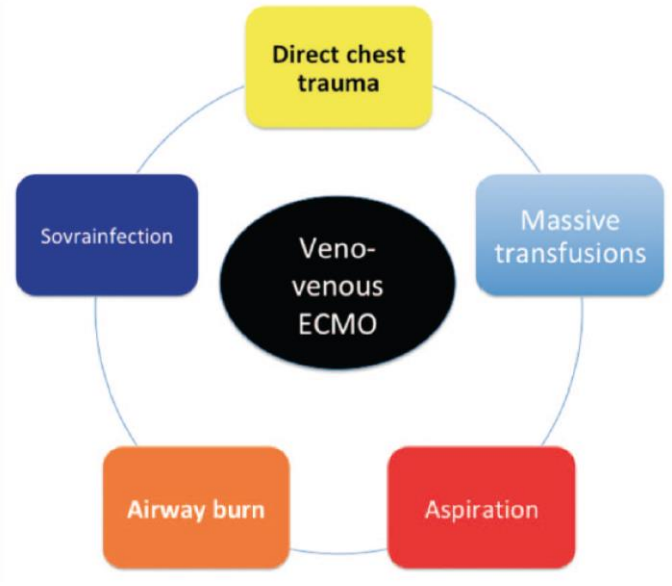
First trauma patient on by-pass:

- ✓24 yo male
- ✓Motorcycle accident
- ✓Aortic rupture
- ✓Surgery on by-pass
- ✓Post-traumatic ARDS
- ✓ECLS for 75hrs
- ✓Survived wo deficits

N Engl J Med 1972

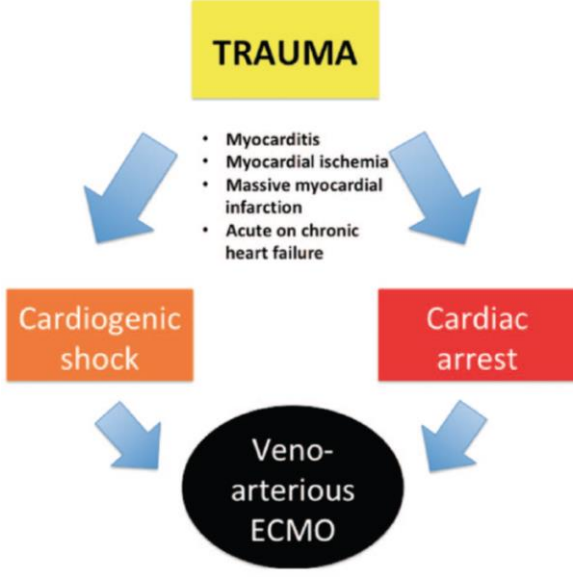
Q #2: Is trauma a contraindication to ECMO?

POST-TRAUMATIC ARDS



DIRECT CARDIAC INJURY

Leading to CS or CA



Modified from Curr Opin Anesth 2019

Q #2: Is trauma a contraindication to ECMO?

Indications and outcomes of extracorporeal life support in trauma patients

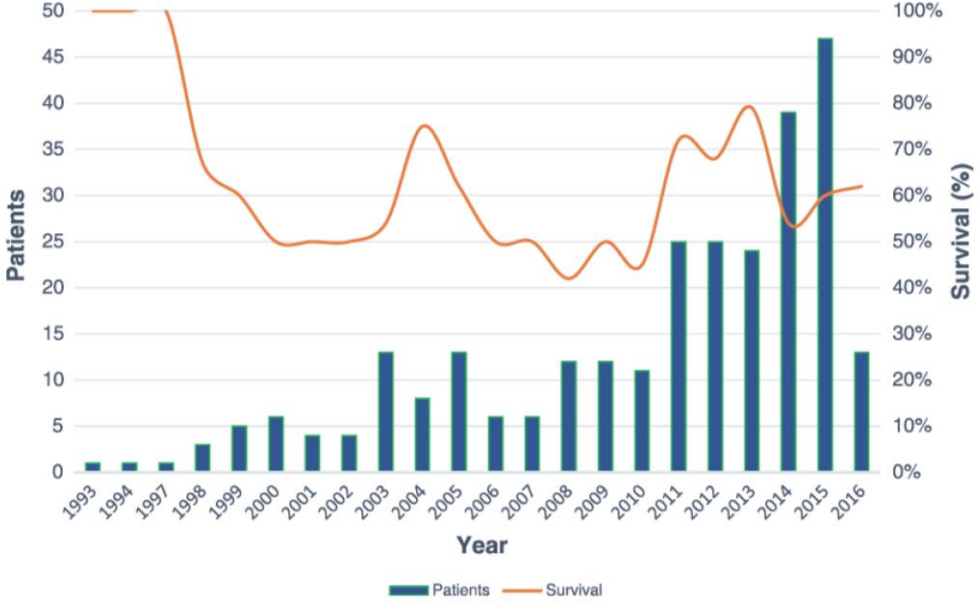


TABLE 2. Trauma Diagnoses and Indications for ECLS Support

Index Trauma Diagnosis	n	%	ECLS Indication	n	%
Thoracic injury	76	27.2	ARDS/lung failure	138	49.5
Spine fracture	42	15.1	Trauma NOS	34	12.1
Abdominal injury	34	12.2	Extremity fracture	15	5.4
Orthopedic fracture	33	11.8	Hemothorax/pneumothorax	12	4.3
Burns	33	11.8	Pulmonary infection	11	3.9
Skull fracture	13	4.6	Burns	10	3.6
Traumatic brain injury	10	3.6	Pulmonary contusion	10	3.6
Vascular injury	8	2.9	Shock	8	2.9
Spinal cord injury	5	1.8	Cardiogenic shock	8	2.9
Other	25	9.0	Abdominal injury	5	1.8
Total	279	100	Pulmonary embolism	4	1.4
			Spinal cord injury	2	0.7
			Acute myocardial infarction	2	0.7
			Viral pneumonia	2	0.7
			Drowning	2	0.7
			Hypothermia	1	0.4
			Fat embolism	1	0.4
			Other	14	5.0
Total	179	100%	Total	179	100%

Q #2: Is trauma a contraindication to ECMO?

Extracorporeal life support in trauma: Worth the risks? A systematic review of published series

TABLE 3. Ranges of Outcomes Reported for Variables of Interest

Variable	Range Among Included Studies
Mean age	5–72 y (12 out of 215 patients were <16 y of age)
Blunt trauma	81–100%
ISS	18–73
Duration from trauma to ECLS	<1–38 d
Duration on ECLS	<1–43 d
Death from bleeding	0–38% (<15% in studies after 1995)
Death from sepsis/MSOF	0–30%
[illegible]	[illegible]
VV-ECLS survival to discharge	56–89%
VA-ECLS survival to discharge	42–63%
[illegible]	[illegible]

Reports by Senunas et al., Huang et al., and Arlt et al. were not included in the pooled analysis because of significant overlap of their reported patients with other included series. Denominators were based on the total number of patients where the outcomes of the variable of interest were specifically reported.

ISS, Injury Severity Score; ECLS, extracorporeal life support; VA, venoarterial; VV, venovenous; MSOF, multisystem organ failure.

Conclusion

The use of ECLS in trauma patients when needed may provide survival benefits that significantly overweigh the feared risk of bleeding associated.

J Trauma Acute Care Surg 2017

Q #2: Is trauma a contraindication to ECMO?

ECMO

Offloads the venous side

Controls Temperature

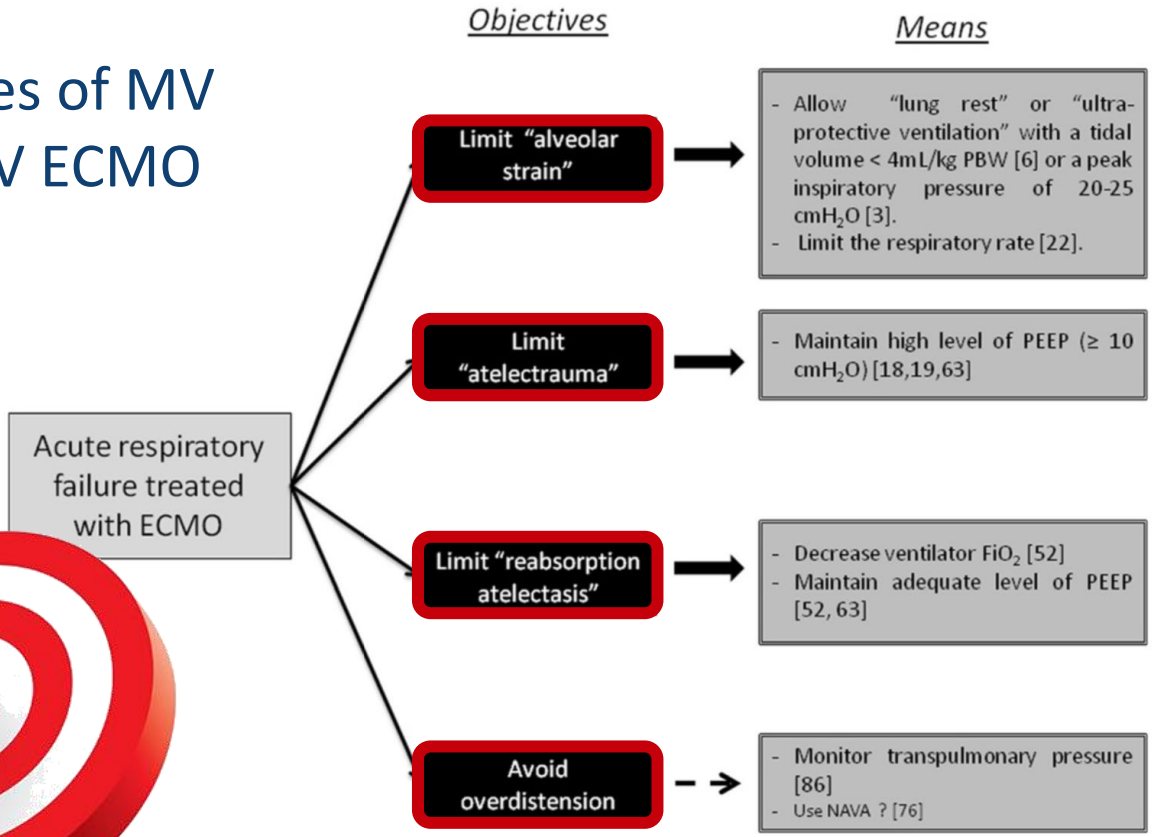
Restores CO

Clears lactates

Improves acidosis

Q #3: How should we ventilate?

Objectives of MV during VV ECMO



Schmidt M, Critical Care 2014

Q #3: How should we ventilate?

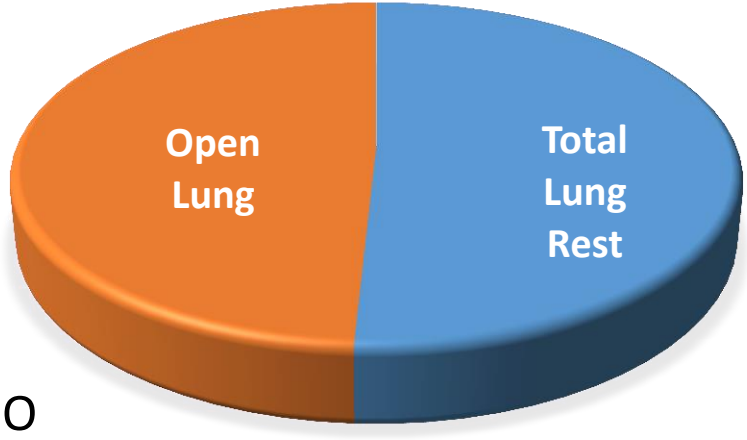
TOTAL LUNG REST

OPEN LUNG APPROACH

Q #3: How should we ventilate?

International survey on the management of mechanical ventilation during ECMO in adults with severe respiratory failure

- ✓173 adult respiratory ECMO centres
- ✓Only 27.1% of ECMO centres had a protocol for MV on ECMO
- ✓55.8% of centres limited plateau pressure to less than 30 cmH_2O
- ✓45.7% used low PEEP and low plateau pressure to allow “lung rest” during ECMO
- ✓44.2% preferred an open lung ventilation strategy with moderate/high PEEP values



Minerva Anestesiol 2015

Q #3: How should we ventilate?

Walking the tight rope…

TOTAL REST

- ✓**Less strain**
- ✓Need for higher BF to obtain adequate oxygenation
- ✓More frequently persisting hypoxemia
- ✓RV does not like lung collapse
- ✓**Need to convert to VA in some patients**

TOTAL REST STRATEGY

PRO:
- Minimize Overdistention
- Lower Airway Pressure

CON:
- Atelectrauma
- Right Ventricular Failure
- Higher Intrapulmonary Shunt

OPEN LUNG STRATEGY

PRO:
- Minimize Atelectrauma
- Lower Vt/EELV ratio

CON:
- Overdistention

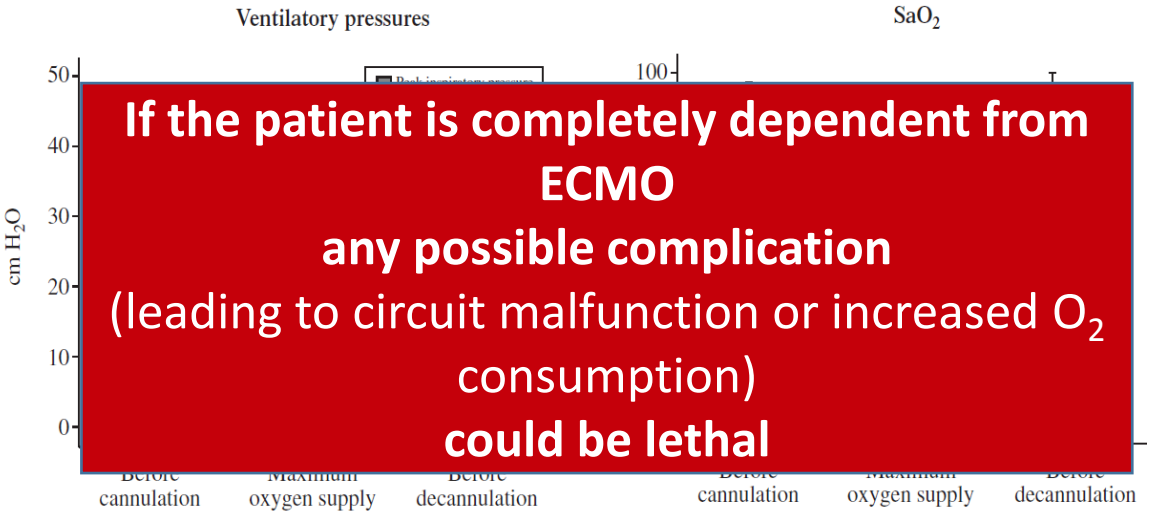
Pesenti A., Med Klin Intensivmed Notfmed 2018

OPEN LUNG

- ✓**Less cyclic closure/reopening**
- ✓Lower BF may be sufficient
- ✓Lower incidence of RV failure and conversion to VA
- ✓Might lead to overdistention
- ✓**Might be less 'protective'**

Q #3: How should we ventilate?

Extracorporeal membrane oxygenation for pandemic H1N1 2009 respiratory failure



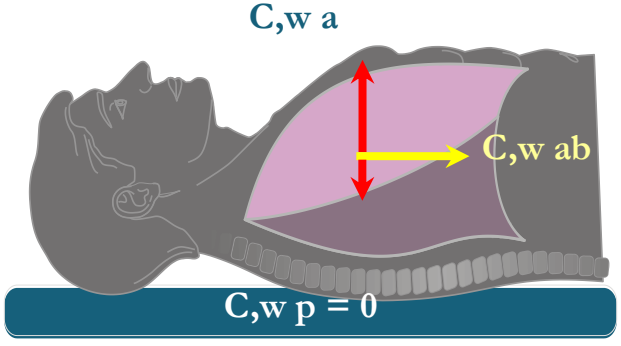
If the patient is completely dependent from ECMO
any possible complication
(leading to circuit malfunction or increased O_2 consumption)
could be lethal

33%

Four patients were converted from v-v to v-a ECMO, three because of right heart failure and one because of life threatening arrhythmias with circulatory instability that did not respond to conventional treatment.

Minerva Anestesiol 2010

Q #3: How should we ventilate?



…upside down you turn me…

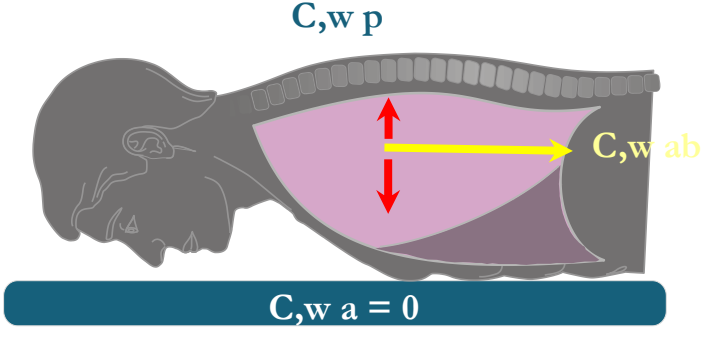
An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome

Eddy Fan, Lorenzo Del Sorbo, Ewan C. Goligher, Carol L. Hodgson, Laveena Munshi, Allan J. Walkey, Neill K. J. Adhikari, Marcelo B. P. Amato, Richard Branson, Roy G. Brower, Niall D. Ferguson, Ognjen Gajic, Luciano Gattinoni, Dean Hess, Jordi Mancebo, Maureen O. Meade, Daniel F. McAuley, Antonio Pesenti, V. Marco Ranieri, Gordon D. Rubenfeld, Eileen Rubin, Maureen Seckel, Arthur S. Slutsky, Daniel Talmor, B. Taylor Thompson, Hannah Wunsch, Elizabeth Uleryk, Jan Brozek, and Laurent J. Brochard; on behalf of the American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine

This official clinical practice guideline of the American Thoracic Society (ATS), European Society of Intensive Care Medicine (ESICM), and Society of Critical Care Medicine (SCCM) was approved by the ATS, ESICM, and SCCM, March 2017

Question 2: Should Patients with ARDS Receive Prone Positioning?

Recommendation. We recommend that adult patients with severe ARDS receive prone positioning for more than 12 hours per day (strong recommendation, moderate-high confidence in effect estimates).



Am J Resp Crit Care Med 2017

Q #3: How should we ventilate?

- ✓Non-adherence to evidence-based management of ARDS is common
- ✓The question is no longer whether ECMO works, but “by how much does ECMO work, in whom, and at what cost?”
- ✓We very strongly advocate for widespread adoption of proven conventional management approaches

Lancet 2019

Unproven and Expensive before Proven and Cheap: Extracorporeal Membrane Oxygenation versus Prone Position in Acute Respiratory Distress Syndrome

Xuehan Li[1,2,3], Damon C. Scales[3,4], and Brian P. Kavanagh[1,3]

Am J Respir Crit Care Med 2018

Q #3: How should we ventilate?

Application of prone position in hypoxaemic patients supported by veno-venous ECMO ☆

Alberto Lucchini [a,d,*], Christian De Felippis [b], Giulia Pelucchi [a], Giacomo Grasselli [c], Nicolò Patroniti [a], Luigi Castagna [c], Giuseppe Foti [a], Antonio Pesenti [c], Roberto Fumagalli [d,e]

- ✓PP during ECMO was not associated with major adverse events.
- ✓In hypoxaemic patients, PP can improve oxygenation
- ✓PP during VV-ECMO is a safe procedure when **performed by trained staff in a recognised ECMO centre**.

Int Crit Care Nurs 2018

Q #3: How should we ventilate?

Spontaneous breathing during veno-venous extracorporeal membrane oxygenation

Stefania Crotti, Nicola Bottino, Elena Spinelli

PROs

- ✓Better V_A/Q matching
- ✓Muscle tone preservation
- ✓Less atelectasis
- ✓Less VAP
- ✓Lower intrathoracic pressures
- ✓Better venous return
- ✓Less sedation, less delirium
- ✓Active physio
- ✓Interaction with staff and relatives

CONs

- ✓unassisted spontaneous hyperventilation has to be avoided
- ✓higher work of breathing
- ✓increased oxygen consumption
- ✓Hypoventilation might happen
- ✓the risk of cannulae and devices displacement is higher in awake patients

J Thorac Dis 2018

Q #3: How should we ventilate?

Ventilation-induced lung injury exists in spontaneously breathing patients with acute respiratory failure: Yes

Laurent Brochard[1,2*]

- ✓In patients under partial ventilatory assist, clinicians should not consider that their patients are “protected” because they set only modest levels of positive airway pressure during inspiration using pressure support ventilation. To better understand what forces the patient is generating, **a monitoring of respiratory muscle activity and/or respiratory drive is necessary.**

Intensive Care Med 2017

OI #1: We are below standards

Position paper for the organization of ECMO programs for cardiac failure in adults

✓In order to optimize outcomes, we recommend that, whenever possible, centers performing ECMO for cardiac failure achieve a minimum ECMO case volume of 30 cases per year, with a substantial proportion being for cardiac failure

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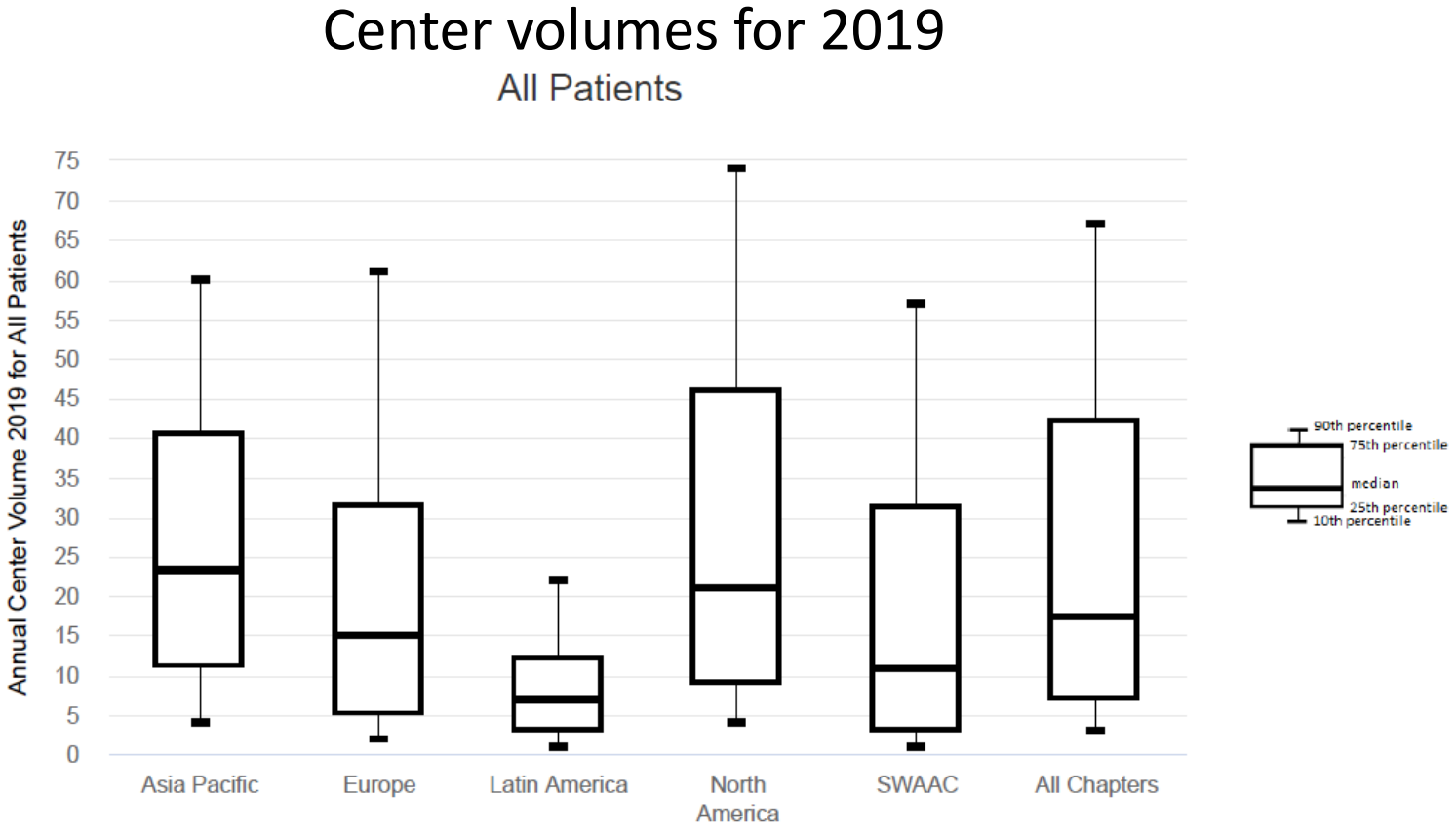
OI #1: We are below standards



OI #2: We don't have enough evidence

Position paper for the organization of ECMO programs for cardiac failure in adults

Table 3 Indications for venoarterial ECMO and quality of evidence

	Highest level of evidence
Indications	
Myocardial infarction-associated cardiogenic shock	Cohort studies
Fulminant myocarditis	Cohort studies
Sepsis-associated cardiomyopathy	Cohort studies
Adult congenital heart disease with acute decompensated heart failure	Case series
Post-cardiotomy cardiogenic shock	Cohort studies
RV support during LVAD implantation	Cohort studies
Bridge to VAD or heart transplantation	Cohort studies
Post-transplantation graft failure	Cohort studies
ECPR	Cohort studies with matched propensity analyses
Cardiogenic shock post-cardiac arrest	Cohort studies with matched propensity analyses
Refractory ventricular arrhythmia	Cohort studies
Pulmonary hypertension with RV failure	Case series
Massive pulmonary embolism	Cohort studies

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OI #2: We don't have enough evidence

Use of ECMO in ARDS: does the EOLIA trial really help?

Luciano Gattinoni*, Francesco Vasques and Michael Quintel

EOLIA Authors' conclusion: "Among patients with very severe ARDS, 60day mortality was not significantly lower with ECMO than with a strategy of conventional mechanical ventilation that included ECMO as rescue therapy".

However:

a) **Emergency ECMO improves outcome by "buying time" in extremely hypoxemic patients.**
   Of the 35 patients switched from conventional therapy to rescue ECMO (median SaO2 77%; nine cardiac arrest events), 15 survived. It is unlikely that they would have survived without ECMO, regardless of the statistical relevance of these observations.

b) **ECMO improves outcome by reducing the invasiveness of mechanical ventilation.**
   During ECMO, tidal volume was reduced by 43% and respiratory rate by 23%, while PEEP remained essentially unchanged. This represents an estimated 66% reduction in the mechanical power applied to the lungs (from 28 J/min to 10 J/min). This reduction was associated with a higher survival rate (81/124patients) in the ECMO group (vs 68/125 controls).

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OI #2: We don't have enough evidence

Do we need randomized clinical trials in extracorporeal respiratory support? Yes

Alain Combes[1,2*], Antonio Pesenti[3] and Daniel Brodie[4]

Do we need randomized clinical trials in extracorporeal respiratory support? No

Luciano Gattinoni[*] and Michael Quintel

Do we need randomized clinical trials in extracorporeal respiratory support? We are not sure

Jean-Louis Vincent[1*] and Laurent J. Brochard[2,3]

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OI #3: We have too many complications

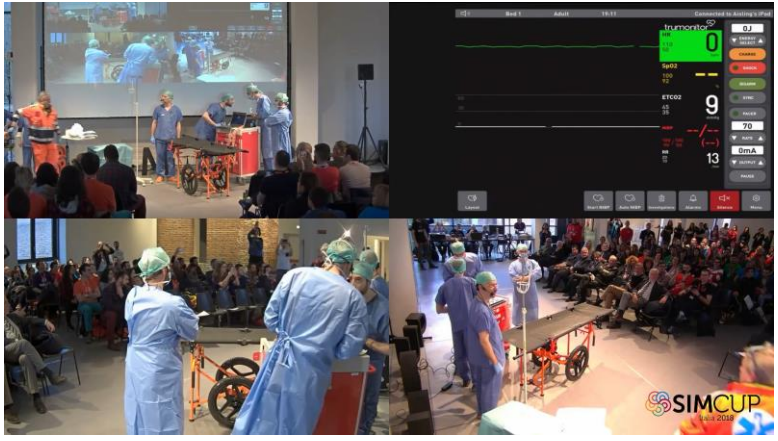
Table 3
Reporting and Definitions of ECMO Complications.

Complication	Reported	Common definitions used	Total studies n, (%)
Bleeding	28/46 (61%)	Bleeding requiring RBC's/transfusion (median ≥ 2 units, range 1-5U)	7/46 (15%)
		≥1Unit	4/46 (9%)
		≥2Units	1/46 (2%)
		≥3Units	1/46 (2%)
		≥4Units	1/46 (2%)
		≥5Units	1/46 (2%)
		Bleeding requiring surgical intervention	4/46 (9%)
		Bleeding from cannulation or surgery	3/46 (7%)
		ELSO[1] or ECABG[2] or INTERMACS[3] definitions	3/46 (7%)
		Any bleeding definition	24/46 (52%)
Vascular complications	26/46 (57%)	Ischaemia or thromboembolism	21/46 (46%)
		Vascular injury requiring surgical repair	17/46 (37%)
		Compartment syndrome	3/46 (7%)
		Fasciotomy	3/46 (7%)
		Amputation	3/46 (7%)
		Any vascular complications defined	23/46 (50%)
CNS injury	25/46 (54%)	CVA or ICH (not further defined)	8/46 (17%)
		Blood or ischaemia on CT/MRI	5/46 (11%)
		INTERMACS or ICD-9 or CPC scale definitions	3/46 (7%)
Renal failure	24/46 (52%)	AKI requiring renal replacement therapy #	10/46 (22%)
		RIFLE classification	3/46 (7%)
		KDIGO[6], AKIN or ICD9 codes each	3/46 (7%)
		Any renal failure definition	21/46 (46%)
Infection/sepsis	19/46 (41%)	Sepsis (not defined)	4/46 (9%)
		CDC[6] or INTERMACS[7] definitions each	4/46 (9%)
		Positive sputum or blood cultures	2/46 (4%)
		Any Infection/sepsis definition	17/46 (37%)
Cannula infection	9/46 (20%)	Local cannula site infection	4/46 (9%)
		Positive cultures	2/46 (4%)
		CLABSI or CRI criteria	2/46 (4%)
		Any cannula infection definition	8/46 (17%)
Equipment failure	9/46 (20%)	Circuit change	5/46 (11%)
		Oxygenator change	4/46 (9%)
		Circuit thrombosis	2/46 (4%)
		Equipment failure defined	9/46 (20%)

ECMO - Extracorporeal membrane oxygenation; ELSO – Extracorporeal life support organization; CNS – central nervous system; ICH – Intracranial haemorrhage; CVA – Cerebrovascular accident; RIFLE - Risk, Injury, Failure, Loss, and End-stage Kidney definition; RRT – Renal replacement therapy; RBCs – Red blood cells; CT – Computerised Tomography; MRI – Magnetic resonance imaging; INTERMACS - Interagency Registry for Mechanically Assisted Circulatory Support; CDC – Centers for Disease Control; CLABSI - Central Line Associated Blood Stream Infection ICD-9 – International classification of diseases. ECABG – European coronary artery bypass graft bleeding definition; CPC – Cerebral performance category; KDIGO – Kidney disease: improving global outcomes definition;

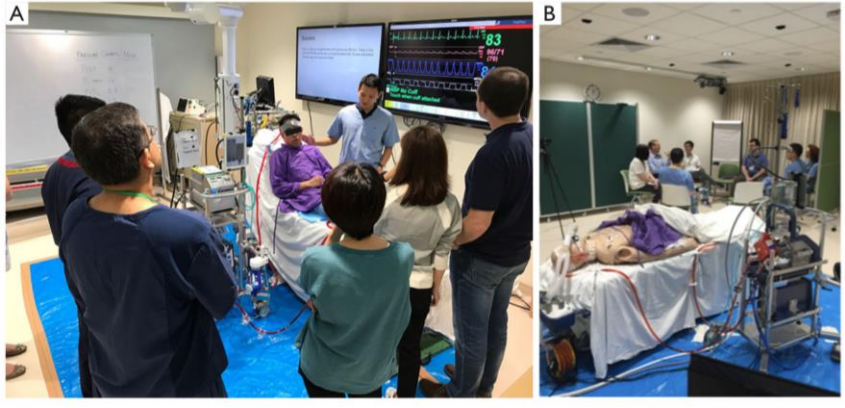
J Crit Care 2019

OI #3: We have too many complications



Simulation training for crises during venoarterial extracorporeal membrane oxygenation

Simon W. C. Sin[1,2], Pauline Y. Ng[1,2], Wallace C. W. Ngai[1], Peter C. K. Lai[1], Andy Y. T. Mok[1], Ricky W. K. Chan[1]



J Thorac Dis 2019

OI #4: We should improve outcome

- ✓Ongoing research
- ✓Reduction of complications

- ✓Center performance

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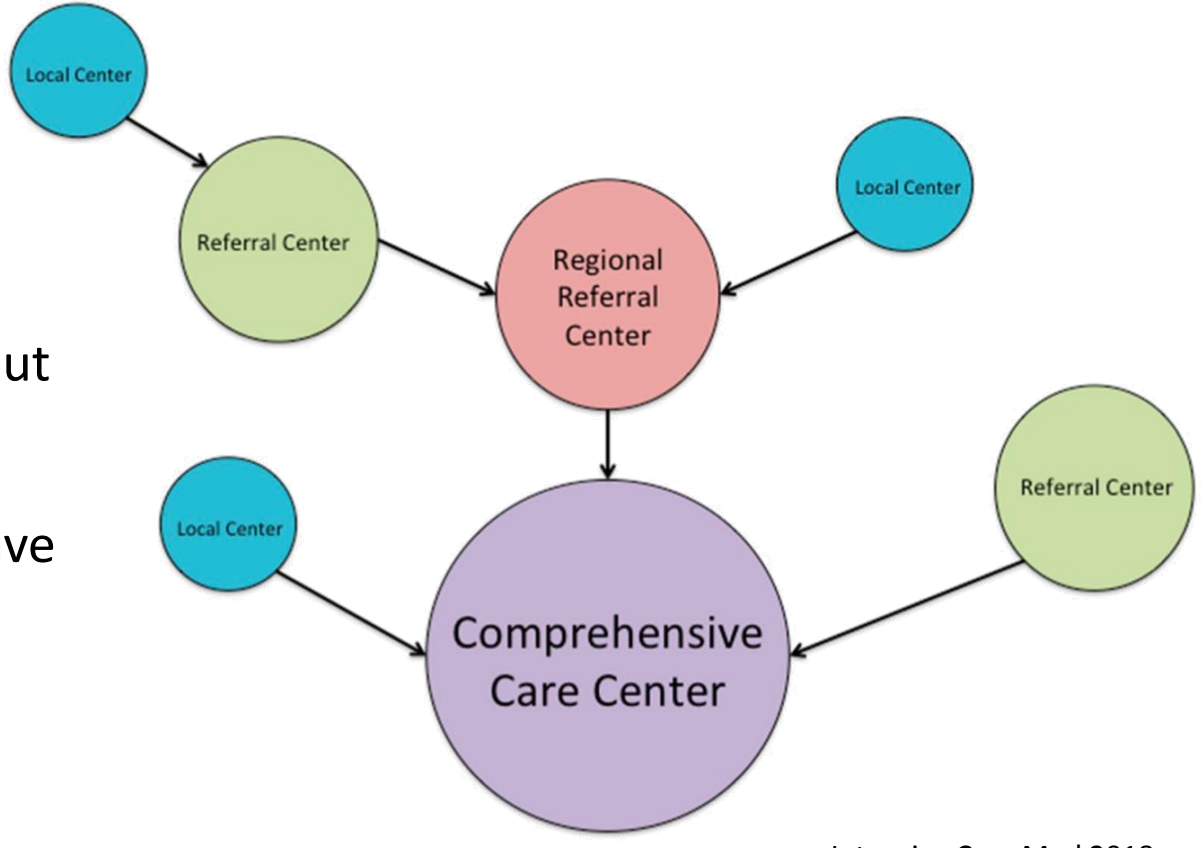
OI #4: We should improve outcome

NETWORKING

- ✓Regional referral centers capable of performing ECMO, including ECMO transport, but without access to long-term heart replacement therapies, should have collaborative relationships with comprehensive care centers



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OI #4: We should improve outcome

MONITORING

- ✓No defined indications exist on monitoring ECMO patients
- ✓No sistematic audit is performed in most centers

Guidelines for Adult Respiratory Failure
August, 2017

Echocardiography is an excellent tool to assess hemodynamic function and help guide management during VV ECLS.

Take-home points

- ✓**ECMO SAVES LIVES**
- ✓Many open issues remain, RCTs may not be the (only) way to answer, collaboration is essential
- ✓As for all aspects in the care of the critically ill, sanga's *mantra* is… MEASURE, MEASURE, MEASURE!

docsanga@gmail.com
fabio.sangalli@unimib.it