Pulmonary Hypertension and RV Failure during Prolonged VV ECMO Support

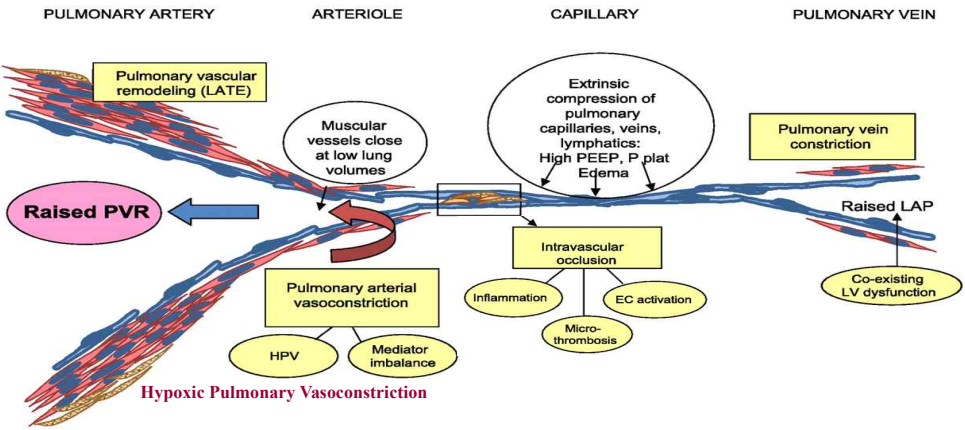
전 경 만

성균관의대 삼성서울병원 호흡기내과

SMC 삼성서울병원

Pathophysiology of Pulmonary HTN in ARDS

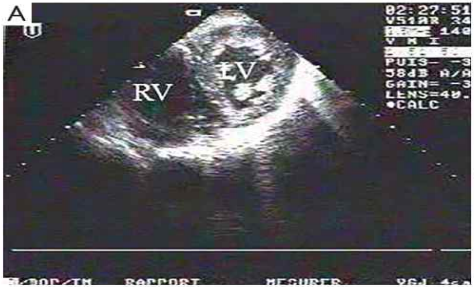
Increased Pulmonary Vascular Resistance (PVR)



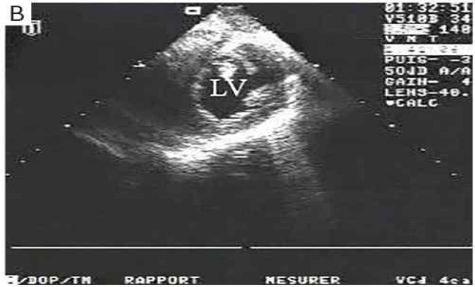
Am J Physiol Lung Cell Mol Physiol 2012;302: L803

Pathophysiology of RV Dysfunction in ARDS

Hypercapnic Increase in PVR



Pplat 22 cmH_2O
$PaCO_2$ 71 mmHg
P/F 103 mmHg



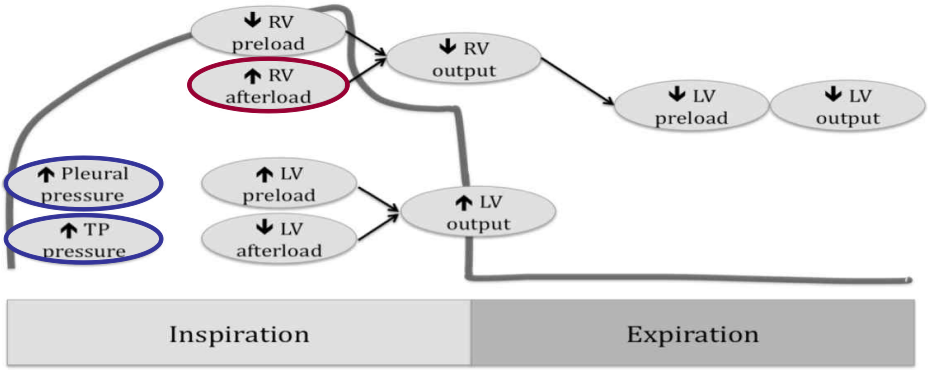
Pplat 23 cmH_2O
$PaCO_2$ 52 mmHg
P/F 88 mmHg

▶ Effect of a fast change in $PaCO_2$ (90 minutes) on the right ventricle in a patient ventilated for severe ARDS.

J Thorac Dis 2017;9:1420

Pathophysiology of RV Dysfunction in ARDS

Positive Pressure Ventilation (Driving Pressure)



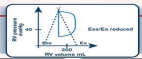
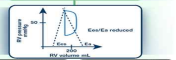
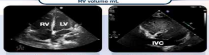
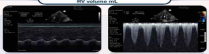
▶ Positive-pressure MV causes an increase in driving or transpulmonary pressure, which acts as a back pressure for pulmonary venous return and may increase RV afterload.

Crit Care 2000;4:282

RV Protective Ventilation

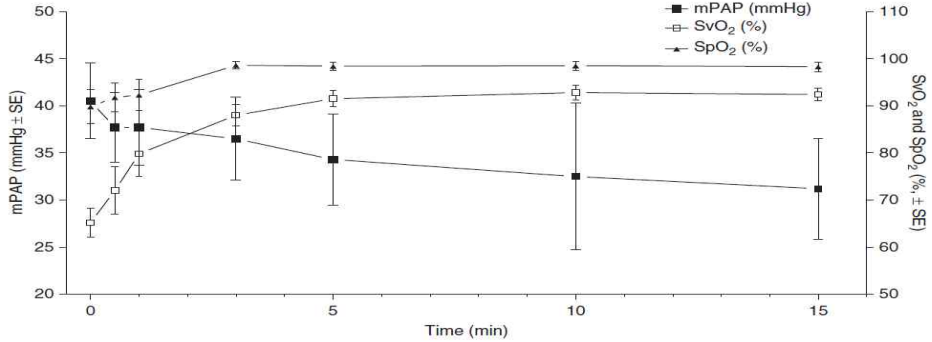
Protecting the Right Ventricle Network (PRORVnet)

RV injury in ARDS

	A: RV meets flow demand				B: RV does not meet flow demand
Major Phenotypes	NO				YES
Clinically shocked					
RV adaptation to elevated afterload	1- Isolated RV dilatation	2- RV dilatation + RV-PA uncoupled	3- RV dilatation + RV-PA uncoupled	4- RV dilatation + RV function impaired + RV-PA uncoupled	RV dilatation + RV function impaired + RV-PA uncoupled
PV Loops					
Echocardiography	 RVEDA/LVEDA ratio > 0.6 TAPSE > 17m	RVEDA/LVEDA ratio > 0.6 TAPSE > 17mm TAPSE/PASP ratio > 0.63 mm/mmHg	 RVEDA/LVEDA ratio > 0.6 TAPSE > 17mm TAPSE/PASP ratio < 0.63 mm/mmHg	RVEDA/LVEDA ratio > 0.6 TAPSE/PASP ratio < 0.63 mm/mmHg TAPSE < 17mm	 RVEDA/LVEDA ratio > 1 TAPSE/PASP ratio < 0.63 mm/mmHg TAPSE < 17mm
Echocardiography-Pulmonary artery doppler waveform	• Pulmonary artery acceleration time < 100 ms • Pulmonary acceleration time/RVET ratio < 0.29 • Mid-systolic notching of pulmonary artery doppler waveform				
Signs of systemic congestion	• CVP > 8mmHg • Dilated IVC with loss of respiratory variability (in spontaneously breathing patients) • Biphasic renal vein waveform • Pulsatile portal vein waveform • Hepatic vein S wave < D wave				• CVP > 15mmHg • Markedly dilated IVC • Monophasic renal vein waveform • Dilated hepatic veins and reversal of S wave • To- and fro- portal vein waveform
Management considerations	• Inhaled or systemic pulmonary vasodilators • Restrictive approach to fluid management • Promptly treat vasodilatory states with vasopressors (e.g. norepinephrine or vasopressin) • Avoid persistent acidemia	In addition consider: • Use of low dose inodilators: dobutamine, enoximone or milrinone • Early use of renal replacement therapy for AKI, manage fluid balance and/or acid-base abnormalities			In addition consider: • Inotropes • VV-ECMO, VAV-ECMO or VPA-ECMO with ultra-protective ventilation
Management-RV protective ventilation	• Driving pressure < 18 cmH_2O • Plateau pressure < 27 cmH_2O • Assess recruitability and PEEP optimization			• Consider prone ventilation • Avoid hypercapnia	

Intensive Care Med 2023;49:99

RV Unloading Following VV ECMO

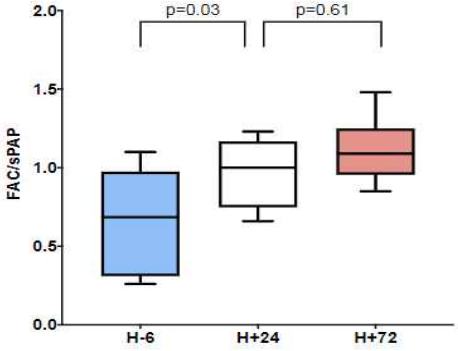


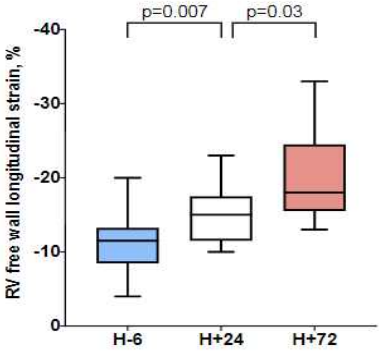
▶ Initiation of VV ECMO in respiratory failure is associated with immediate RV unloading associated with an increase in SvO_2 and a decrease in $PaCO_2$

Am J Respir Crit Care Med 2015;191:346

Reversal of RV Dysfunction with VV ECMO

COVID-19 Pneumonia





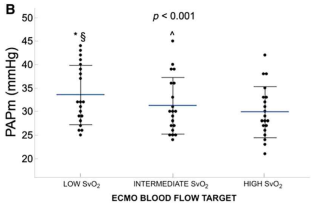
FAC/sPAP, fractional area change of right ventricle/systolic pulmonary artery pressure

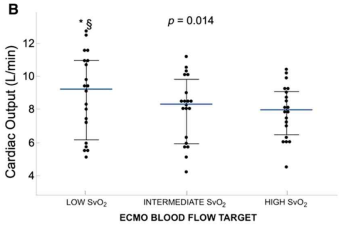
Am J Respir Crit Care Med 2023;207:78

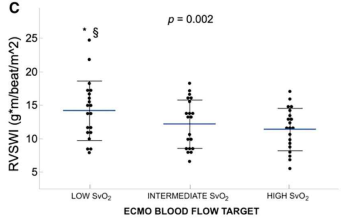
Effect of High ECMO Flow on PAP, CO, RVSWI

Direct RV Unloading

Variables	ECMO Blood Flow Target		
	Low Sv_{O_2}	Intermediate Sv_{O_2}	High Sv_{O_2}
ECMO settings			
Blood flow rate, L/min	1.51 [1.16–1.94]*†	2.44 [2.03–2.93]‡	3.43 [3.01–3.75]
Blood gases			
Sv_{O_2}, %	73.9 ± 2.8*†	79.4 ± 2.7‡	86.7 ± 3.5







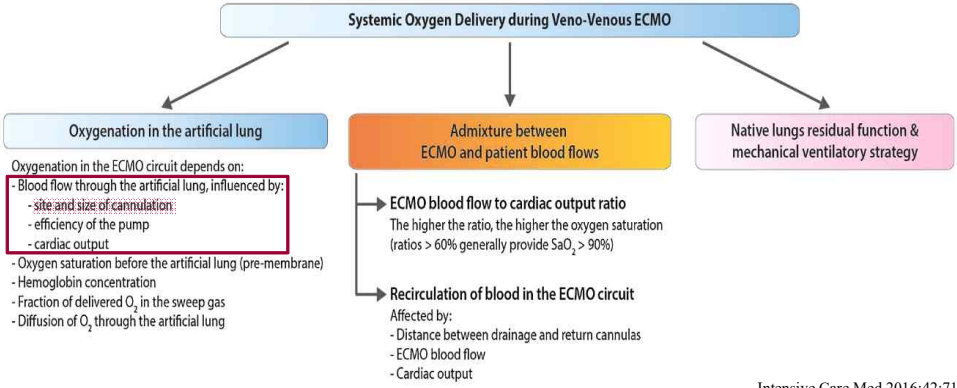
▶ Increased ECMO blood flow rate resulting in higher SvO_2 decreases pulmonary artery pressure, cardiac output, and right heart workload.

Am J Respir Crit Care Med 2024;210:629

Hypoxemia despite VV ECMO Support

Factors Contributing to Oxygen Delivery

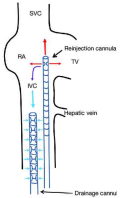
Why systemic oxygen delivery is still inadequate in this patient?

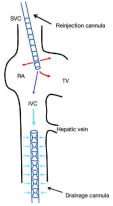


Intensive Care Med 2016;42:712

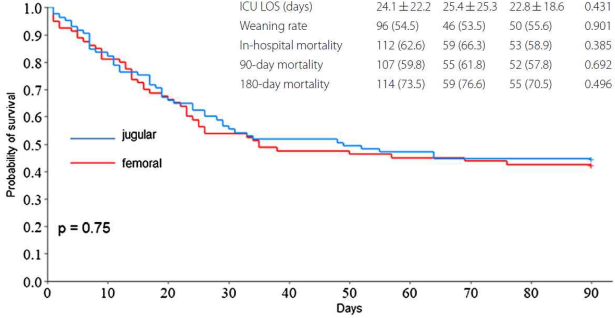
Comparison of Classic Cannulations

Vf-Vf vs.Vf-Vj



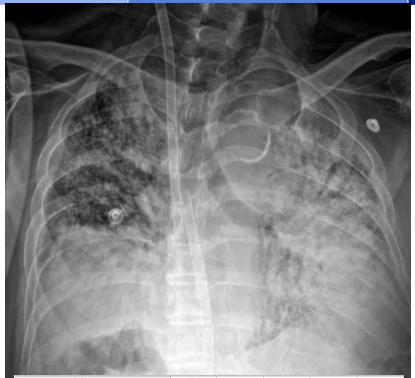


	Total ($n=180$)	Jugular ($n=90$)	Femoral ($n=90$)	P
Tracheostomy	78 (43.6)	39 (43.3)	39 (43.8)	1.0
ECMO duration (days)	16 ± 18.2	17.6 ± 21.2	14.5 ± 14.6	0.248
Interval MV–ECMO (days)	4.3 ± 7.5	4.4 ± 8.8	4.3 ± 6.1	0.879
Hospital stay (days)	56.1 ± 65.1	57.9 ± 60.9	54.3 ± 69.4	0.714
ICU LOS (days)	24.1 ± 22.2	25.4 ± 25.3	22.8 ± 18.6	0.431
Weaning rate	96 (54.5)	46 (53.5)	50 (55.6)	0.901
In-hospital mortality	112 (62.6)	59 (66.3)	53 (58.9)	0.385
90-day mortality	107 (59.8)	55 (61.8)	52 (57.8)	0.692
180-day mortality	114 (73.5)	59 (76.6)	55 (70.5)	0.496

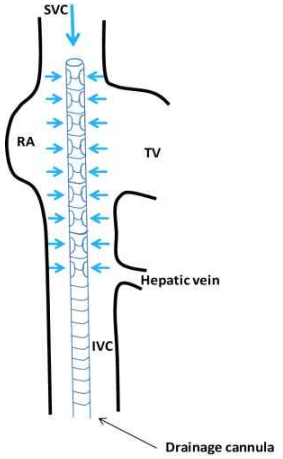


Ann Intensive Care 2020;10:86

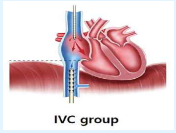
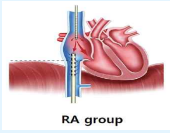
More Cephalad Position of Drainage Cannula



ECMO	Type	VV					
	Equipment	PLS					
	ECMO flow(L/min)	7	6.7	7	7.1	6.8	
	RPM(ECMO)	4,550					
	FiO2(%)	100					
	Sweep gas flow(L/min)	4					
Oxygen Therapy							
	Oxygen T... Device	Room Air					
	pO2 (mmHg)						102.7



Effect of Enhanced Venous Drainage

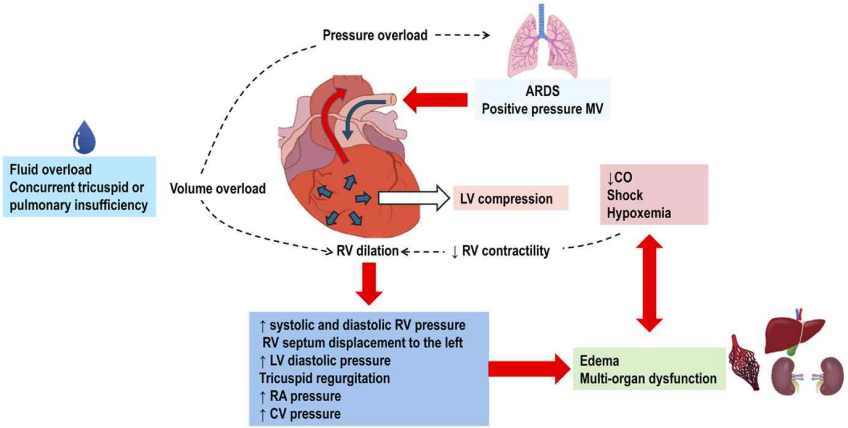
	 IVC group	 RA group	P value
ECMO flow	3.7 ± 1.0	4.0 ± 0.9	0.07
Negative fluid balance	31.4%	57.4%	0.01
Mean body weight loss	0.1 ± 3.1 kg	1.1± 2.5 kg	0.05
Awake ECMO	22.9%	42.6%	0.04

▶Patients with more cephalad cannula placement were more tolerant of volume removal and more likely to achieve net negative volume status, and were more frequently able to wean to minimal sedation, allowing for a larger proportion of awake ECMO.

Ann Thorac Surg 2023;115:1016

Iatrogenic Drivers of RV Dysfunction on Prolonged ECMO

Volume Overload



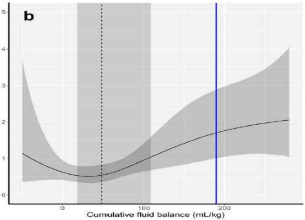
Front Physiol. 2024;15:1478514

Cumulative Fluid Balance during ECMO

Multicenter Cohort, Korea

Table 5 Cox regression analyses for 90-day mortality with cumulative fluid balance, cumulative input, and output

Models	Variables	Non-cardiovascular disease	
		HR (95% CI)	*P* value
Model 1	CFB*	1.46 (1.17–1.83)	< 0.001
Model 2	CFB*	1.55 (1.16–2.09)	0.003
Model 3	Cumulative input*,†	5.53 (2.60–11.75)	< 0.001
	Cumulative total output*,†	0.25 (0.14–0.45)	< 0.001
Model 4	Cumulative input*,†	1.92 (1.08–3.42)	0.027
	Cumulative urine output*,†	0.84 (0.75–0.93)	0.001



CFB Cumulative fluid balance

Model 1: Additionally adjusted for age, sex, Charlson comorbidity index, Acute Physiology and Chronic Health Evaluation II score, and propensity score

Model 2: Model 1 + daily fluid balance before ECMO*,¶

Model 3: Model 2 + cumulative input + cumulative total output without CFB

Model 4: Model 2 + cumulative input + cumulative urine output without CFB

*Data were log-transformed

†During 3 days from extracorporeal membrane oxygenation (ECMO) commencement

¶Daily fluid balance during intensive care unit admission before ECMO commencement

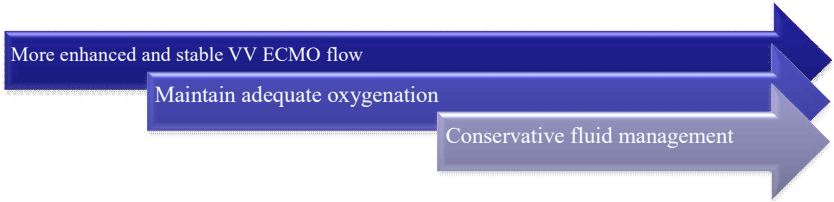
Propensity score was obtained by logistic regression analysis with covariables body mass index, ECMO pump time, ECMO blood flow rate, albumin, total carbon dioxide, acute kidney injury stage

The 27 (3.7%) patients who were lost to follow-up were treated as censored

Crit Care 2018;22:270

RV Protective Strategy for Prolonged VV ECMO

Enhanced and Stable VV ECMO Flow



Appropriate positioning of drainage cannula to maximize venous drain

Adjustment of VV ECMO flow based on the oxygenation

Reduced unnecessary volu me replacement to increase ECMO flow

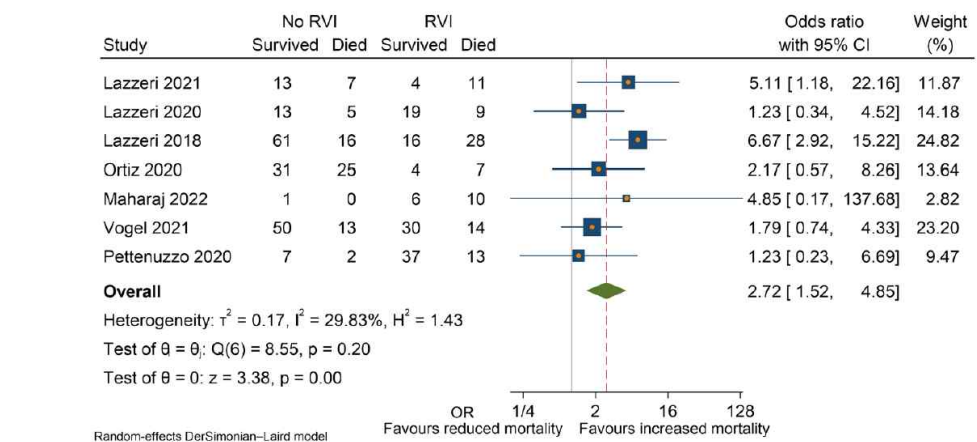
Enhanced negative fluid balance to reduce the risk of RV dilatation

Suggested Medical Management

Suggestion	Rationale	Limitations
Negative fluid balance	Reduces RV preload, septal shift, venous con gestion	Risk of hypovolemia and underfilling
Inhaled pulmonary vasodilators (iNO)	Decrease PVR without systemic hypotension	~30% responder rate
Inotropic support: dobutamine, milrinone, or epinephrine for RV contractility	Maintains coupling and forward flow	Arrhythmia; tachycardia worsens RV filling
Vasopressor support: norepinephrine or va sopressin to maintain MAP	Preserves RV coronary perfusion	Excessive vasoconstriction raises PVR
Anticoagulation	Prevents circuit and pulmonary thrombosis	Bleeding risk

RV Injury and Mortality of ARDS on VV ECMO

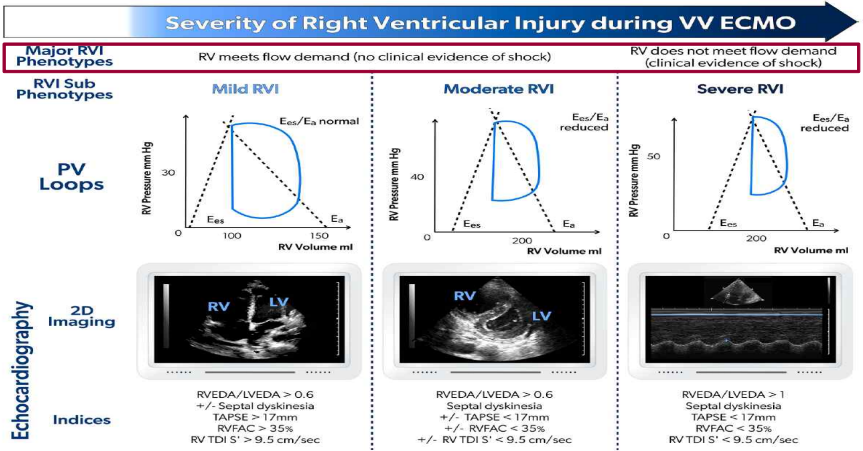
Systematic Review



Protecting the Right Ventricle network (PRORVnet), ASAIO J 2023;69:e14

Consensus Definition of RV Injury during VV ECMO

Protecting the Right Ventricle Network (PRORVnet), 2024



Intensive Care Med 2024; 50:1411

RV Injury Sub Phenotypes

Dynamic Spectrum (Dilatation ▶ Dysfunction ▶ Failure)

Mild RV injury

Isolated RV dilatation without systemic venous congestion

- ↑ RV size, RV/LV area ratio
- Early afterload mismatch, may progress

Moderate RV injury

RV dilatation and abnormal markers of RV function (RV dysfunction) while the RV flow output remains sufficient for tissue needs

- Reduced TAPSE/FAC/TDI S′/strain
- Hemodynamically significant, treatable stage

Severe RV injury

RV fails (RV failure) to maintain sufficient flow output and resultant systemic venous congestion with shock

- Low output, venous congestion, organ injury
- Associated with prolonged ECMO, ↑ mortality

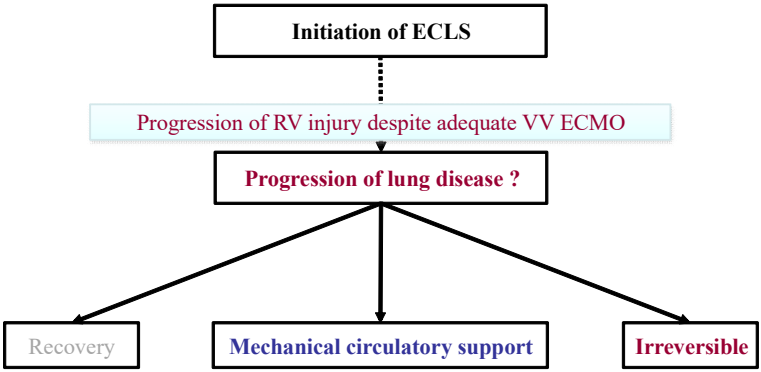
Diagnosis and Monitoring of RV Injury during VV ECMO

Syndrome-based Multimodal Assessment

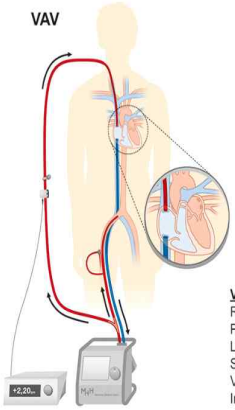
Clinical / laboratory	Echocardiography	Invasive hemodynamics (selected)	Organ function
• ↑ vasopressor, tachycardia, oliguria, lactate rise, edema or congestion, low flow tolerance	• RV size, RV/LV ratio, septal shift, TR, TAPSE, FAC, TDI S′, RV strain	• mPAP, PAOP, CI, SvO_2 in severe PH, shock, transplant candidates	• Renal and hepatic function, bilirubin, lactate trends

▶ Serial, multimodal assessment is essential; trends outweigh single measurements

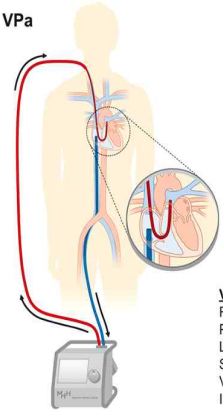
RV dysfunction during Prolonged VV ECMO



RV Unloading or Bypass for RV Failure



VAV cannulation
RaP may decrease
PaPmean may decrease
LVEDP may decrease or increase
SBP increases
Vasopressor dose decreases
Inotrope dose decreases

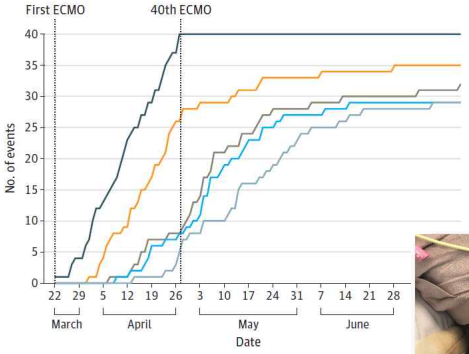


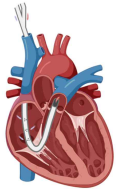
VPa cannulation
RaP decreases
PaPmean increases
LVEDP may increase
SBP may increase
Vasopressor dose may decrease
Inotrope dose may decrease

Napp LC, Bauersachs J. Triple Cannulation ECMO [Internet]. Extracorporeal Membrane Oxygenation: Advances in Therapy. InTech; 2016. Available from: http://dx.doi.org/10.5772/63392

V-PA ECMO for COVID-19 ARDS

Illinois, US (n = 40)

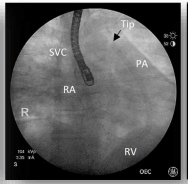




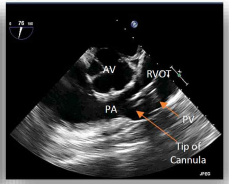
15% of mortality

- Single-access, dual-stage cannula to PA
- Early mobility

Cannula Insertion



Fluoroscopy



Trans-Esophageal Echocardiography

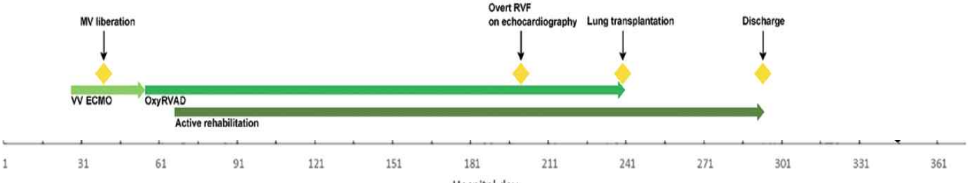
JAMA Surg 2020;155:990

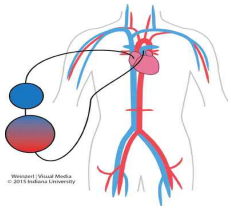
Veno-Pulmonary Cannulation

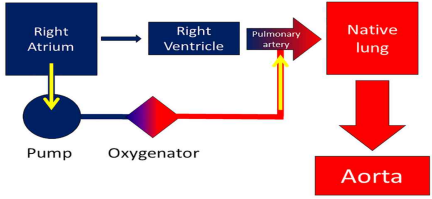
- Benefit
  - Eliminating recirculation
  - Mechanical support to RV
  - Facilitate rehabilitation in awake patients
- Pitfalls
  - Insertion with echocardiography or fluoroscopy
  - Risk of pulmonary edema in patients with LV failure
  - Risk of pulmonary hemorrhage

Prolonged VPA ECMO (OxyRVAD)

SMC Experience (213 days)







ASAIO J 2016;62:e37

ASAIO J 2021;67:e127

RV Injury during Prolonged VV ECMO

Summary

- RV injury during VV ECMO is common and should be considered as dynamic spectrum (dilatation ▸ dysfunction ▸ failure)
  - Mechanisms are multifactorial; management must be physiology-based & integrated
  - Serial multimodal assessment and trends are crucial for early recognition and staging

- RV protective strategies
  - Efforts to provide adequate support with VV ECMO
    - More enhanced and stable VV ECMO flow by adequate cannulation
  - Efforts to avoid complications
    - Restrictive fluid management
    - Adequate medical management
    - Preventive measure to reduce additional lung injury: awakening, tracheostomy with subglottic drainage
- In refractory RV failure, timely escalation to VVA or oxygenated RVAD (veno-pulmonary ECMO) may be life-saving, particularly transplant candidates