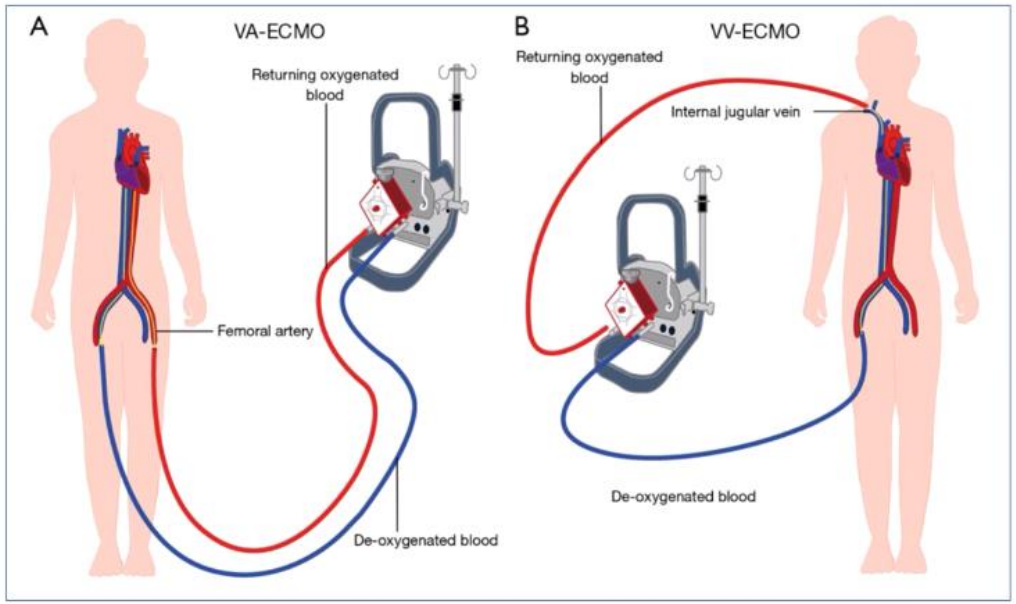
Extra-Corporeal Life Support (ECLS) in ARDS



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29.06.1400

PROLONGED EXTRACORPOREAL OXYGENATION FOR ACUTE POST-TRAUMATIC RESPIRATORY FAILURE (SHOCK-LUNG SYNDROME)

Use of the Bramson Membrane Lung

J. Donald Hill, M.D., Thomas G. O'Brien, M.D., James J. Murray, M.D., Leon Dontigny, M.D., M. L. Bramson, A.C.G.I., J. J. Osborn, M.D., and F. Gerbode, M.D.

Abstract A 24-year-old man sustained subadventitial transection of the thoracic aorta and multiple orthopedic injuries resulting from blunt trauma. The aortic injury was repaired. Because respiratory failure occurred four days later and worsened despite maximal conventional supportive therapy, partial venoarterial perfusion with peripheral cannulation, with use of the Bramson-membrane heart-lung machine, was initiated and continued for 75 hours. At a by-pass flow of 3.0 to 3.6 liters per minute, oxygen tension increased from 38 to 75 mm of mercury, inspired oxygen concentration was reduced from 100 to 60 per cent, and peak airway pressure decreased from 60 to 35 cm of water. The shock-lung syndrome was reversed, and the patient recovered.

End-stage shock lung may be reversible if the patient receives adequate gas exchange through partial extracorporeal circulation with an appropriate membrane lung.

SHOCK lung as a clinical entity is now a well recognized phenomenon after trauma, extensive surgery, hemorrhage, burn or shock.[1,2] Thus far, no single treatment has been consistently successful.[3,4] In the case reported below prolonged partial venoarterial extracorporeal circulation was successfully used in the treatment of shock lung after extensive trauma.

Case Report

Injury and Diagnosis

A 24-year-old man was admitted to the emergency room of the Santa Barbara Cottage Hospital about 30 minutes after being struck by an automobile. He had not lost consciousness. Pain was severe in the pelvis and lower extremities. The blood pressure was 74/30, the pulse 134, and the respirations 32. Mediastinal widening was noted on the x-ray film (Fig. 1*A*).

The diagnoses were comminuted fractures of the left tibia and fibula, dislocation of the right knee, with fracture of the tibial plateau, fractures of both right pubic rami and the left acetabulum, dislocation of the right sacroiliac joint, probable subadventitial transection of the thoracic aorta, root or peripheral nerve injury of the right lower extremity, and hypovolemia.

Abbreviations Used
F_{IO_2}: inspired oxygen concentration
P_{aCO_2}: arterial carbon dioxide tension
P_{aO_2}: arterial oxygen tension

Intravenous fluids and blood were given. A thoracic aortogram demonstrated a subadventitial traumatic aneurysm, distal to the left subclavian artery.

Emergency Surgery

With the use of partial peripheral (left-groin) venoarterial bypass, the aortic tear was repaired through a left thoracotomy incision. The heart and lungs appeared normal. The

From the Department of Cardiovascular Surgery, Presbyterian Hospital, and the Heart Research Institute, Institute of Medical Sciences, Pacific Medical Center, San Francisco, and the departments of Surgery and Medicine, Santa Barbara Cottage Hospital, Santa Barbara, Cal. (address reprint requests to Dr. Hill at the Pacific Medical Center, 2200 Webster St., Room 305, San Francisco, Cal. 94115).

Aided in part by a grant (HE 06311) from the U.S. Public Health Service.

Extracorporeal support of ARDS was first applied in 1972.

The NEW ENGLAND JOURNAL of MEDICINE

March 23, 1972
N Engl J Med 1972; 286:629-634
DOI: 10.1056/NEJM197203232861204

November 16, 1979

Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

Warren M. Zapol, MD; Michael T. Snider, MD, PhD; J. Donald Hill, MD; et al

» Author Affiliations

JAMA. 1979;242(20):2193-2196. doi:10.1001/jama.1979.03300200023016

The first randomized trial ever performed in ALI/ARDS showed that patients treated with Extracorporeal support or with Conventional ventilation had similar mortality, equal to about 90%.

Preliminary Communication

TREATMENT OF ACUTE RESPIRATORY FAILURE WITH LOW-FREQUENCY POSITIVE-PRESSURE VENTILATION AND EXTRACORPOREAL REMOVAL OF CO_2

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Summary Terminal respiratory failure was reversed in three patients with a combination of extracorporeal CO_2 removal through a membrane lung and oxygen diffusion into the diseased lungs between mechanical breaths induced at a frequency of 2–3/min. The technique seems to prevent the pulmonary barotrauma and extrapulmonary derangements caused by conventional mechanical ventilation.

(*JAMA* 1986;256:881-886)

August 15, 1986

Low-Frequency Positive-Pressure Ventilation With Extracorporeal CO2 Removal in Severe Acute Respiratory Failure

Luciano Gattinoni, MD; Antonio Pesenti, MD; Daniele Mascheroni, MD; et al

» Author Affiliations

JAMA. 1986;256(7):881-886. doi:10.1001/jama.1986.03380070087025

43 patients

Abstract

Forty-three patients were entered in an uncontrolled study designed to evaluate extracorporeal membrane lung support in severe acute respiratory failure of parenchymal origin. Most of the metabolic carbon dioxide production was cleared through a low-flow venovenous bypass. To avoid lung injury from conventional mechanical ventilation, the lungs were kept "at rest" (three to five breaths per minute) at a low peak airway pressure of 35 to 45 cm H_2O (3.4 to 4.4 kPa). The entry criteria were based on gas exchange under standard ventilatory conditions (expected mortality rate, >90%). Lung function improved in thirty-one patients (72.8%), and 21 patients (48.8%) eventually survived. The mean time on bypass for the survivors was 5.4 ± 3.5 days. Improvement in lung function, when present, always occurred within 48 hours. Blood loss averaged 1800±850 mL/d. No major technical accidents occurred in more than 8000 hours of perfusion. Extracorporeal carbon dioxide removal with low-frequency ventilation proved a safe technique, and we suggest it as a valuable tool and an alternative to treating severe acute respiratory failure by conventional means.

Suggestion of benefit in 1980s

Extracorporeal CO2 removal with low-frequency ventilation proved a safe technique, and we suggest it as a valuable tool and an alternative to treating severe acute respiratory failure by conventional means.

A randomized study performed in 1994 (40 patients) **did not show** any survival benefit with extracorporeal CO2 removal support influenced by bleeding complications

Clinical Trial > Am J Respir Crit Care Med. 1994 Feb;149(2 Pt 1):295-305.
doi: 10.1164/ajrccm.149.2.8306022.

Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO2 removal for adult respiratory distress syndrome

A H Morris [1], C J Wallace, R L Menlove, T P Clemmer, J F Orme Jr, L K Weaver, N C Dean, F Thomas, T D East, N L Pace, M R Suchyta, E Beck, M Bombino, D F Sittig, S Böhm, B Hoffmann, H Becks, S Butler, J Pearl, B Rasmusson

Despite the discouraging results, in Europe few centers continued to use V-V ECMO support as a last resource in selected series of patients

Clinical Trial > Intensive Care Med. 1997 Aug;23(8):819-35. doi: 10.1007/s001340050418.

High survival rate in 122 ARDS patients managed according to a clinical algorithm including extracorporeal membrane oxygenation

K Lewandowski [1], R Rossaint, D Pappert, H Gerlach, K J Slama, H Weidemann, D J Frey, O Hoffmann, U Keske, K J Falke

The **rebirth of the technique**, however, was due to its use as a **rescue therapy** during H1N1 flu epidemics in Australia and New Zealand in severely hypoxemic patients untreatable with conventional method

CARING FOR THE CRITICALLY ILL PATIENT

JAMA-EXPRESS

Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators*

Context The novel influenza A(H1N1) pandemic affected Australia and New Zealand during the 2009 southern hemisphere winter. It caused an epidemic of critical illness and some patients developed severe acute respiratory distress syndrome (ARDS) and were treated with extracorporeal membrane oxygenation (ECMO).

This report showed a survival rate higher than 70%

Interest in ECMO was renewed after the publication of CESAR trial in 2009.

Randomized Controlled Trial > Lancet. 2009 Oct 17;374(9698):1351-63.
doi: 10.1016/S0140-6736(09)61069-2. Epub 2009 Sep 15.

180 patients

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 [1], 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, CESAR trial collaboration

Showed clear benefits on outcome when severely hypoxemic patients were treated within an expert high–case volume center (with ECMO capability) when compared with nonspecialized hospitals

The CESAR trial:

- **First, of the 90 patients assigned for consideration of ECMO, 22 ultimately did not receive ECMO.**
- **Secondly, although a lung protective ventilation strategy was recommended, it was not mandated, and therefore ventilation strategies could differ between patients.**

This study must therefore **not be considered as a pure trial** comparing ECMO with traditional mechanical ventilation, but more in the context of conventional management vs. management at an ECMO-designated center

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2018 VOL. 378 NO. 21

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*

EOLIA ClinicalTrials

CONCLUSIONS:
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

This conclusion was **complicated by the large crossover** rate from the control to the ECMO group for refractory hypoxemia

EOLIA Clinical Trials

Without crossover,

- it is likely that the absolute risk reduction between the intervention and control groups would have achieved statistical significance

ECMO: THE EVIDENCE FOR ITS USE IN ARDS

TABLE 20.1 Clinical Trials of ECMO for the Treatment of ARDS.

Study	Study Design	Control	Intervention	Conclusions
ECMO in severe ARDS[30]	Prospective RCT, nonblinded	Mechanical ventilation	Mechanical ventilation plus partial VA ECMO	Mortality unchanged
CESAR trial[10]	Prospective RCT, nonblinded	Mechanical ventilation (non-standardized protocol)	Transfer to ECMO capable hospital, option for ECMO initiation	Improved survival without disability if transferred to ECMO capable facility
ELOIA[31]	Prospective RCT, nonblinded	Mechanical ventilation (standardized protocol)	Mechanical ventilation plus VV ECMO	Mortality not statistically changed
XTRAVENT[32]	Prospective RCT, nonblinded	Mechanical ventilation (6 mL/kg)	Mechanical ventilation (3 mL/kg) plus $ECCO_2$ removal	Mortality not statistically changed
PCIRV/$ECCO_2$ REMOVAL[33]	Prospective RCT, nonblinded	Mechanical ventilation	Mechanical ventilation plus $ECCO_2$ removal	Mortality not statistically changed

$ECCO_2$, extracorporeal CO_2 removal; *ECMO*, extracorporeal membrane oxygenation; *PCIRV*, pressure control inverse ratio ventilation; *RCT*, randomized controlled trial; *VA ECMO*, venoarterial extracorporeal membrane oxygenation; *VV ECMO*, venovenous extracorporeal membrane oxygenation

Great improvement of this technology primarily aiming at CO2 removal

› Anaesthesist. 2004 Sep;53(9):813-9.

Anaesthesist 2004 · 53:813–819
DOI 10.1007/s00101-004-0699-8
Online publiziert: 18. Juni 2004

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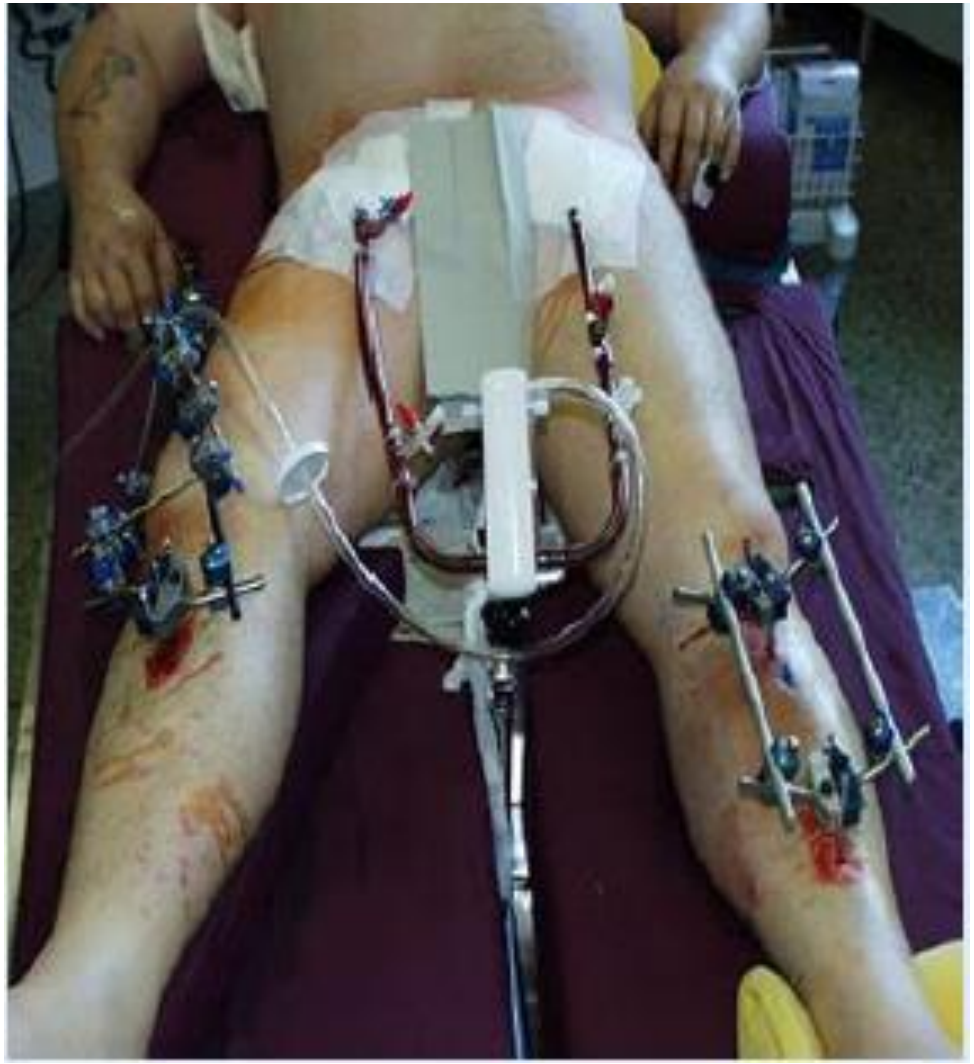
Pumpenfreie extrakorporale Lungenunterstützung mit arteriovenösem Shunt beim schweren akuten Lungen-versagen des Erwachsenen

Bericht über 30 Einsätze

Conclusion:

- pECLA represents a feasible and **effective treatment in patients with severe ARDS.**
- Compared with pump-driven systems pECLA is characterised by low costs and reduced personnel requirements.

Implanted pECLA system in one patient after multiple trauma.



- **iLA can be applied to the patient for up to 29 days.**
- **Blood flow 0.5-4.5 l/min**
- **integrated CRRT connector**
- **High degree of biocompatibility thanks to heparin coating**
- **Flow sensor attached to the membrane system**
- **The hose is connected to the O2 supply**

MANAGEMENT OF COVID-19 PATIENTS

Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization

Badulak, Jenelle[*,†]; Antonini, M. Velia[‡,§]; Stead, Christine M.[¶]; Shekerdemian, Lara[‖]; Raman, Lakshmi[#]; Paden, Matthew L.[**]; Agerstrand, Cara[††,‡‡]; Bartlett, Robert H.[§§]; Barrett, Nicholas[¶¶,‖‖]; Combes, Alain[##,***]; Lorusso, Roberto[†††]; Mueller, Thomas[‡‡‡]; Ogino, Mark T.[§§§]; Peek, Giles[¶¶¶]; Pellegrino, Vincent[‖‖‖]; Rabie, Ahmed A.[###]; Salazar, Leonardo[****]; Schmidt, Matthieu[††††,‡‡‡‡]; Shekar, Kiran[§§§§]; MacLaren, Graeme[¶¶¶¶]; Brodie, Daniel[††,‡‡]; ELSO COVID-19 Working Group Members

Author Information

ASAIO Journal: May 2021 - Volume 67 - Issue 5 - p 485-495
doi: 10.1097/MAT.0000000000001422

Conventional selection criteria for COVID-19–related ECMO should be used

- **The actual indications for ECMO depend on the patient's need and the physician's request.**
- **The choice of the technique may vary from low-flow bypass with CO2 removal to high-flow ECMO with total oxygenation support.**
- **If the aim is the treatment of life-threatening hypoxemia, the clear-cut indication is high-flow V-V ECMO.**
- **If the patient, however, presents with severe cardiac failure, V-A ECMO must be used.**

Simplified schema of possible ARDS intervention

	ARDS		
	MILD	MODERATE	SEVERE
ALTERNATIVE TREATMENTS			ECMO
		$ECCO_2$-R	
			Neuromuscular Blockade
			Prone Position
Airway Plateau Pressure	≤30 cm H_2O		
Transpulmonary Pressure	≤20 cm H_2O		
PEEP	≈10 cm H_2O		>15 cm H_2O
Tidal Volume	6 mL/kg IBW		
Strain	≤1.5–2		

BOX 42-1 Indications for ECMO in Cases of Severe ARDS[22]

Severe hypoxemia—P/F ratio < 50-80
Severe hypercarbia associated with acidemia (pH < 7.15)
Excessive end-inspiratory plateau pressure (>35-45 cm H_2O) in the presence of deep sedation and use of NMBs
Failed proning maneuver
Potentially reversible cause of respiratory failure
Absence of conditions associated with poor prognosis

Ideal candidates for ECMO are young patients with severe ARDS and no other organ dysfunction

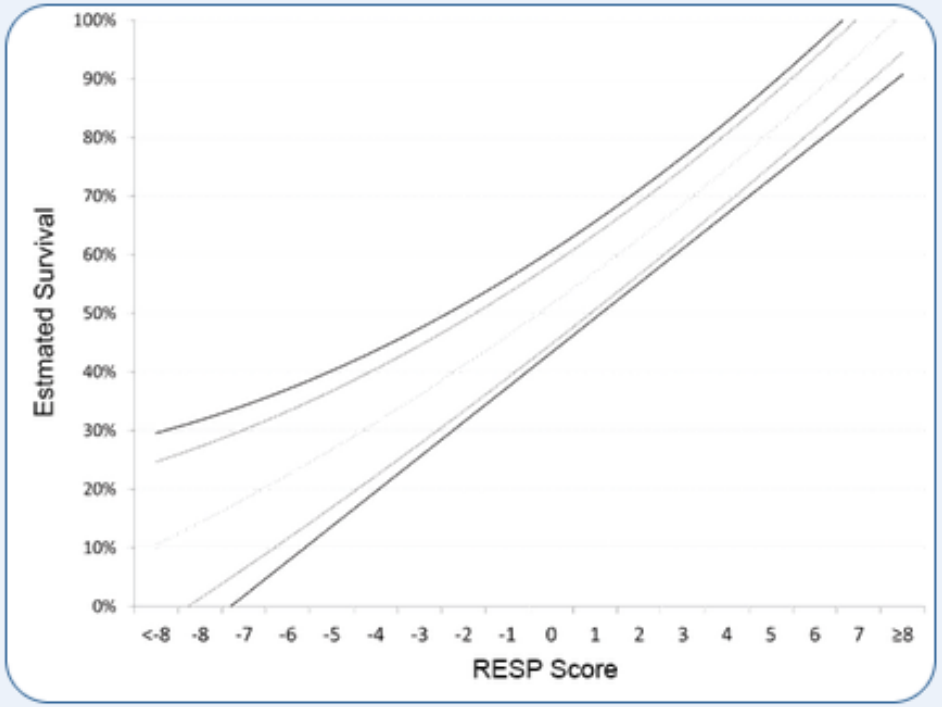
It is designed to assist prediction of survival for adult patients undergoing ECMO for respiratory failure.

www.respscore.com

The RESP Score

The RESP Score has been developed by ELSO and The Department of Intensive Care at The Alfred Hospital, Melbourne. It is designed to assist prediction of survival for adult patients undergoing Extra-Corporeal Membrane Oxygenation for respiratory failure. It should not be considered for patients who are not on ECMO or as substitute for clinical assessment.

For more information see:
Schmidt M, Bailey M, Sheldrake J, et al. Predicting Survival after ECMO for Severe Acute Respiratory Failure: the Respiratory ECMO Survival Prediction (RESP)-Score. Am J Respir Crit Care Med. 2014.



The patient's RESP Score is

0

Age (years:)
- 18-49
- 50-59
- ≥60

Immunocompromised: NO

Mechanical ventilation prior to initiation of ECMO
- <48 hours
- 48 hours - 7 days
- >7 days

Acute Respiratory diagnosis group
- Viral pneumonia
- Bacterial pneumonia
- Asthma
- Trauma/burn
- Aspiration pneumonitis
- Other acute respiratory diagnosis
- Non-respiratory and chronic respiratory diagnoses

Central nervous system dysfunction: NO

Acute associated (non-pulmonary) infection: NO

Neuro-muscular blockade before ECMO: NO

Nitric oxide use before ECMO: NO

Bicarbonate infusion before ECMO: NO

Cardiac arrest before ECMO: NO

$PaCO_2$ ≥75 mmHg / 10kpa: NO

Peak inspiratory pressure ≥42cmH_2O: NO

Ventilation on VV ECMO

- Acute Inflammatory stage:
  - Protective lung strategy
  - Common mistake - recruit lung volume during the acute inflammatory stage early in ECMO

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

CESAR

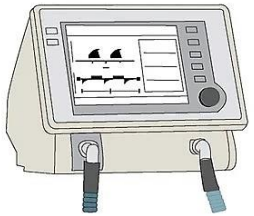
- Example of "Rest Settings":
  - Pressure control ventilation (PCV)
  - Peak inspiratory pressure (PIP) < 20 cm H_2O
  - PEEP 10 cm H_2O
  - Respiratory rate (RR) 10 breaths/minute
  - FiO_2 30%

Mechanical ventilation during ECMO
"ultra-protective lung ventilation"

- FiO2 is reduced to 0.3 (or the lowest possible).
- TV is decreased **to 2– 4 ml/ kg** of predicted body weight; many patients, however, have tidal volumes **of 1< ml/ kg** predicted body weight
- Respiratory rate < 10-15 / min (6-10)
- ΔP is reduced to < 10 cmH2O.
- PEEP can be gradually reduced to 10-15 cmH_2o.

Clinical management and daily monitoring of ECMO for ARDS.

Clinical Management

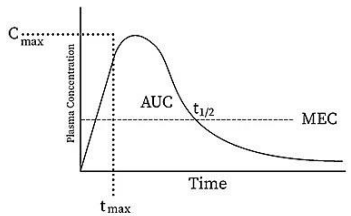


Ultra-protective ventilation

- FiO_2 : 0.3-0.5
- <u>VCV mode:</u> PEEP ≥ 10 cm H_2O; VT lowered to obtain a P_{plat} ≤ 24 cm H_2O and $\Delta P \leq 15$ cm H_2O; RR ≤ 10-20/min[a]
- <u>BIPAP / APRV:</u> P_{high} ≤ 24 cm H_2O; P_{low} ≥ 10 cm H_2O; RR ≤ 10-20/min[a]

Anticoagulation

- UFH to a target aPTT of 40 to 55 seconds or anti-Xa activity between 0.2 and 0.3 IU / mL
- Target aPTT of 60 to 75 seconds or anti-Xa activity between 0.3 and 0.5 IU/mL for COVID-19 patients



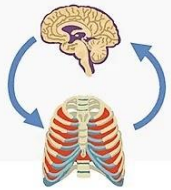
PK / PD

- Sequestration by the ECMO membrane **(Lipophilic)**
- Increased volume of distribution
- Alterations in drug clearance

Early physical rehabilitation and mobilisation

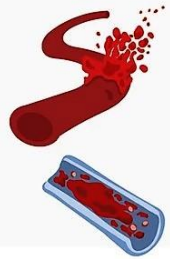
- Patient awake and cooperative (RASS -1 to +1)
- Experienced, trained staff
- Optimal staffing (2 for in-bed rehab, 4-5 for out of bed rehab)
- One staff member allocated to protecting the secured ECMO lines

Daily Monitoring



✓ Avoid rapid decrease in $PaCO_2$

✓ Monitor respiratory drive (RR, $P_{0.1}$)



✓ Fibrinogen
✓ Platelets
✓ Anticoagulation level

✓ P_{ven} , P_{art} , and ΔP on ECMO

✓ Clinical hemolysis
✓ Free hemoglobin

✓ ECMO lines secured

✓ Careful monitoring of cannula sites
✓ Sterile dressing

[a] Modified EOLIA settings with a set RR lower than in EOLIA

RESEARCH Open Access

Prone positioning in severe ARDS requiring extracorporeal membrane oxygenation

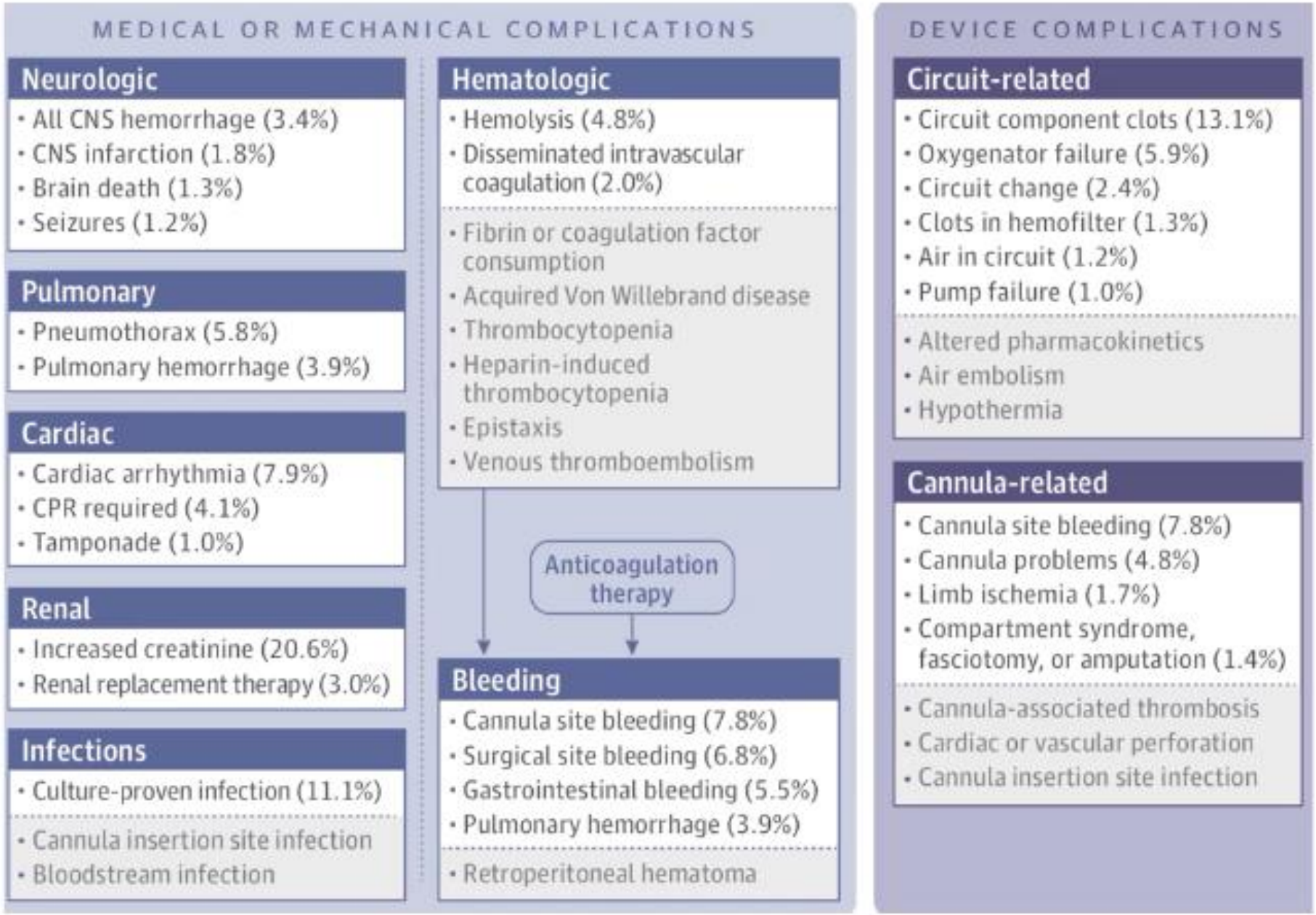
Jonathan Rilinger[1,2*], Viviane Zotzmann[1,2], Xavier Bemtgen[1,2], Carin Schumacher[1,2], Paul M. Biever[1,2], Daniel Duerschmied[1,2], Klaus Kaier[3], Peter Stachon[1,2], Constantin von zur Mühlen[1,2], Manfred Zehender[1,2], Christoph Bode[1,2], Dawid L. Staudacher[1,2] and Tobias Wengenmayer[1,2]

REVIEW

Extracorporeal life support for adults with acute respiratory distress syndrome

Alain Combes[1,2*], Matthieu Schmidt[1,2], Carol L. Hodgson[3], Eddy Fan[4,5], Niall D. Ferguson[6,7], John F. Fraser[8], Samir Jaber[9,10], Antonio Pesenti[11], Marco Ranieri[12], Kathryn Rowan[13], Kiran Shekar[14,15], Arthur S. Slutsky[16,17] and Daniel Brodie[18,19]

2 recent retrospective series of severe ARDS patients showed that prone positioning, while on-ECMO demonstrated higher ECMO-weaning and survival rates


MEDICAL OR MECHANICAL COMPLICATIONS
Neurologic
• All CNS hemorrhage (3.4%)
• CNS infarction (1.8%)
• Brain death (1.3%)
• Seizures (1.2%)
Pulmonary
• Pneumothorax (5.8%)
• Pulmonary hemorrhage (3.9%)
Cardiac
• Cardiac arrhythmia (7.9%)
• CPR required (4.1%)
• Tamponade (1.0%)
Renal
• Increased creatinine (20.6%)
• Renal replacement therapy (3.0%)
Infections
• Culture-proven infection (11.1%)
• Cannula insertion site infection
• Bloodstream infection
Hematologic
• Hemolysis (4.8%)
• Disseminated intravascular coagulation (2.0%)
• Fibrin or coagulation factor consumption
• Acquired Von Willebrand disease
• Thrombocytopenia
• Heparin-induced thrombocytopenia
• Epistaxis
• Venous thromboembolism
Anticoagulation therapy
Bleeding
• Cannula site bleeding (7.8%)
• Surgical site bleeding (6.8%)
• Gastrointestinal bleeding (5.5%)
• Pulmonary hemorrhage (3.9%)
• Retroperitoneal hematoma
DEVICE COMPLICATIONS
Circuit-related
• Circuit component clots (13.1%)
• Oxygenator failure (5.9%)
• Circuit change (2.4%)
• Clots in hemofilter (1.3%)
• Air in circuit (1.2%)
• Pump failure (1.0%)
• Altered pharmacokinetics
• Air embolism
• Hypothermia
Cannula-related
• Cannula site bleeding (7.8%)
• Cannula problems (4.8%)
• Limb ischemia (1.7%)
• Compartment syndrome, fasciotomy, or amputation (1.4%)
• Cannula-associated thrombosis
• Cardiac or vascular perforation
• Cannula insertion site infection

Future studies:

- ❑ Timing of ECMO initiation in ARDS
- ❑ Sedation requirements
- ❑ Patients' ability to ambulate
- ❑ Use of spontaneous ventilation while on ECMO to reduce diaphragmatic dysfunction
- ❑ How long patients can be managed on ECMO and still have a chance for lung recovery

RECOMMENDATIONS:

- The incorporation of low stretch ventilation, early muscle relaxants, and prone positioning should all be considered first-line therapies for ARDS (conventional care).
- It is widely believed that a cohort of patients with severe ARDS would probably die without ECMO—this was demonstrated during the H1N1 influenza epidemic of 2009-10.
- To date, a mortality benefit of utilizing ECMO has not been demonstrated in ARDS. The major RCT (ELOIA) was terminated early, with a 28% crossover (to ECMO) rate probably confounding the data.
- Any mortality benefit for ECMO is likely to be achieved in high-volume centers that have expertise in both conventional strategies and the use of ECMO.