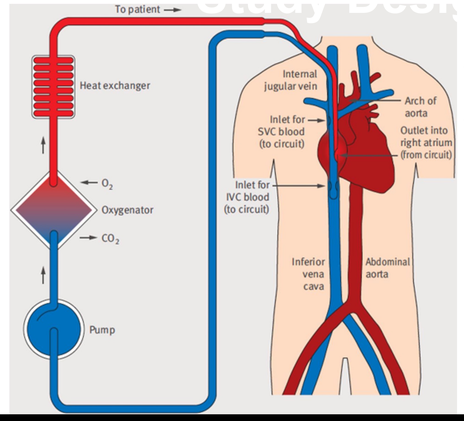
Extracorporeal Membrane Oxygenation (ECMO) for Severe Asthma Exacerbations Requiring Mechanical Ventilation

Jonathan K. Zakrajsek [1,2], Sung-Joon Min[3], Richard R. Allen[4] , P. Michael Ho [2,5] ,Arun Kannappan[1], Tyree H. Kiser[2,6], Meghan D. Althoff[1,2], Peter D. Sottile[1,2], Paul M. Reynolds [2,6], Ellen L. Burnham[1,2], Marc Moss[1,2], Marc Mikkelson[1], and R. William Vandivier [1,2] [1]Division of Pulmonary Sciences and Critical Care Medicine. Department of Medicine. University of Colorado Anschutz Medical Campus. Aurora, Colorado; [2]Colorado Pulmonary Outcomes Research Group (CPOR), University of Colorado Anschutz Medical Campus, Aurora, CO; [3]Division of Health Care Policy and Research, University of Colorado Anschutz Medical Campus, Aurora, Colorado; [4]Peak Statistical Services. Evergreen, Colorado; [5]Division of Cardiology. Department of Medicine. University of Colorado Anschutz Medical Campus. Aurora, Colorado; [6]Department of Clinical Pharmacy. University of Colorado Anschutz Medical Campus. Aurora, Colorado.

Introduction:

Asthma patients placed on a ventilator have a mortality of 7-15%. The tragedy is that the underlying pathophysiology of asthma exacerbations is reversible if given enough time. Standard therapies for asthma include systemic corticosteroids and short-acting bronchodilators. Standard therapies work but they take time, which some patients don't have. Severely ill patients can develop respiratory failure with high blood CO_2 and decreased blood pH requiring mechanical ventilation. These patients often have high lung pressures, which increases the risk for ventilator-induced lung injury. For these severe patients salvage therapies like permissive hypercapnia and inhaled anesthetics can be used but sometimes they don't work quickly enough. Extracorporeal membrane oxygenation (ECMO) is now being used to bridge the most severely ill asthma patients until standard therapies start take effect. The knowledge of ECMO in asthma is limited to case reports, case series, and registry studies that lack critical controls. To date, no randomized controlled trials or observational cohort studies have been performed.

ECMO Circuit



Venovenous (vv) ECMO

Venoarterial (va) ECMO

Hypothesis:

ECMO is associated with reduced mortality in severe asthma exacerbations treated with standard therapies and mechanical ventilation.

Study Design:

- Retrospective Epidemiologic Cohort Study
- Premier Database from 2010-2020

Primary Outcome: Hospital mortality

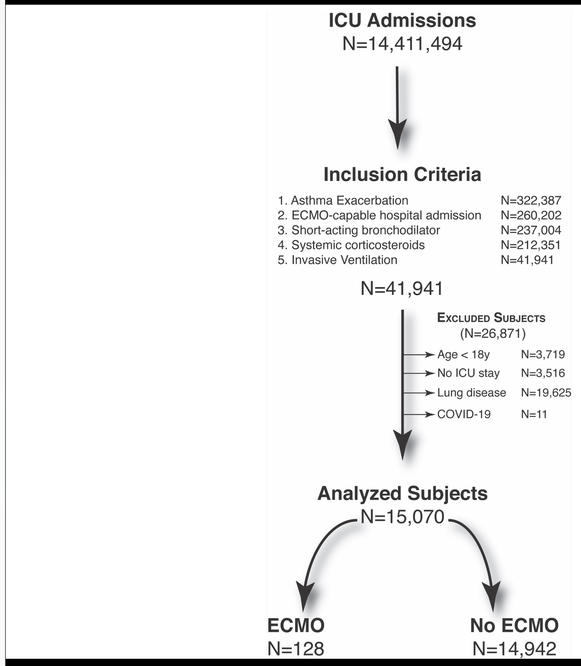
Key Secondary Outcomes:
- ICU length of stay (LOS)
- Hospital LOS
- Length of mechanical ventilation
- Total hospital cost

Safety Outcomes:
- Hemorrhage
- Infection
- Neurologic or cardiac complications
- Pneumothorax

Data Analysis:

- Covariate adjusted analysis of 128 ECMO vs 14,943 NO ECMO subjects (total cohort)
- Propensity score adjusted analysis of the total cohort
- Propensity score matched analysis of 1 ECMO to 2 No ECMO patients (93 vs 186)

Flow Diagram:



Results:

Characteristics	ECMO N (%)	No ECMO N (%)	P-value	Standardized Mean Diff
N	128	14,943		
Age, y	37.9 (13.3)	45.4 (17.2)	< 0.0001	-0.490
Female	70 (54.7)	9,677 (64.8)	0.02	-0.207
White	59 (46.1)	7,349 (49.2)	0.34	-0.062
Hospital Transfer			0.002	
• Transfer from Acute Care Hospital	51 (39.8)	1,824 (12.2)	< 0.0001	0.663
Critical Illness-Related Diagnosis				
• Shock (Non-Septic)	15 (11.7)	559 (3.7)	< 0.0001	0.302
• Acute Kidney Failure	32 (25.0)	2,453 (16.4)	0.01	0.213

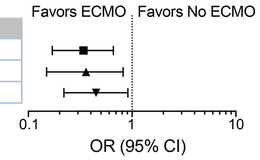
Characteristics	ECMO N (%)	No ECMO N (%)	P-value	Standardized Mean Diff
N	128	14,943		
Hospital Beds			<0.0001	
> 500	90 (70.3)	6,354 (42.5)		0.584
Teaching Status			<0.0001	
• Teaching	107 (83.6)	8,172 (54.7)		0.659
Attending Physician			0.002	
• Hospitalist	57 (44.5)	9,693 (64.9)		-0.417
• Pulmonologist	21 (16.4)	1,439 (9.6)		0.202
• Surgery	11 (8.6)	35 (0.2)		0.416
• Intensivist	12 (9.4)	912 (6.1)		0.123

Results:

Characteristics	ECMO N (%)	No ECMO N (%)	P-value	Standardized Mean Diff
N	128	14,943		
ECMO				
• vvECMO	106 (82.8)			
• vaECMO	8 (6.3)			
• vvECMO & vaECMO	14 (10.9)			
Therapies				
• Antibiotics	122 (95.3)	12,139 (81.2)	0.0002	0.448
• Continuous Neuromuscular Blockade	77 (60.2)	1,545 (10.3)	<0.0001	1.221
• IV Magnesium Sulfate	96 (75.0)	8,845 (59.2)	0.0004	0.341
• Ketamine	72 (56.3)	2,783 (18.6)	<0.0001	0.844
• IV Bicarbonate	76 (59.4)	2,590 (17.3)	<0.0001	0.959
• Heliox	10 (7.8)	450 (3.0)	<0.0001	0.213
• Inhaled Anesthetics	6 (4.7)	174 (1.2)	0.0008	0.210
• Vasopressors	108 (84.4)	5,228 (35.0)	<0.0001	1.165
• Renal Replacement Therapy	30 (23.5)	725 (4.9)	<0.0001	0.553

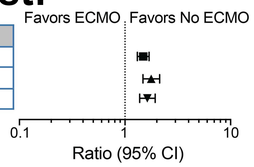
Mortality:

	OR (95% CI)	p-value
Covariate adjusted (Full Cohort)	0.34 (0.17-0.66)	<0.01
Propensity score adjusted (Full Cohort)	0.36 (0.15-0.82)	0.02
Propensity score matched (1:2)	0.45 (0.22-0.91)	0.03



Total Hospital Cost:

	Ratio (95% CI)	p-value
Covariate adjusted (Full Cohort)	1.49 (1.31-1.69)	<0.0001
Propensity score adjusted (Full Cohort)	1.77 (1.48-2.13)	<0.0001
Propensity score matched (1:2)	1.63 (1.38-1.93)	<0.0001



Adverse Effects:

	ECMO (N=93)	No ECMO (N=186)	p-Value	Standardized Mean Difference
	No. (%)	No. (%)		
Hemorrhage	10 (10.8)	2 (1.1)	0.002	0.419
Brain Death	0 (0.0)	8 (4.3)	0.99	0.300
Cardiac Arrest/Arrhythmia	17 (18.3)	31 (16.7)	0.74	0.043
Infection of Catheter/Surgical Site	1 (1.1)	0 (0)	--	0.147
Pneumothorax	4 (4.3)	7 (3.8)	0.83	0.027

Limitations:

- The Premier database does not contain blood gas results, ventilator settings or ventilator pressures
- Small number of ECMO patients
- Confounding by indication is always possible
- Selection bias is always possible

Conclusions:

ECMO was associated with lower mortality, higher costs, increased hemorrhage and decreased brain death, suggesting that select asthma exacerbation patients may benefit from ECMO.

Funding: K. Louise Coulter Pulmonary Research and Health Sciences Fellowship Award