

Rescue Therapies for Intractable Hypoxemia: Do These Make a Difference?

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DISCLOSURE

The content of this presentation does not relate to any product of a commercial entity; therefore, I have no relationships to report.

Objectives

Briefly provide overview of potential rescue therapies for refractory hypoxemia

Describe the use of ECMO in pediatric lung failure

Briefly describe High Frequency Percussive Ventilation and it's use at one institution

Refractory Hypoxemia in ARDS

- The use of rescue therapies has increased in efforts to limit toxicology of ventilation
 - Risk versus benefits
- Initiated when evidence of tissue related hypoxic injury due to hypoxemia, hypo-perfusion, and cellular dysfunction
 - SpO₂ > 88%; PaO₂ > 60 mmHg
 - How low is too low?



Rescue Therapies

Therapy	Benefit	Mortality Effect
Nitric Oxide ¹	↑Oxygenation	N/S adult, peds
Prone Positioning ²	No increase in complications	↓ Adults (28 and 90 day)
HFOV ³	Adult study terminated early	↑ Adults
Steroids	Early ARDS: ↓Vent days; ↑Oxygenation Late ARDS-none	N/S
Surfactant ⁴	No difference in oxygenation, vent days	N/S peds
ECMO	To be discussed	???? Peds

1. Adhikari et al. *CCM*. 2014; 42:404. (meta-analysis)
2. Guerin et al, *NEJM*. 2013; 368: 2159 (PROSEVA multicenter)
3. Ferguson et al. *NEJM*. 2013; 368:795 (OSCILLATE multicenter)
4. Wilson et al. *PCCM*. 2013; 14:657. (PALISI multicenter)

Recent Recommendations

- Consensus Recommendations from the Pediatric Acute Lung Injury Consensus Conference-PCCM 2015
- 27 experts over 2 years
 - taxonomy to define pediatric acute respiratory distress syndrome (PARDS)
 - make recommendations regarding treatment and research priorities.
 - Use of data and a modified Delphi approach

Consensus Recommendations

- OI > P/F: strong agreement
 - Use of P/F for NIPPV
 - Use of OSI or SpO₂/FIO₂ if needed
- iNO-consider in pulmonary hypertension or RV dysfunction: strong agreement
 - ? Rescue or bridge to ECMO
- Surfactant: not recommended
- Liquid Ventilation: not recommended



Consensus Recommendations

- Prone Positioning-consider in severe PARDS: weak agreement
- Strong Agreement on no recommendation for other adjunct therapies such as helium, prostaglandins, TNF, NAC, etc.

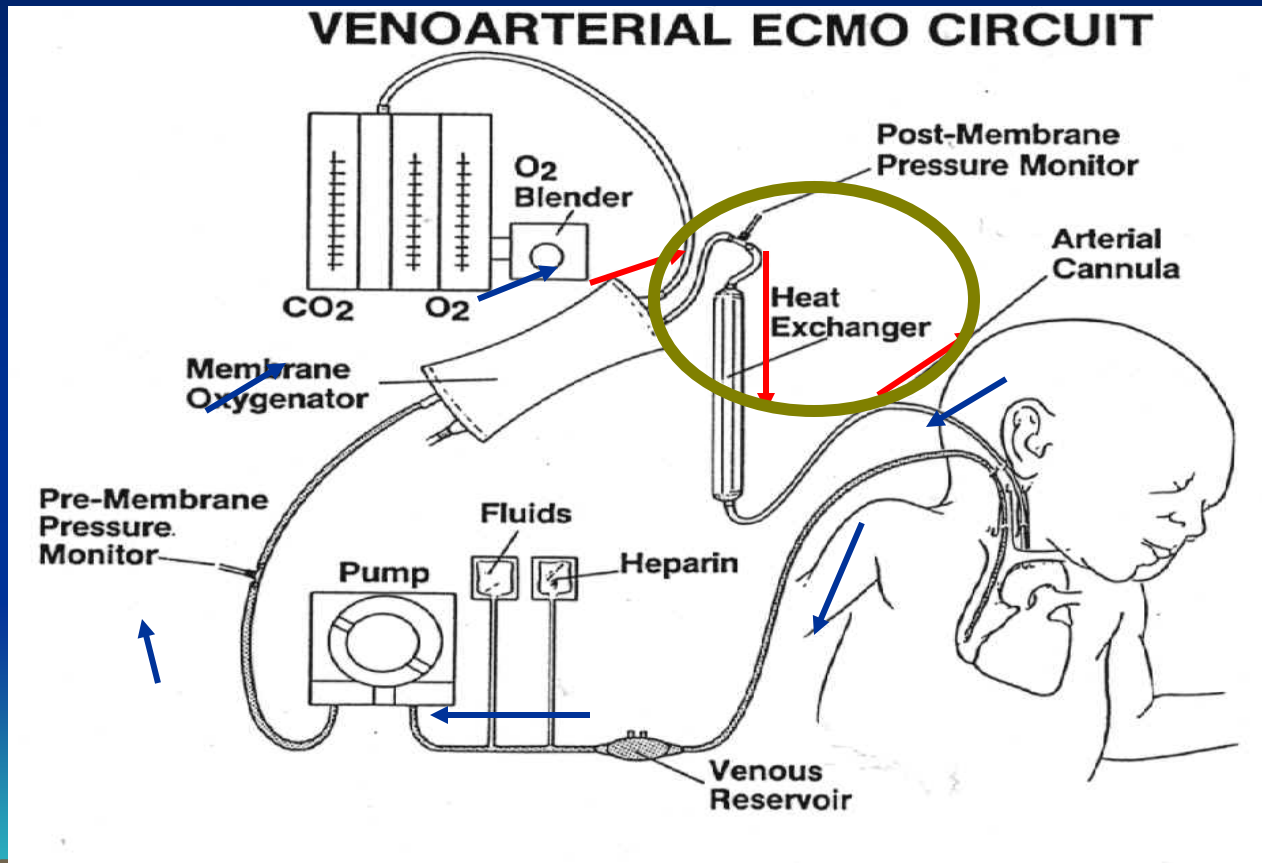


Consensus Recommendations

- ECMO-use in severe PARDS if cause is reversible and patient suitable candidate: strong agreement
 - Decisions should be based on structured evaluation, serial evaluation, and quality of life assessments
 - ECMO centers should have clear leadership, support, and participate in registries



Extracorporeal Membrane Oxygenation (ECMO)



Pediatric ECMO Indications- Respiratory

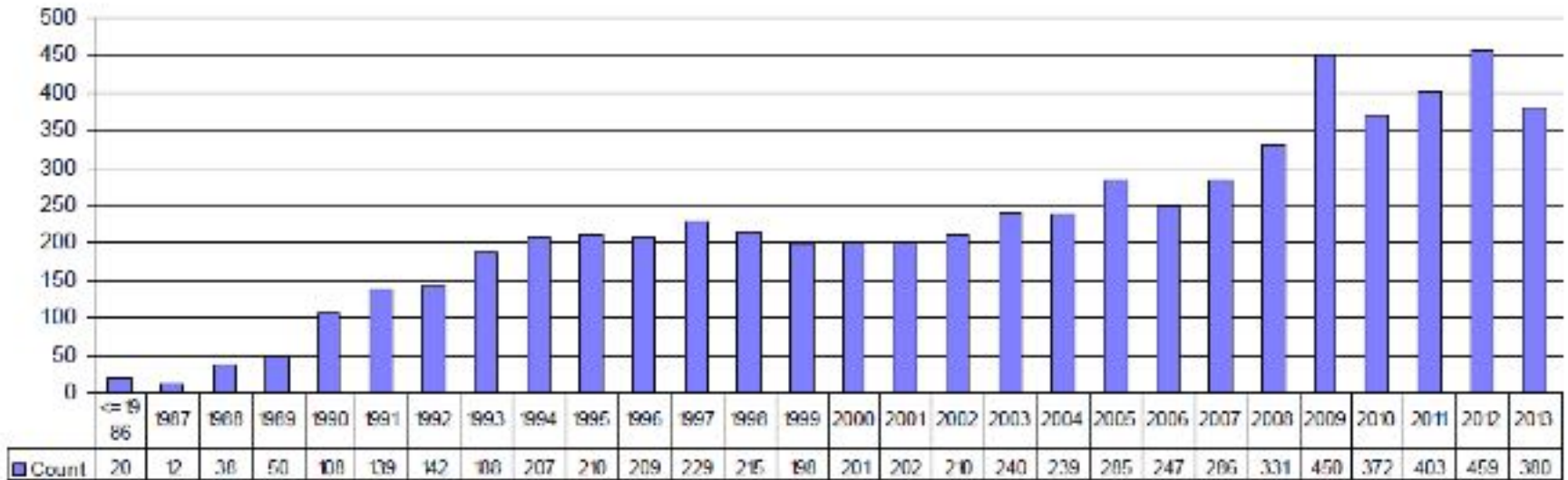
- Reversible disease
- No CNS bleeding
- Acceptable baseline function
- No severe immune disorders (BMT, poor prognosis CA)
- Failure of conventional respiratory support (OI>40)

$$OI = \frac{MAP(\text{FiO}_2) 100}{PaO_2}$$

- Intractable air leak

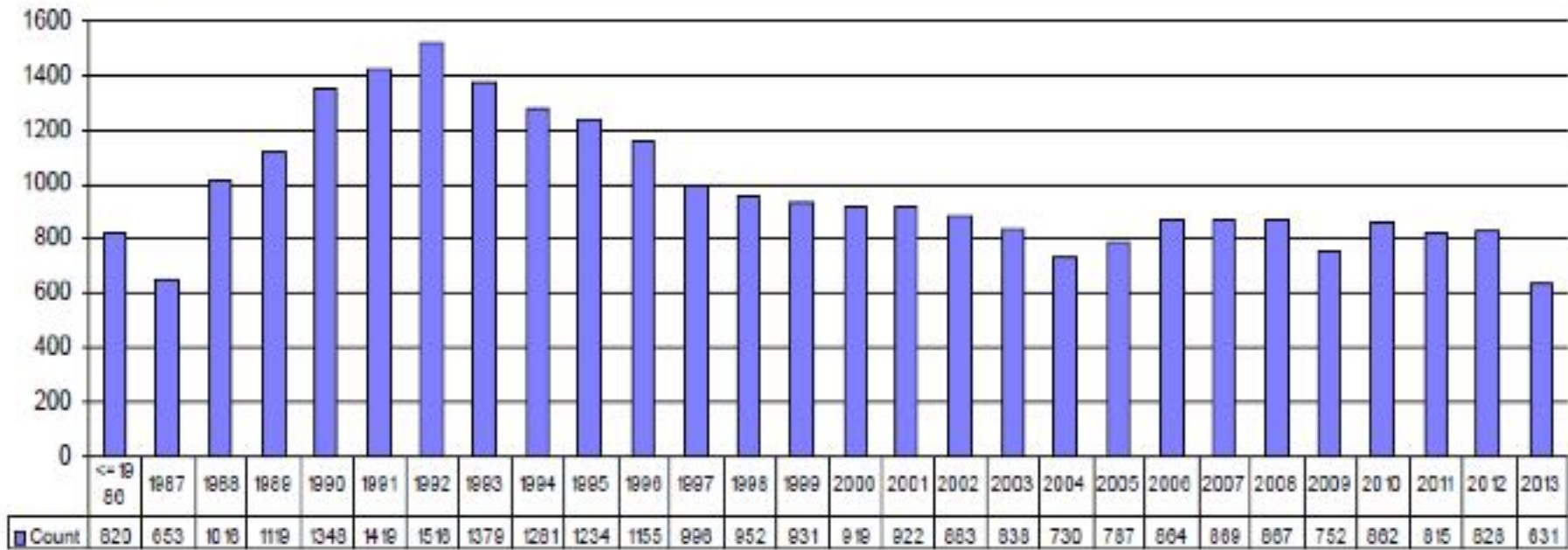
ELSO 2013

Annual Respiratory Pediatric Runs



ELSO 2013

Annual Respiratory Neonatal Runs



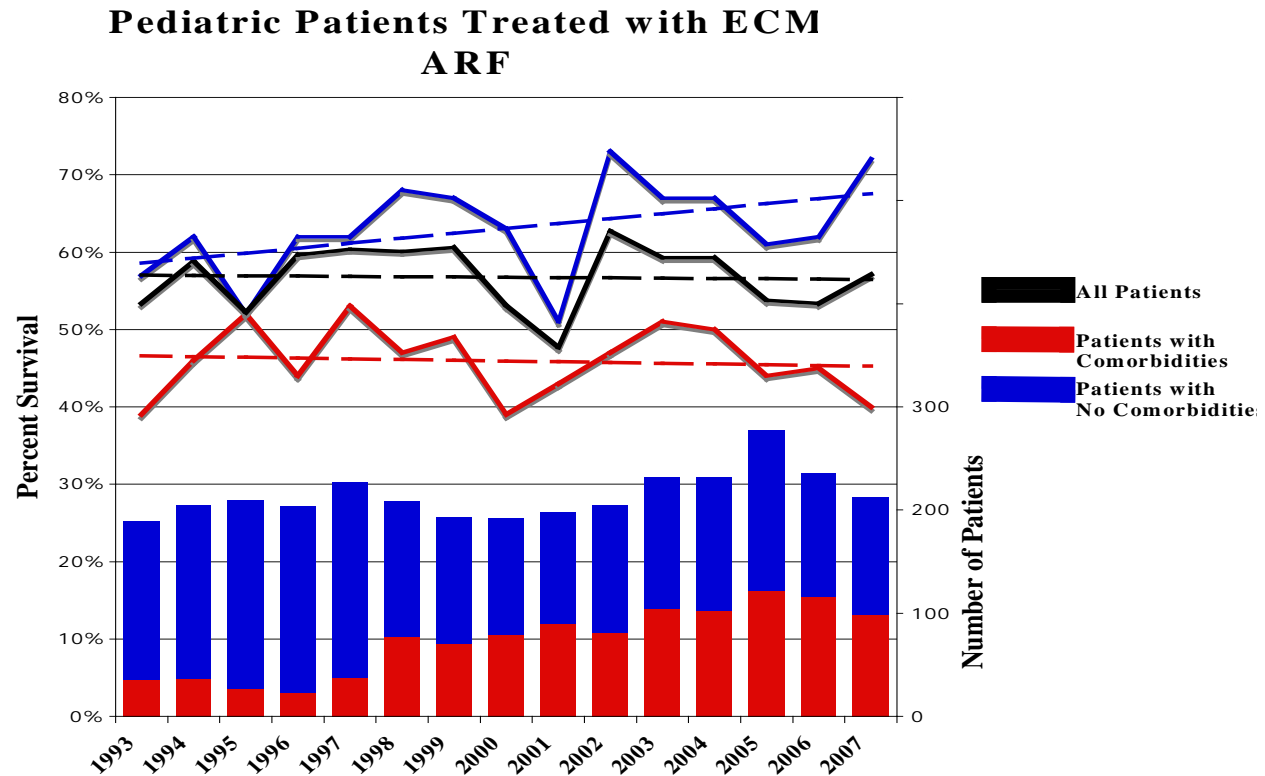
Survival-Pediatric Respiratory ECMO

- 57% over past 15 years
- 61% in 2013 among 282 cases
- Little variation
- Increased co-morbid conditions

Zabrocki, CCM 2011



Survival and Co-morbid Conditions



Survival-Pediatric Respiratory ECMO

PRIMARY DIAGNOSIS	N	SURVIVAL
ARF, Non-ARDS	607	49%
RSV Pneumonia	496	70%
Bacterial PNA	476	57%
Other Viral PNA	378	56%
Other	285	51%
ARDS, Sepsis	235	40%
Aspiration PNA	225	71%
ARDS, Trauma/Post-op	159	59%
Pertussis	85	39%
Status Asthmaticus	71	83%
Pulmonary Hemorrhage	51	69%
Influenza	47	57%
Submersion Injury	43	65%
Pneumocystis PNA	25	48%
ARDS, Other Cause	17	47%
Fungal Pneumonia	13	23%
Total	3213	57%

Survival-Pediatric Respiratory ECMO

COMORBID CONDITIONS	N	SURVIVAL
Acute or Chronic Renal Failure	329	33%
Chronic Lung Disease / BPD	296	59%
CHD- Two Ventricle	195	52%
Cardiac Arrest	88	38%
Cancer	84	30%
CHD- Single Ventricle	75	60%
Transplant – Non BMT	70	39%
Cardiomyopathy / Myocarditis	61	43%
Primary Immunodeficiency	59	34%
Liver Failure	51	16%
Bone Marrow Transplant	22	5%
Any Comorbid Condition	1104	46%
No Comorbid Condition	2109	63%

Death from Pediatric Respiratory Failure

- Sepsis 1.53 (1.11-2.11)
- Aspiration 0.59 (0.42-0.83)
- Asthma 0.37 (0.12-0.87)
- Submersion 0.50 (0.23-1.1)
- ARDS 1 reference group
 - Bacterial pneumonia, ARDS trauma, influenza, other viral pneumonia
- Liver failure 4.33 (1.95-9.62)
- Renal failure 2.2 (1.68-2.89)
- Cancer 2.56 (1.55-2.43)
- Ventilation > 2 weeks 2.55 (1.9-3.42)

Complications

- CNS infarct 7.4% neonate / 4% pediatric
- CNS bleed 7% neonate / 6% pediatric
- Seizures 9.4% neonate / 5.9% pediatric
- Infection 6% neonate / 18% pediatric
- Mechanical 15% (decreasing)

Rehder, PCCM 2013



Bleeding

- ELSO registry (2002-2013) by Werho PCCM 2015
 - 39% had hemorrhagic complication (49% cardiac vs 32% other)
- ELSO Registry (2005-2011) by Dalton PCCM 2015
 - Bleeding in 38%; Thrombosis in 31% excluding CDH
 - Bleeding decreased survival by 40% (RR 0.59 (CI 0.53-0.66))
 - Thrombosis decreased survival by 33% (RR 0.67 (CI 0.67-0.74))
 - Risk factors: longer ECMO run, VA cannulation
 - ICH 11%

Long Term Survival

Great Ormond Street, UK (1992-2010)

TABLE 1. Early Mortality Proportions, Late Mortality Proportions, Estimated Overall 5-Yr Survival Rates, and Estimated 5-Yr Survival Rates in Patients Alive at 90 D Post-Extracorporeal Life Support by Diagnosis

Diagnosis (n)	Early Survival to 90 d (%)	Late Mortality > 90 d (%)	Estimated 5-Yr Survival Overall (95% CI)	Estimated 5-Yr Survival in Patients Alive at 90 d (95% CI)
Meconium aspiration syndrome (122)	110 (90.2)	2 (1.6)	88.0% (80.6–92.7)	97.9% (92.0–99.5)
Congenital diaphragmatic hernia (49)	28 (57.3)	7 (14.3)	42.1% (28.0–55.5)	73.6% (52.3–86.5)
Neonatal other (120)	71 (59.2)	7 (5.8)	53.4% (43.9–61.9)	90.1% (80.3–95.7)
Pediatric other (38)	24 (63.2)	2 (5.3)	55.6% (37.4–70.4)	88.6% (60.6–97.1)
Pediatric viral (68)	48 (70.6)	5 (7.4)	67.0% (54.4–76.9)	95.4% (82.9–98.8)
Pediatric bacterial (54)	34 (63)	1 (1.9)	61.1% (46.8–72.6)	97.0% (80.4–99.6)
Congenital heart disease (169)	70 (41.4)	11 (6.5)	32.3% (25.1–39.8)	79.9% (66.5–88.4)
Acquired heart disease (121)	84 (69.4)	11 (9.1)	59.1% (49.0–67.9)	85.2% (73.0–92.2)

Iguchi, PCCM 2013

Cost-Effectiveness of Neonatal Extracorporeal Membrane Oxygenation

- 7-Year Results From the United Kingdom Collaborative ECMO Trial
 - Neonatal ECMO reduced death & severe disability
 - Mean health service costs during the first 7 years of life were 3x greater than conventional treatment
 - The incremental cost per life year gained was estimated at £13,385
 - The incremental cost per disability-free life year gained was estimated at £23,566

Petrou Peds 2006



Summary

- Data strongly suggests a role for ECMO in pediatric respiratory failure
- Growing use in pediatric respiratory failure especially in those with co-morbid conditions
- Studies addressing risk factors for short and long term outcomes including risk factors for poor outcomes needed
- Collaborative guidelines on ventilator management, anticoagulation, adjunct therapies while on ECMO needed

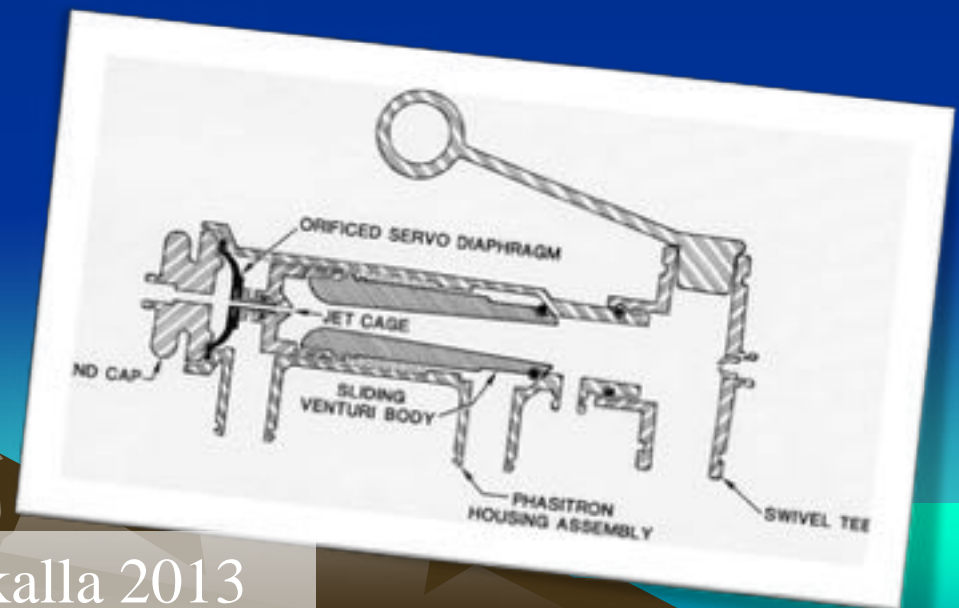


The End

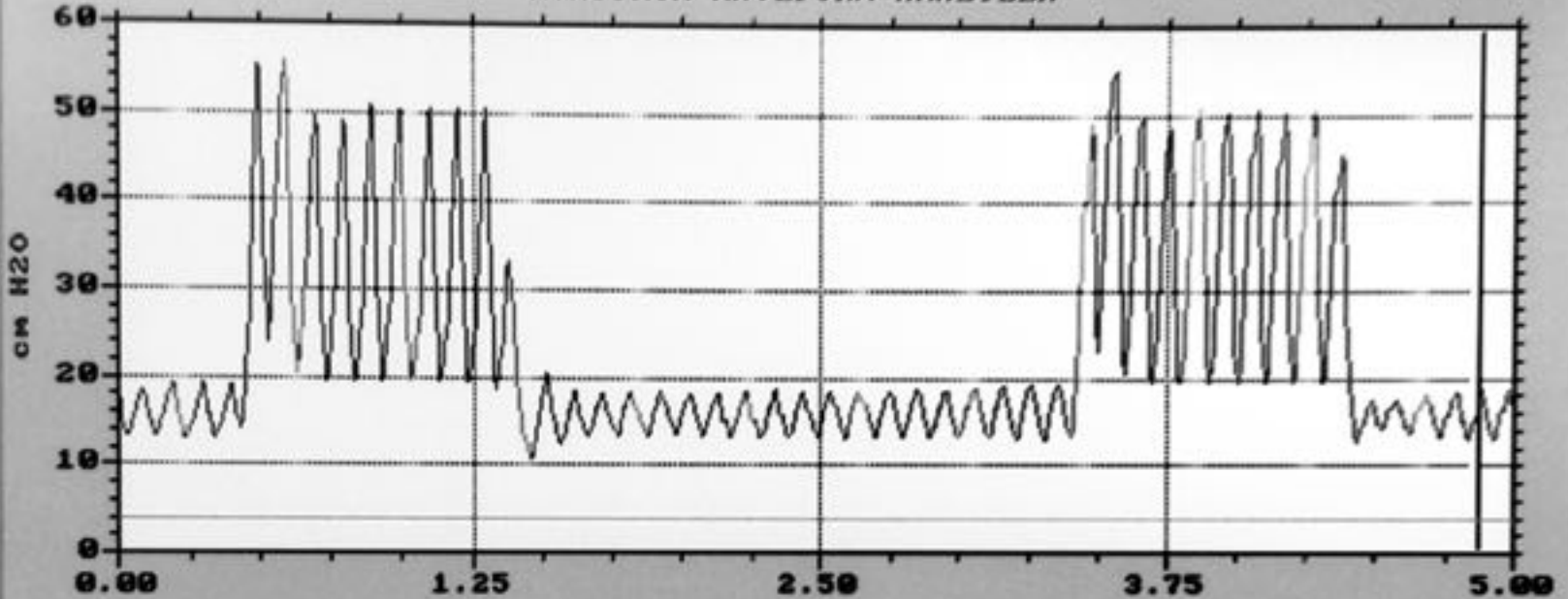


High Frequency Percussive Ventilation (HFPV)

- Pressure-controlled conventional breaths
- Continuous oscillatory rate
- Time-cycled, pneumatically powered
- Described uses: burns, neonates, adults



MONITRON WAVEFORM ANALYZER



I:E Ratio

1:2.2

Inspiration Time

0.9
Seconds

Mean Pressure

22
cm H2O

i:e Ratio

1:1.2

Expiration Time

2.1
Seconds

Convective Rate

20
Cycles/Min

Percussive Rate

570
Cycles/Min



Alarm OK

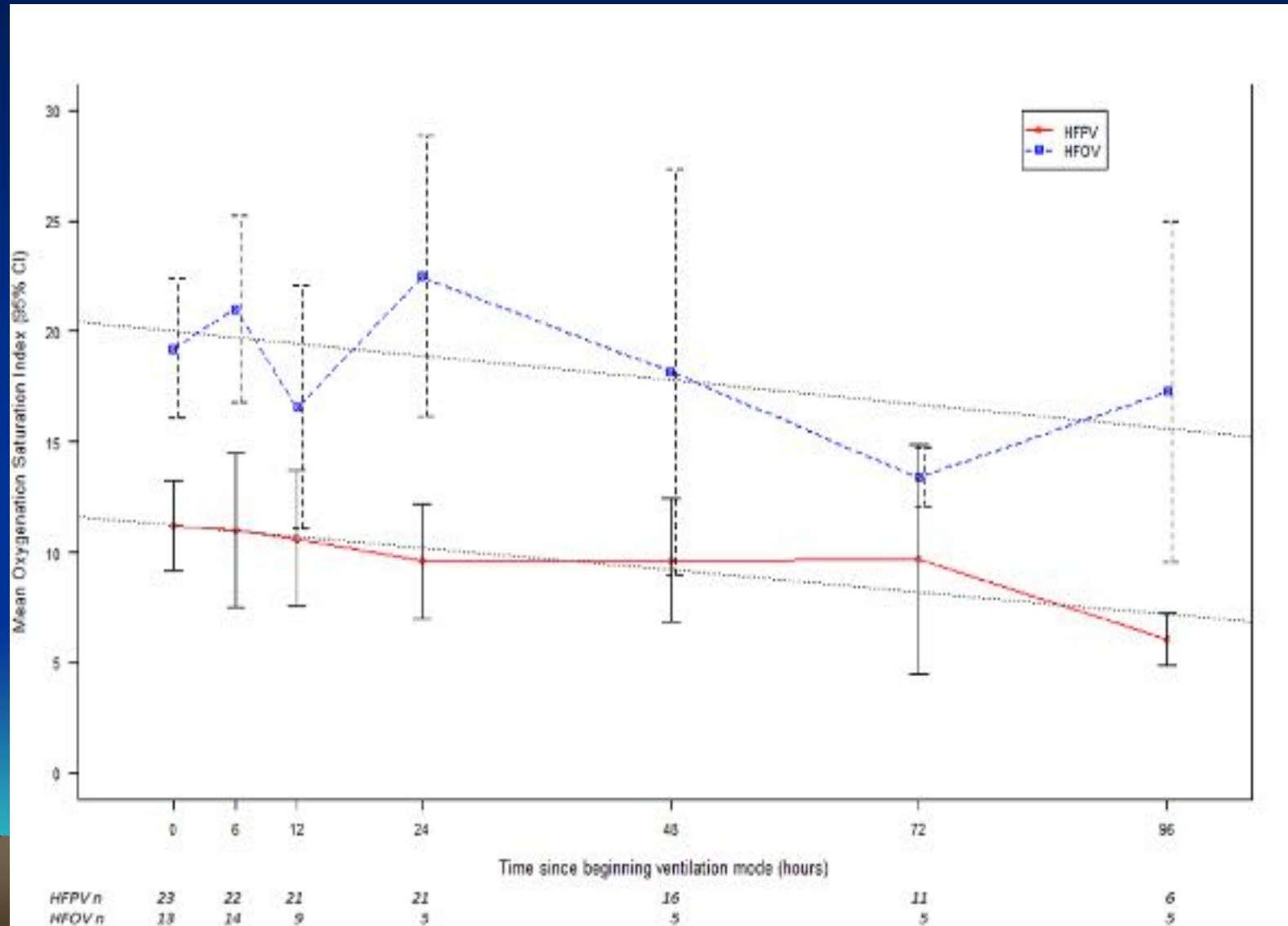
Patient characteristics

		HFPV first	HFOV first
		n = 27	n = 16
		n (%) or mean (\pm SD)	n (%) or mean (\pm SD)
Demographics	Age (months)	57 (\pm 79)	52 (\pm 59)
	Weight (kg)	19 (\pm 24)	17 (\pm 15)
	Male	12 (44%)	9 (56%)
Baseline characteristics	Prob of death (PIM2)	11% (\pm 20%)	32% (\pm 30%)
	Immunocompromised	4 (15%)	6 (38%)
	Prematurity	10 (37%)	3 (19%)
	Chronic Lung Disease	8 (30%)	2 (13%)
	Acute Respiratory Illness	21 (78%)	5 (31%)
	Sepsis	4 (15%)	3 (19%)
Prior ancillary therapies	Inhaled Nitric Oxide	1 (4%)	2 (13%)
	Albuterol	10 (37%)	1 (6%)
	DNase	5 (19%)	1 (6%)
	Corticosteroids	2 (7%)	5 (31%)
	Chest Percussive Therapy	8 (30%)	1 (6%)
	Inotrope/Vasopressor	5 (19%)	7 (44%)
	ECMO	1 (4%)	0 (0%)

Patient characteristics

		HFPV first	HFOV first
		n = 27	n = 16
		n (%) or mean (±SD)	n (%) or mean (±SD)
Reason for	Oxygenation	4 (15%)	14 (88%)
HFV initiation	Ventilation	8 (30%)	1 (6%)
	Secretion management	14 (52%)	0
	Not documented	1 (4%)	1 (6%)
Oxygenation	Oxygenation index	14 (± 7.4) *n=9	25 (± 11) *n=10
impairment	Oxygen Saturation index	11 (± 4.7) *n=23	19 (± 5.2) *n=13
	Mean Airway Pressure	16 (± 2.9) *n=23	19 (± 3.5) *n=13
	FIO ₂	0.65 (± 0.2) *n=23	0.90 (± 0.14) *n=13
	PF ratio	151 (± 68) *n=9	120 (± 120) *n=10
	SF ratio	160 (± 46) *n=23	106 (± 24) *n=13
Ventilation	pCO ₂	60 (± 19) *n=20	56 (± 13) *n=11
impairment			
Outcomes	Total HFPV days	3.7 (± 3.2)	0.7 (± 1.4)
	Total HFOV days	0.6 (± 2.9)	3.4 (± 4.8)
	Total ventilator days	11 (± 7.7)	11 (± 11)
	Total ICU days	15 (± 11)	12 (± 12)
	Mortality	4 (15%)	8 (50%)

Mean Oxygen Saturation Index



Mean PaCO₂

