Respiratory review of 2022

Critical Care Medicine

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송명진

분당서울대학교병원

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Temperature control after cardiac arrest

NEJM. 2021 Jun 17;384(24):2283-2294

Major Clinical Trials for temperature control after cardiac arrest

HACA study group NEJM, N=275
OHCA due to shockable rhythm
33 °C vs 37 °C
Favorable neurologic outcome (90 days) : 55% vs 39%

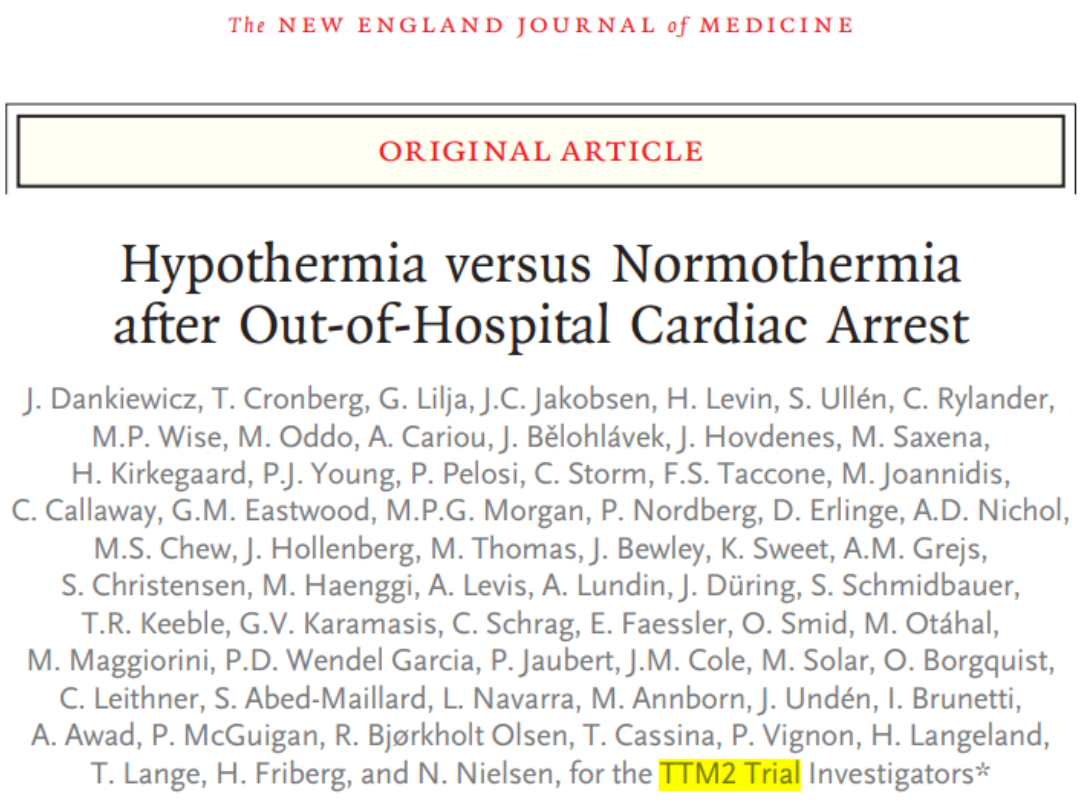
Dankiewicz et al. NEJM, N=1,861
OHCA with presumed cardiac cause
74% were shockable
33 °C vs normothermia <37.8 °C
Death from any cause (6 month) : 50% vs 48%

Bernard et al. NEJM, N=77
OHCA due to V-fib
33 °C vs 37 °C
Favorable neurologic outcome (at discharge) : 49% vs 26%

Nielsen et al. NEJM, N=939
OHCA with presumed cardiac cause
80% were shockable
33 °C vs 36 °C
All cause mortality (through the end of the trial) : 50% vs 48%

Lascarrou et al. NEJM, N=584
OHCA and IHCA, non-shockable
74% were OHCA
33 °C vs 37 °C
Survival c favorable neurologic outcome (90 days) : 10.2% vs 5.7%

TTM-2 Trial

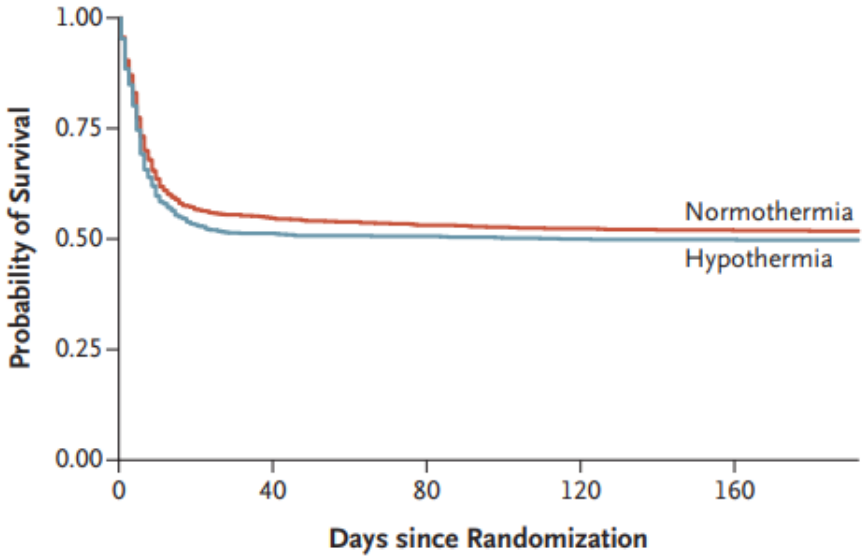


- Design: International, multicenter, open-label, investigator-initiated, randomized, superiority trial
- Population: OHCA irrespective of the initial rhythm (n=1,861)
- Period: Nov 2017 ~ Jan 2020
- Intervention vs. control: 33°C vs. targeted normothermia (< 37.8°C)
- Primary outcome: 6-month mortality

NEJM. 2021 Jun 17;384(24):2283-2294

No significant difference between hypothermia and normothermia in 6-month mortality

265/925 (50%) vs **446/925 (48%)**

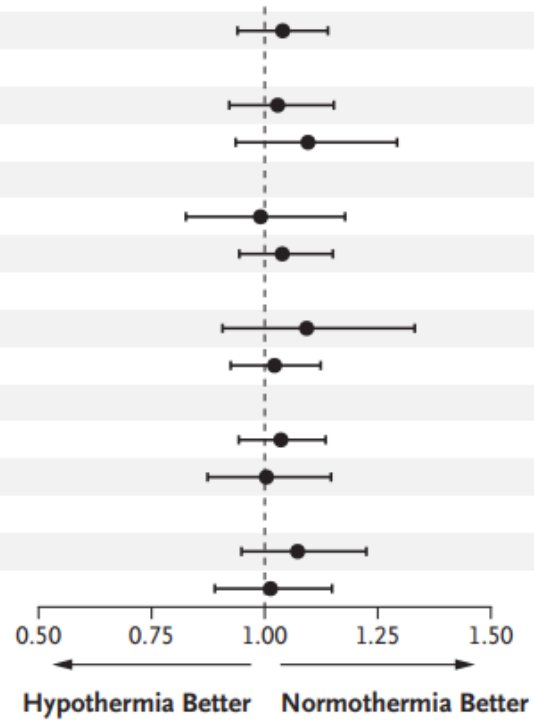


No. at Risk

Normothermia	925	506	491	484	480
Hypothermia	925	474	468	462	461

A Death at 6 Months

Subgroup	Hypothermia	Normothermia	Relative Risk of Death (95% CI)
	no. of patients		
All patients	925	925	1.04 (0.94–1.14)
Sex			
Male	738	729	1.03 (0.92–1.15)
Female	187	196	1.10 (0.94–1.29)
Age			
<65 yr	421	457	0.99 (0.83–1.18)
≥65 yr	504	468	1.04 (0.94–1.15)
Time to ROSC from cardiac arrest			
<25 min	419	416	1.09 (0.91–1.33)
≥25 min	506	509	1.02 (0.92–1.12)
Initial rhythm			
Nonshockable	259	231	1.04 (0.94–1.14)
Shockable	666	694	1.00 (0.87–1.15)
Shock on admission			
Not present	665	651	1.07 (0.95–1.23)
Present	260	274	1.01 (0.89–1.15)



No difference in functional outcome, but arrythmias were more common in hypothermia group

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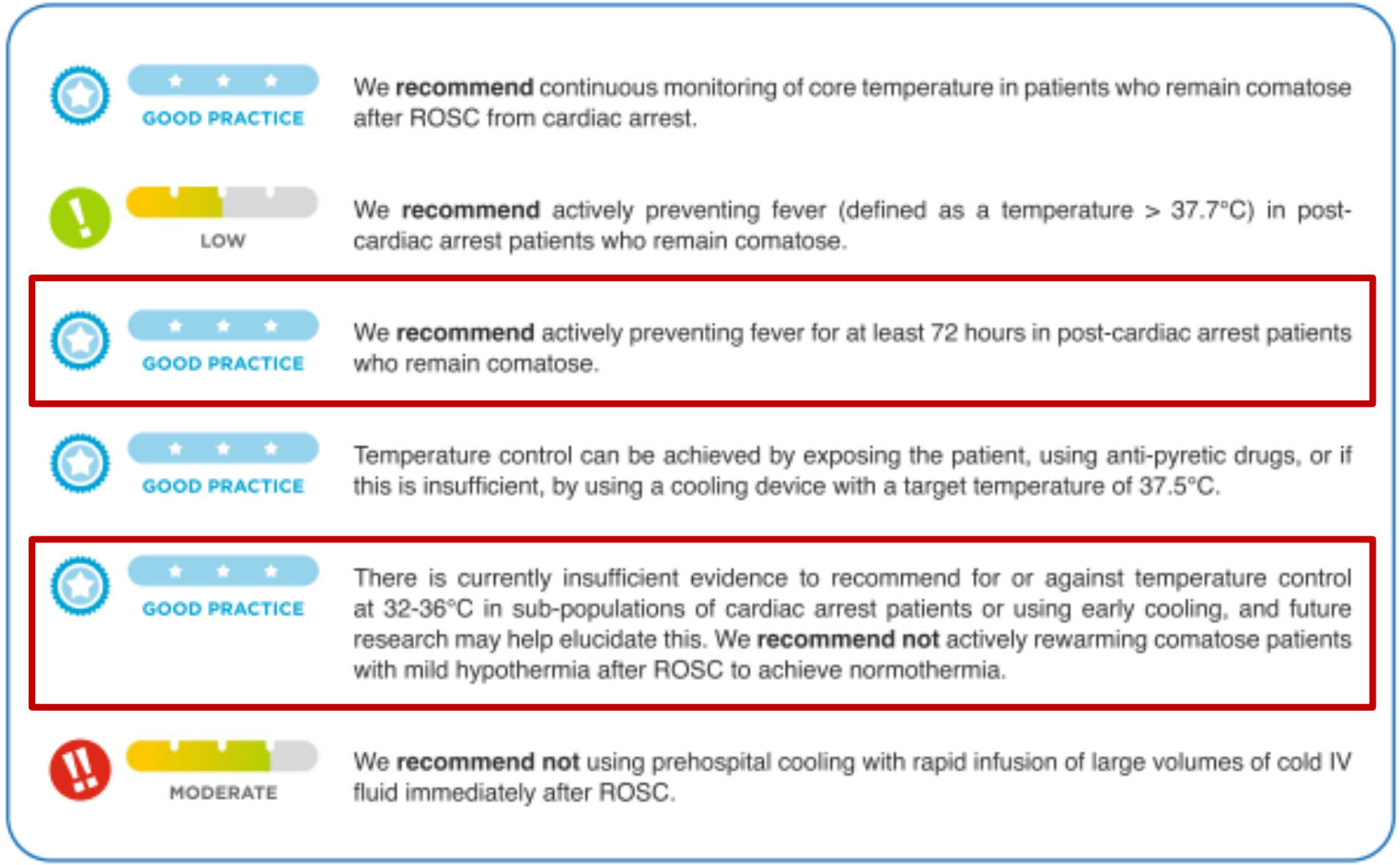
Table 2. Outcomes and Adverse Events.

Outcome or Event	Hypothermia (N=930)	Normothermia (N=931)	Relative Risk (95% CI)*	P Value
Primary outcome: death from any cause at 6 mo — no./total no. (%)	465/925 (50)	446/925 (48)	1.04 (0.94–1.14)	0.37
Main secondary outcome — no./total no. (%)				
Score of 4–6 on modified Rankin scale at 6-mo follow-up†	488/881 (55)	479/866 (55)	1.00 (0.92–1.09)	
Poor functional outcome at 6 mo‡	495/918 (54)	493/911 (54)	1.00 (0.91–1.08)	
Score on modified Rankin scale at 6-mo follow-up — no./total no. (%)†				
0	140/881 (16)	148/866 (17)		
1	87/881 (10)	80/866 (9)		
2	132/881 (15)	127/866 (15)		
3	34/881 (4)	32/866 (4)		
4	16/881 (2)	20/866 (2)		
5	7/881 (1)	13/866 (2)		
6	465/881 (53)	446/866 (52)		
Serious adverse events — no./total no. (%)				
Arrhythmia resulting in hemodynamic compromise	222/927 (24)	152/921 (16)	1.45 (1.21–1.75)	<0.001
Bleeding	44/927 (5)	46/922 (5)	0.95 (0.63–1.42)	0.81
Skin complication related to device used for targeted temperature management	10/927 (1)	5/922 (<1)	1.99 (0.71–6.37)	0.21
Pneumonia	330/927 (36)	322/921 (35)	1.02 (0.90–1.15)	0.75
Sepsis	99/926 (11)	83/922 (9)	1.19 (0.90–1.57)	0.23

ERC-ESICM guidelines on temperature control after cardiac arrest in adults



Intensive Care Med 2022 Mar;48(3):261-269

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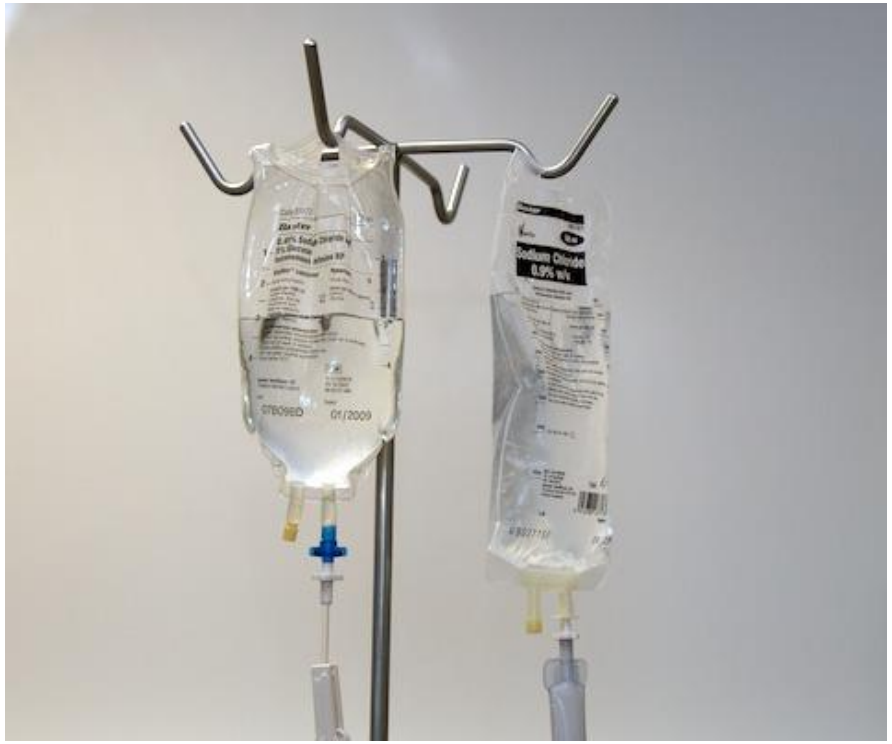
Fluid in ICU

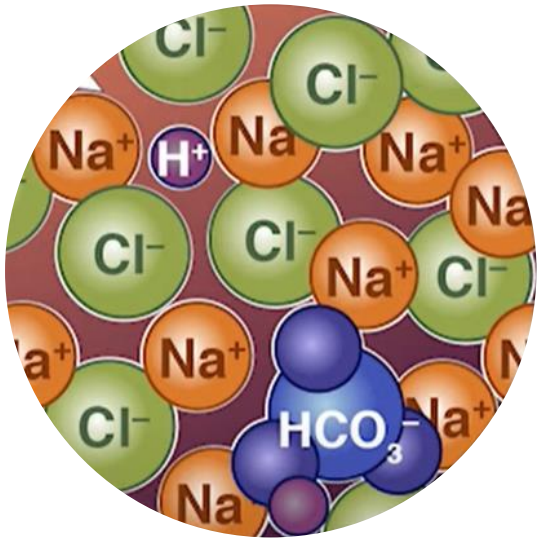
JAMA. 2021 Sep 7;326(9):818-829

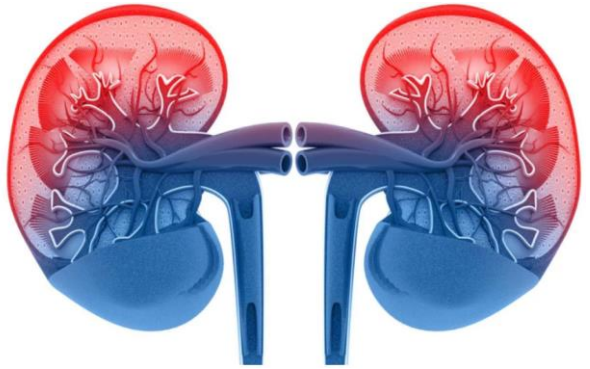
NEJM. 2022 Mar 3;386(9):815-826



Normal saline vs Balanced solution?

0.9% Normal Saline





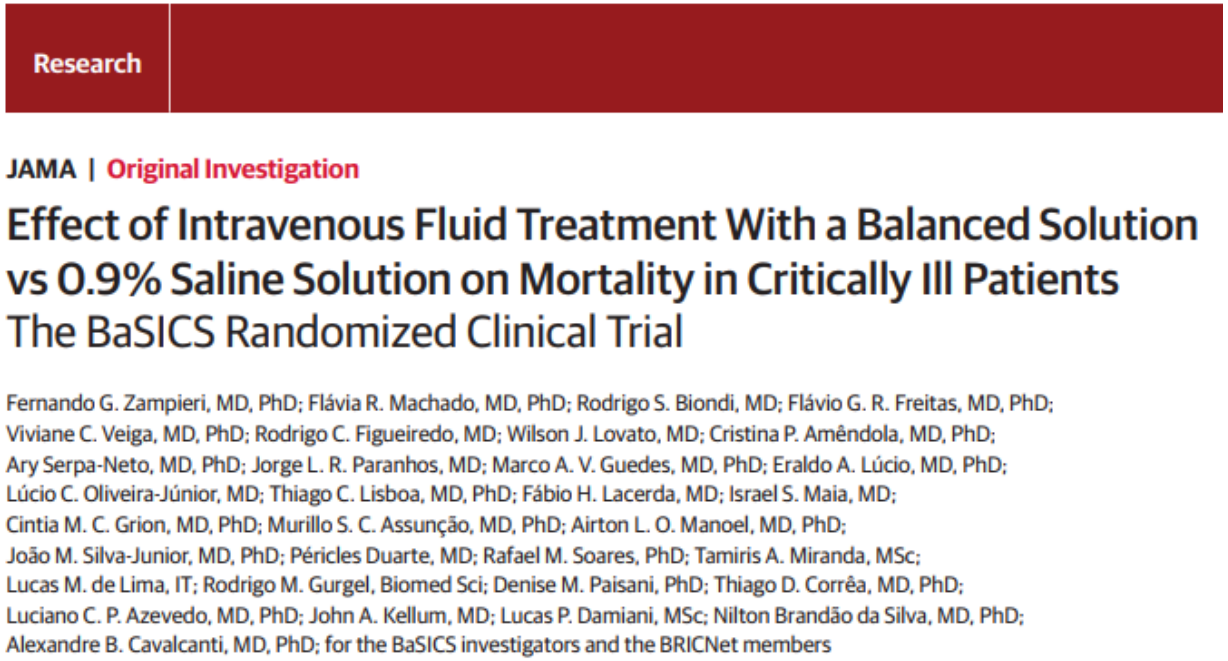
Hyperchloremic metabolic acidosis

Kidney injury

- SPLIT trial (JAMA, 2015)
  - No difference in AKI, new RRT or mortality.
- SMART trial (NEJM, 2018)
  - Favor of balanced solutions in the composite outcome of death from any cause, new RRT, or persistent kidney dysfunction.

JAMA. 2015 Oct 27;314(16):1701-10 (SPLIT)
N Engl J Med. 2018 Mar 1;378(9):829-839 (SMART)

BaSICS Trial



Research

JAMA | Original Investigation

Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients
The BaSICS Randomized Clinical Trial

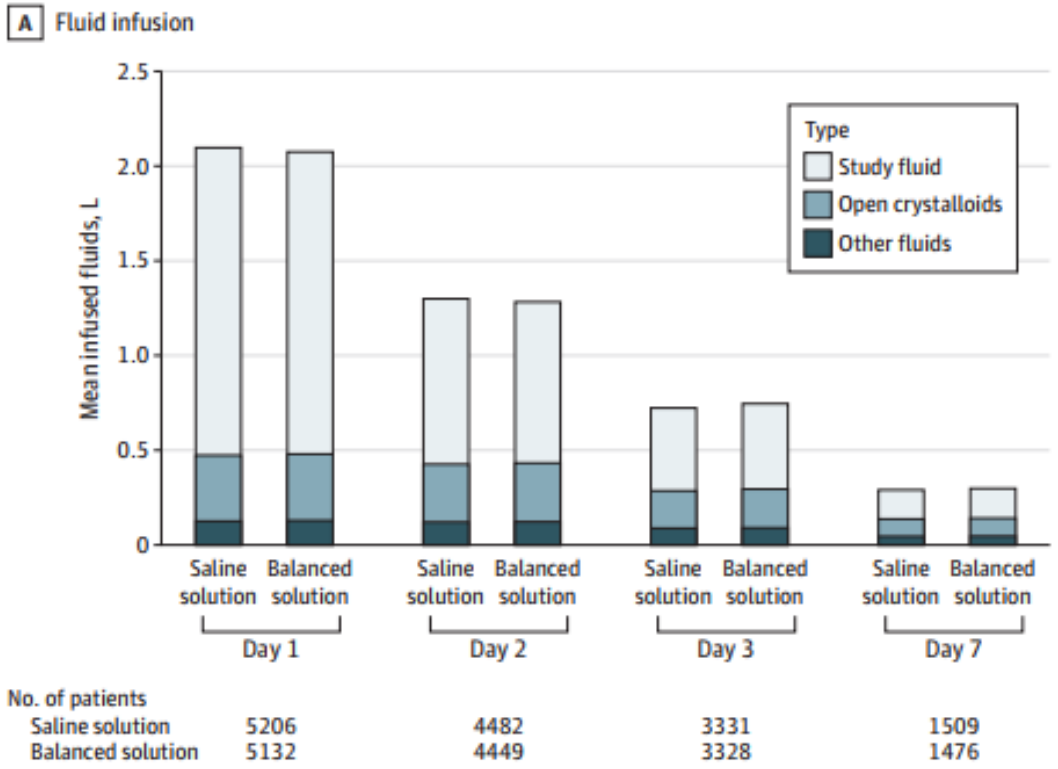
Fernando G. Zampieri, MD, PhD; Flávia R. Machado, MD, PhD; Rodrigo S. Biondi, MD; Flávio G. R. Freitas, MD, PhD; Viviane C. Veiga, MD, PhD; Rodrigo C. Figueiredo, MD; Wilson J. Lovato, MD; Cristina P. Amêndola, MD, PhD; Ary Serpa-Neto, MD, PhD; Jorge L. R. Paranhos, MD; Marco A. V. Guedes, MD, PhD; Eraldo A. Lúcio, MD, PhD; Lúcio C. Oliveira-Júnior, MD; Thiago C. Lisboa, MD, PhD; Fábio H. Lacerda, MD; Israel S. Maia, MD; Cintia M. C. Grion, MD, PhD; Murillo S. C. Assunção, MD, PhD; Airton L. O. Manoel, MD, PhD; João M. Silva-Junior, MD, PhD; Péricles Duarte, MD; Rafael M. Soares, PhD; Tamiris A. Miranda, MSc; Lucas M. de Lima, IT; Rodrigo M. Gurgel, Biomed Sci; Denise M. Paisani, PhD; Thiago D. Corrêa, MD, PhD; Luciano C. P. Azevedo, MD, PhD; John A. Kellum, MD; Lucas P. Damiani, MSc; Nilton Brandão da Silva, MD, PhD; Alexandre B. Cavalcanti, MD, PhD; for the BaSICS investigators and the BRICNet members

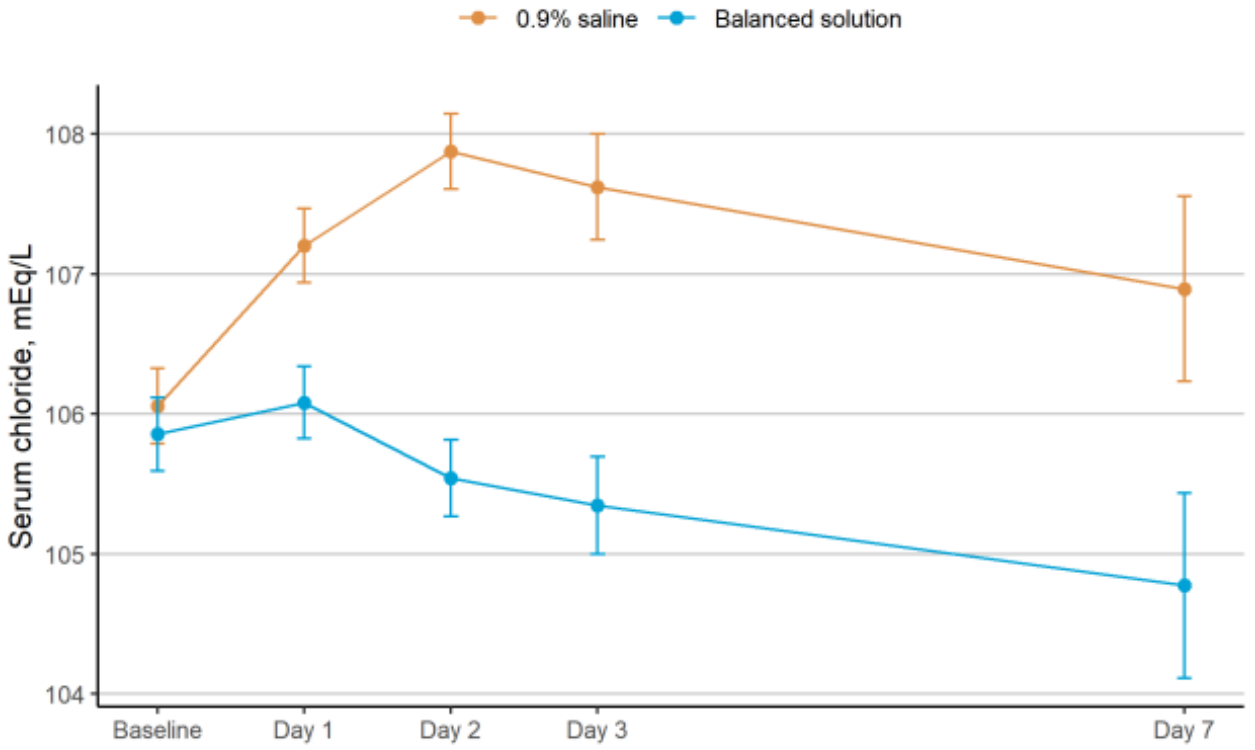
- Design: Double-blind, factorial, randomized clinical trial
- Population: 11,052 patient patients from 75 participating ICUs in Brazil
- Period: May 2017 ~ March 2020
- Intervention vs. control: 2 different fluid types (**Plasma-Lyte 148 vs saline solution**) and 2 different infusion rates (333ml/h vs 999ml/h)
- Primary outcome: 90-day mortality

JAMA. 2021 Sep 7;326(9):818-829

Balanced solution vs Saline solution

Median study fluid administered during the first 3 days was **2.9 L.** (total fluid 4.1L)

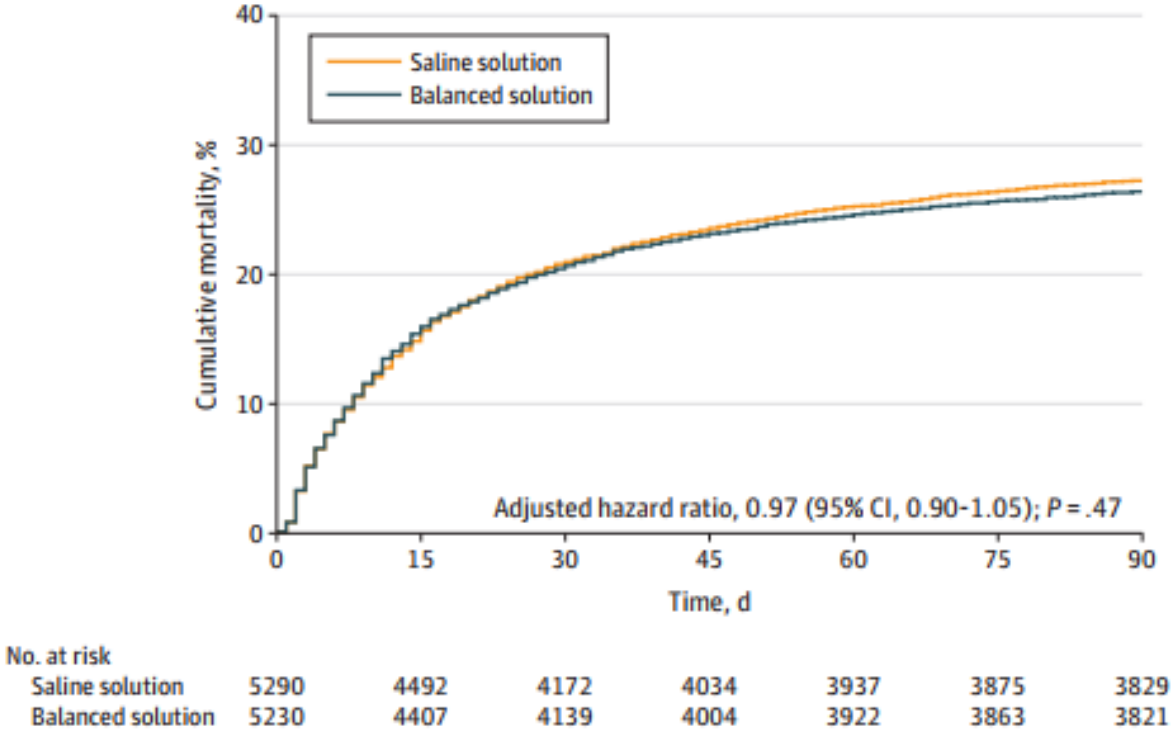




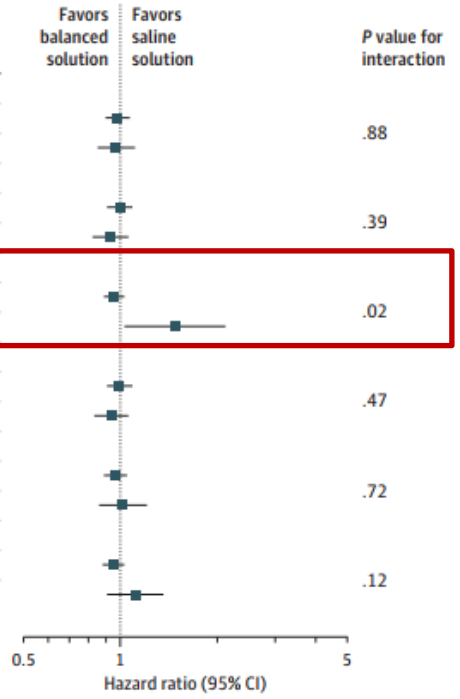
P<.001 for the difference

No difference between balanced and saline in mortality

90d mortality : Balanced vs Normal saline, 26.4% vs 27.2%



Subgroup	No. for 90-d mortality/total (%)[a] Balanced solution	Saline solution[b]	Hazard ratio (95% CI)	P value for interaction
KDIGO stage for acute kidney injury[c]				
<2	989/4360 (22.7)	995/4350 (22.9)	0.98 (0.90-1.07)	.88
≥2	392/870 (45.1)	444/940 (47.2)	0.97 (0.85-1.11)	
Sepsis				
No	928/4260 (21.8)	941/4273 (22.0)	1.00 (0.91-1.09)	.39
Yes	453/970 (46.7)	498/1017 (49.0)	0.93 (0.82-1.06)	
Traumatic brain injury				
No	1303/4981 (26.2)	1389/5053 (27.5)	0.96 (0.89-1.03)	.02
Yes	78/249 (31.3)	50/237 (21.1)	1.48 (1.03-2.12)	
Surgical patients				
No	880/2078 (42.3)	891/2046 (43.5)	0.99 (0.91-1.09)	.47
Yes	501/3152 (15.9)	548/3244 (16.9)	0.94 (0.83-1.06)	
APACHE II score[d]				
<25	1131/4865 (23.2)	1170/4886 (23.9)	0.97 (0.89-1.05)	.72
≥25	250/365 (68.5)	269/404 (66.6)	1.02 (0.86-1.21)	
Administration of saline solution 24 h before randomization, L				
<1.0	1181/4277 (27.6)	1229/4286 (28.7)	0.95 (0.88-1.03)	.12
≥1.0	193/935 (20.6)	203/994 (20.4)	1.12 (0.91-1.36)	



No difference between balanced and saline in outcomes related to renal function

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Outcomes	No./total (%)		Absolute difference (95% CI)	Effect measure (95% CI)
	Balanced solution	Saline solution		
Secondary outcomes				
Incidence of acute kidney failure with need for kidney replacement therapy within 90 d per 1000 patient-days	414/471 (0.88)	445/476 (0.93)	−0.05 (−0.15 to 0.06)	RR, 0.95 (0.83 to 1.08)
At day 1	28/5218 (0.5)	30/5287 (0.6)		
At day 2	115/5174 (2.2)	137/5242 (2.6)		
At day 3	181/5052 (3.6)	213/5123 (4.2)		
At day 7	267/4808 (5.6)	314/4884 (6.4)		
In the hospital (≥1 episode during stay)	393/5218 (7.5)	427/5287 (8.1)	−0.5 (−1.5 to 0.4)	OR, 0.93 (0.81 to 1.06)
Acute kidney injury assessed as KDIGO stage ≥2[b]				
At day 3	850/3128 (27.2)	859/3094 (27.8)	−1.9 (−4.0 to 0.2)	OR, 0.99 (0.88 to 1.11)
At day 7	276/1180 (23.4)	273/1170 (23.3)	−1.5 (−3.6 to 0.6)	OR, 1.07 (0.88 to 1.30)
KDIGO stage ≥2 or death				
At day 3	851/3128 (27.2)	865/3094 (28.0)	−1.9 (−4.0 to 0.2)	OR, 0.98 (0.87 to 1.10)
At day 7	278/1180 (23.6)	275/1170 (23.5)	−1.5 (−3.6 to 0.6)	OR, 1.07 (0.88 to 1.30)

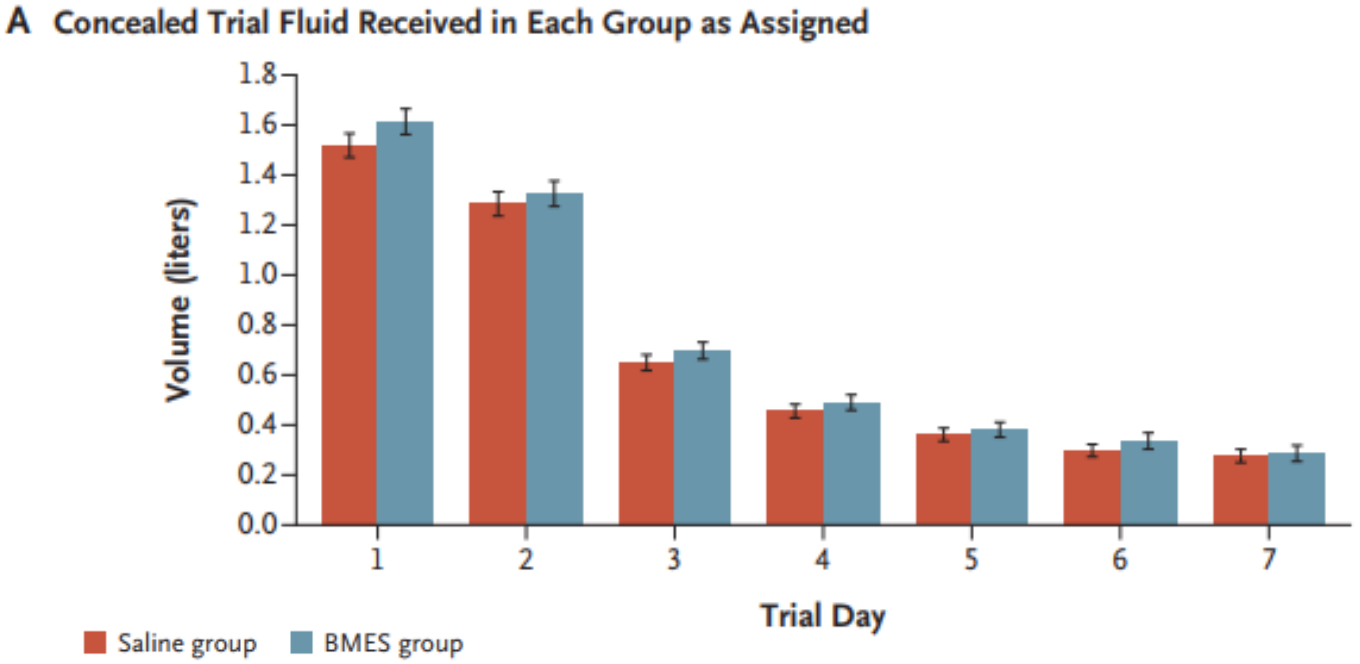
PLUS Trial

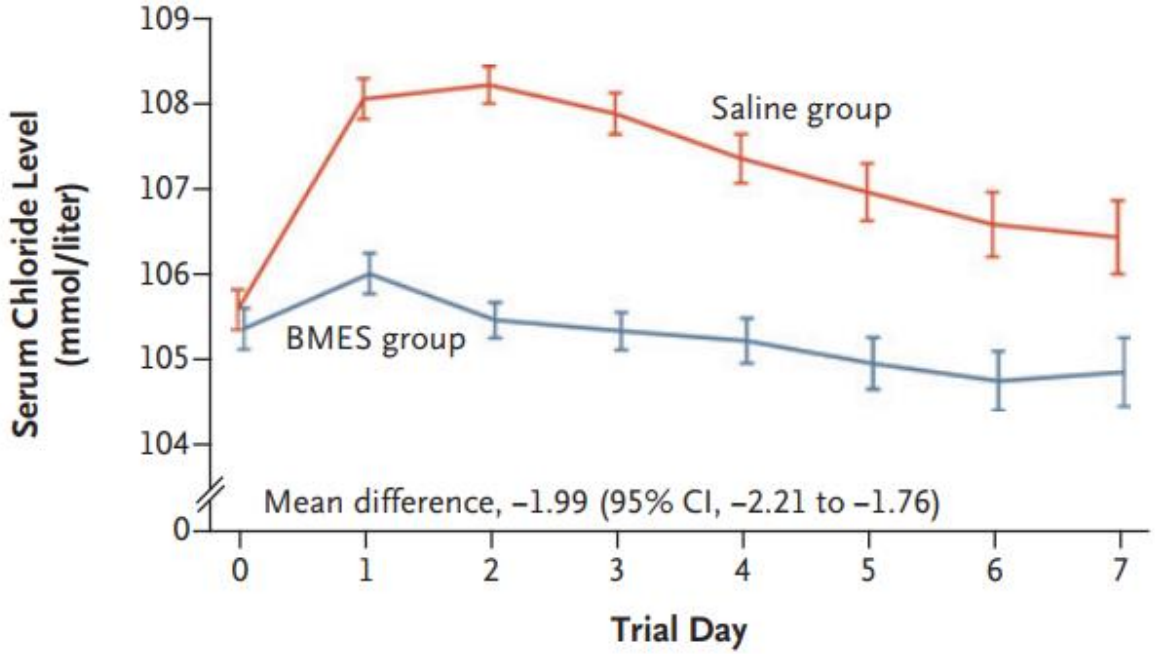
- Design: Investigator-initiated, double-blind, parallel-group, randomized, controlled trial
- Population: 5,037 patients from 53 ICUs in Australia and New Zealand
- Period: Sep 2017 ~ Dec 2020
- Intervention vs. control: BMES (Plasma-Lyte 148) vs. saline
- Primary outcome: 90-day mortality

NEJM. 2022 Mar 3;386(9):815-826

Balanced solution vs Saline solution

Median volume of trial fluid was **3.9 L** in the BMES group and **3.7 L** in normal saline group.

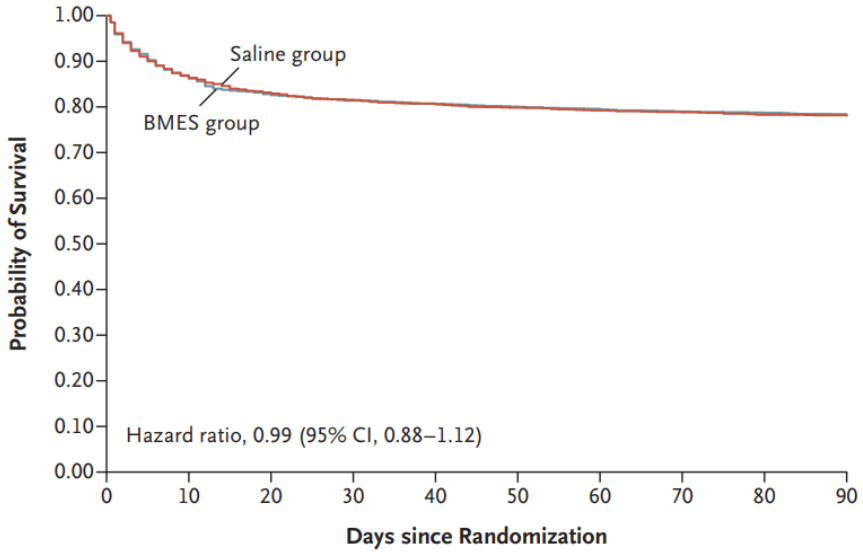




No benefit of BMES compared to saline in 90d mortality

90d mortality : Balanced vs Normal saline, 21.8 % vs 22.0 %

A Kaplan–Meier Estimates of the Probability of Survival

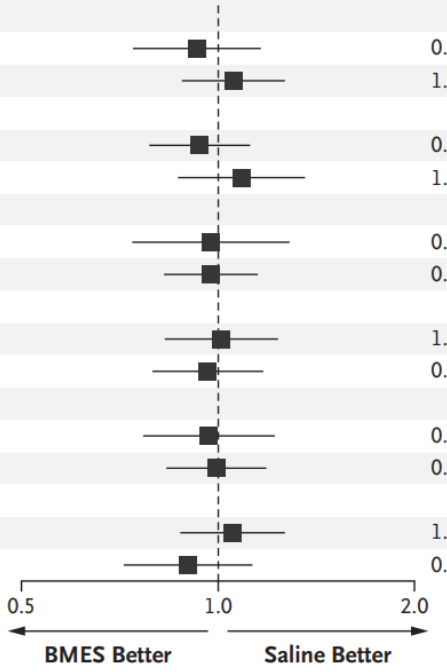


No. of Patients

BMES group	2446	2119	2019	1983	1964	1949	1937	1922	1916	1906
Saline group	2430	2109	2015	1973	1952	1929	1913	1904	1890	1884

B Subgroup Analysis of Death from Any Cause

Subgroup	BMES Group	Saline Group	Odds Ratio (95% CI)
	no. of events/total no. (%)		
Age			
<65 yr	184/1250 (14.7)	188/1207 (15.6)	0.93 (0.74–1.16)
≥65 yr	346/1183 (29.2)	342/1206 (28.4)	1.06 (0.88–1.26)
Sex			
Male	328/1531 (21.4)	323/1437 (22.5)	0.94 (0.79–1.12)
Female	202/902 (22.4)	207/976 (21.2)	1.09 (0.87–1.35)
Kidney injury			
Yes	160/468 (34.2)	155/451 (34.4)	0.98 (0.74–1.29)
No	361/1934 (18.7)	370/1931 (19.2)	0.97 (0.83–1.15)
Sepsis			
Yes	276/1068 (25.8)	265/1026 (25.8)	1.01 (0.83–1.23)
No	254/1362 (18.6)	265/1386 (19.1)	0.97 (0.80–1.17)
Admitted from surgery			
Yes	171/1087 (15.7)	179/1109 (16.1)	0.97 (0.77–1.22)
No	359/1344 (26.7)	351/1304 (26.9)	0.99 (0.84–1.18)
APACHE II score			
<25	287/1753 (16.4)	275/1739 (15.8)	1.05 (0.88–1.26)
≥25	243/678 (35.8)	255/673 (37.9)	0.90 (0.72–1.12)



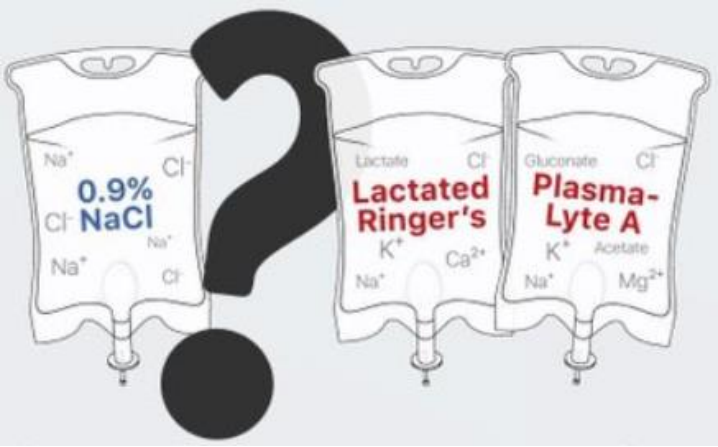
No significant effect of BMES compared to saline on kidney function

	BMES Group (N =2515)	Saline Group (N =2522)	Odds Ratio (95% CI)	Absolute Difference (95% CI)
Receipt of new renal-replacement therapy — no./total no. (%)	306/2403 (12.7)	310/2394 (12.9)	0.98 (0.83 to 1.16)	-0.20 (-2.96 to 2.56)
Maximum creatinine level in the ICU during days 1 to 7 — mg/dl	1.76±1.44	1.75±1.43		0.01 (-0.04 to 0.06)
Maximum increase in creatinine level in the ICU — mg/dl	0.41±1.06	0.41±1.02		0.01 (-0.05 to 0.06)

So then, which fluid do we have to prescribe?

- No measurable risk for administration of 0.9% NaCl when used in small to moderate quantities in critically ill patients who are at relatively low risk for AKI.

- Do not use balanced solution for traumatic brain injury.
- Prefer balanced solution for diabetic ketoacidosis.



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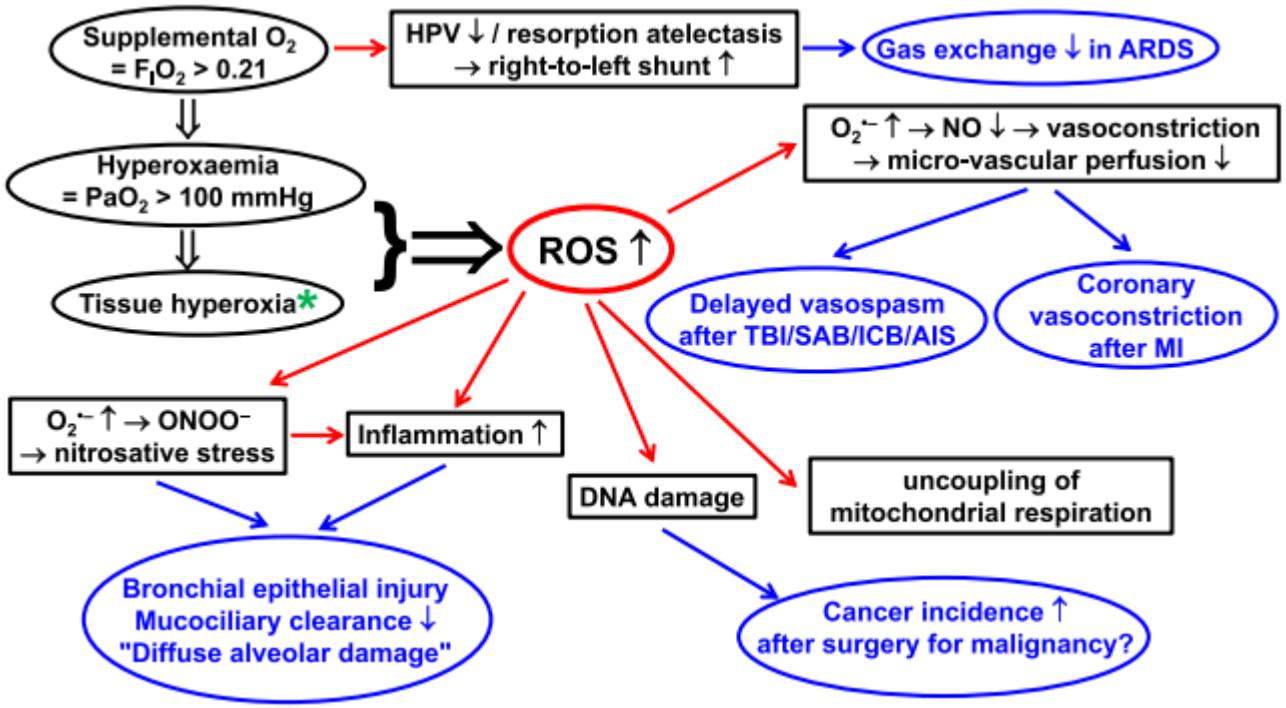
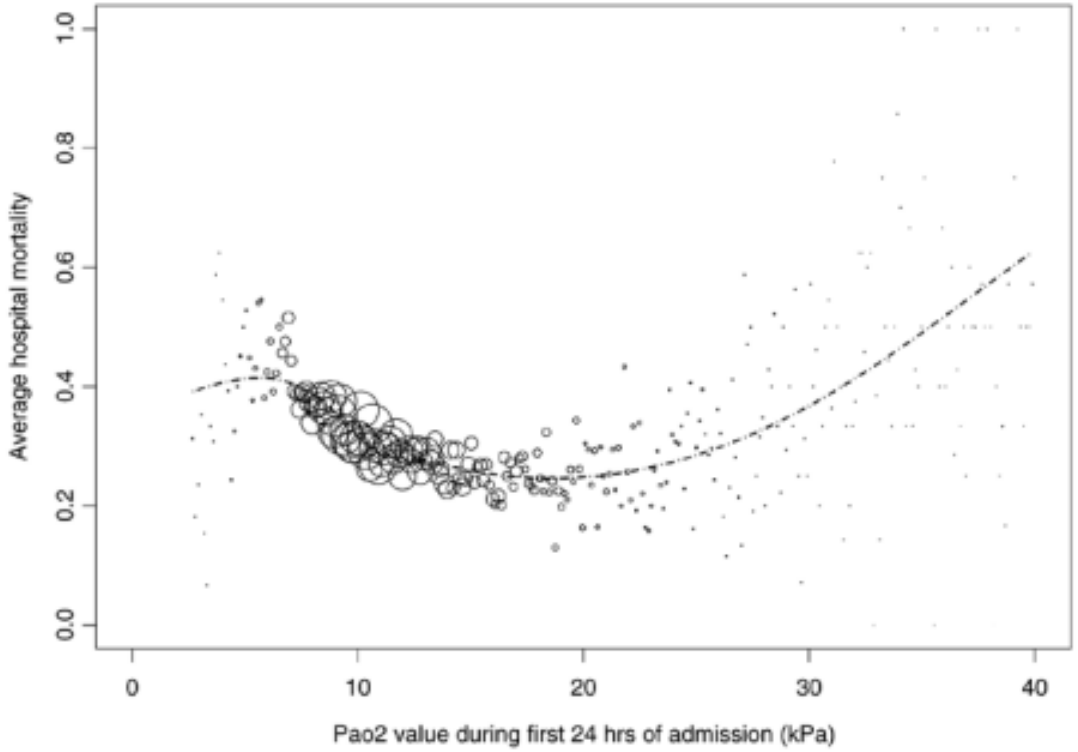
Oxygen therapy in ICU

JAMA. 2021 Sep 14;326(10):940-948

Optimal PaO2 ?





Crit Care. 2021 Dec 19;25(1):440
Crit Care. 2008;12(6):R156

Low vs. high oxygenation target

- Favorable mortality outcomes for Low oxygenation
  - OXYGEN-ICU *JAMA. 2016;316(15):1583-1589*
  - HyperS2S *Lancet Respir Med. 2017;5(3):180-190*

- No difference between low and high oxygenation in mortality
  - ICU-ROX *NEJM. 2020;382(11):989-998*
  - HOT-ICU *NEJM. 2021;384(14):1301-1311*

- *Worrisome safety signal in low oxygenation*
  - $LOCO_2$ *NEJM. 2020;382(11):999-1008*

O2-ICU Trial

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Low-Normal vs High-Normal Oxygenation Targets on Organ Dysfunction in Critically Ill Patients
A Randomized Clinical Trial

Harry Gelissen, MD, MBA; Harm-Jan de Grooth, MD, PhD; Yvo Smulders, MD, PhD; Evert-Jan Wils, MD, PhD; Wouter de Ruijter, MD, PhD; Roel Vink, MD, PhD; Bob Smit, PhD; Jantine Röttgering, MD; Leila Atmowihardjo, MD; Armand Girbes, MD, PhD; Paul Elbers, MD, PhD; Pieter-Roel Tuinman, MD, PhD; Heleen Oudemans-van Straaten, MD, PhD; Angelique de Man, MD, PhD

- Design: multicenter RCT
- Population: 400 patients with systematic inflammation (≥ 2 positive SIRS criteria) from 4 ICUs in the Netherlands
- Period: Feb 2015 ~Oct 2018
- Intervention vs. control: low-normal PaO2 (60-90mmHg) vs high-normal PaO2 (105-135mmHg)
- Primary outcome: $SOFA_{RANK}$
  - Ranking based on the non-respiratory cumulative daily delta SOFA score from day 1 to day 14

JAMA. 2021 Sep 14;326(10):940-948

Low-normal PaO2 target did not significantly reduce organ dysfunction compared with a high-normal target

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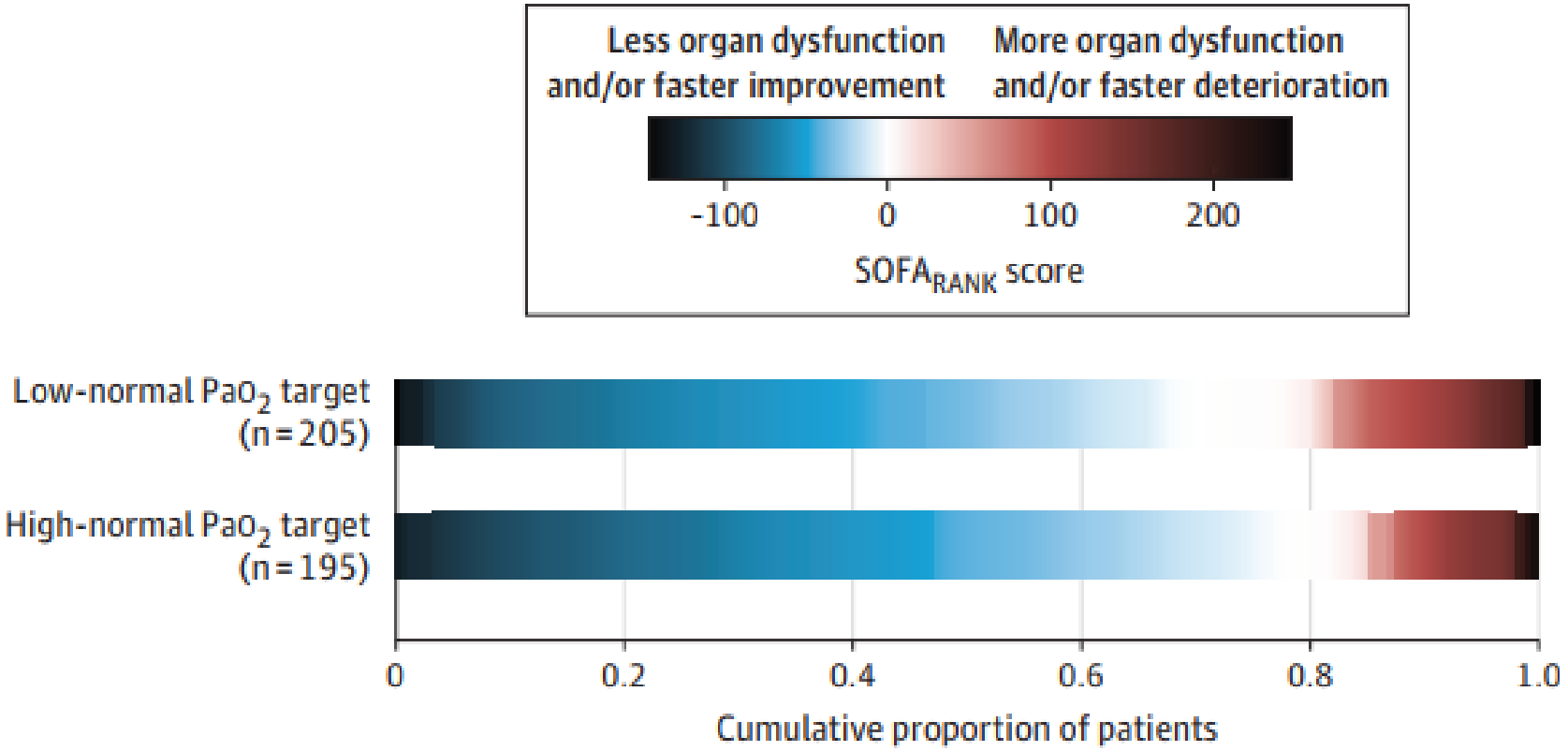
$SOFA_{RANK}$ Low-normal PaO2 vs High-normal PaO2, -35 vs -40, p=0.06



No differences between low- and high-normal PaO2 target in 90-day mortality, duration of MV, or ICU LOS

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Group	Low-normal Pao_2 target (n = 205)	High-normal Pao_2 target (n = 195)	Difference (95% CI)[a]	Odds ratio (95% CI)	*P* value
Intubation during ICU admission, No. (%)[e]	147 (72)	143 (73)	−1 (−11 to 8)	0.92 (0.58 to 1.46)	.74
Duration of mechanical ventilation, median (IQR), d	3.4 (1.2 to 6.8)	3.1 (1.4 to 9.7)	−0.15 (−0.88 to 0.47)[f]		.59
Ventilator-free days to day 14, median (IQR)	9.7 (0 to 13.4)	10.2 (0 to 13.5)	0 (−1.2 to 1.3)		.85
Length of stay in ICU, median (IQR), d	3.9 (2.0 to 8.3)	4.6 (2.0 to 11.1)	−0.34 (−1.14 to 0.37)		.34
Total norepinephrine dose during admission, median (IQR), mg	27.6 (0.7 to 97.2)	27.6 (7.4 to 76.8)	0 (−7.2 to 4.8)		.74
Highest norepinephrine dose during admission, median (IQR), mg/h	0.55 (0.10 to 1.60)	0.60 (0.20 to 1.40)	0 (−0.12 to 0.10)		.77
Mortality, No. (%)					
ICU	50 (24)	49 (25)	−1 (−10 to 8)	0.96 (0.59 to 1.55)	.91
Hospital	66 (32)	61 (31)	1 (−9 to 10)	1.04 (0.67 to 1.63)	.91
At 90 d[e]	72 (35)	67 (34)	1 (−9 to 11)	1.03 (0.67 to 1.59)	.91

Optimal PaO2 ?

- Optimum targets still unknown…
- High oxygenation target has no proven benefit and may increase morbidity and mortality.
- Targeted application of oxygen is needed.

- Ongoing trials of oxygen therapy may provide additional insight.
  - Mega-ROX trial (ACTRN12620000391976)

$ECCO_2R$ in Hypoxemic respiratory failure

JAMA. 2021 Sep 21;326(11):1013-1023

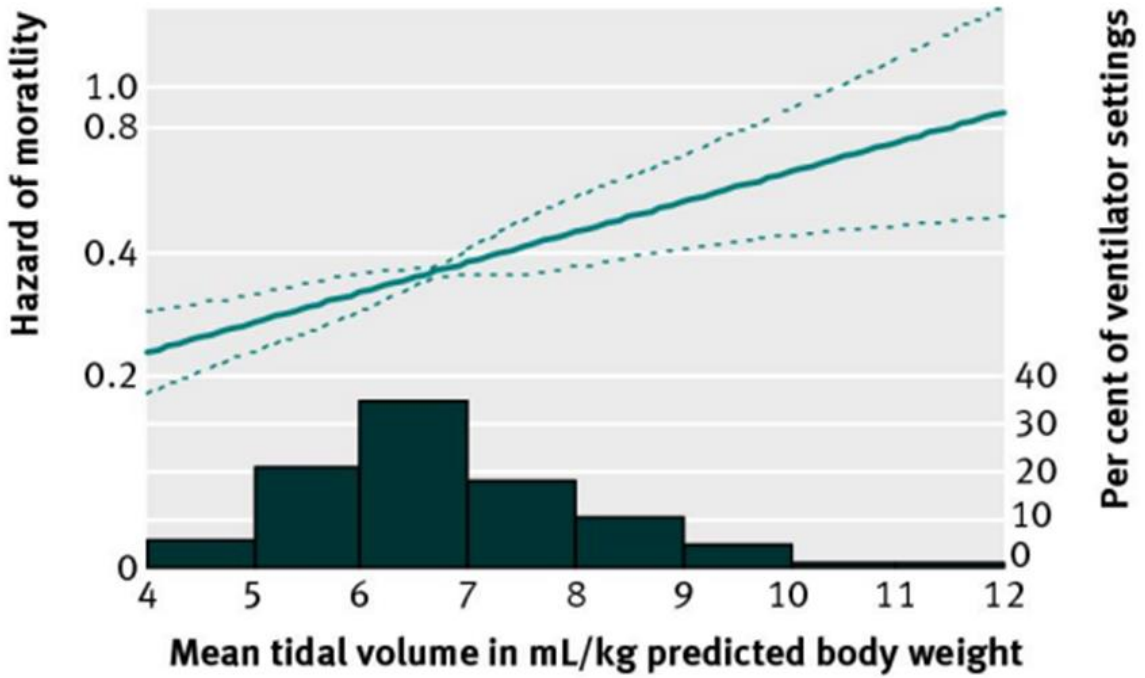
ECCO2R in Hypoxemic respiratory failure

SNUH 분당서울대학교병원 SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

The Evolving Paradigm of Extracorporeal Support for Adults with Acute Respiratory Failure

Salvage — More Protective MV — ?Prevention

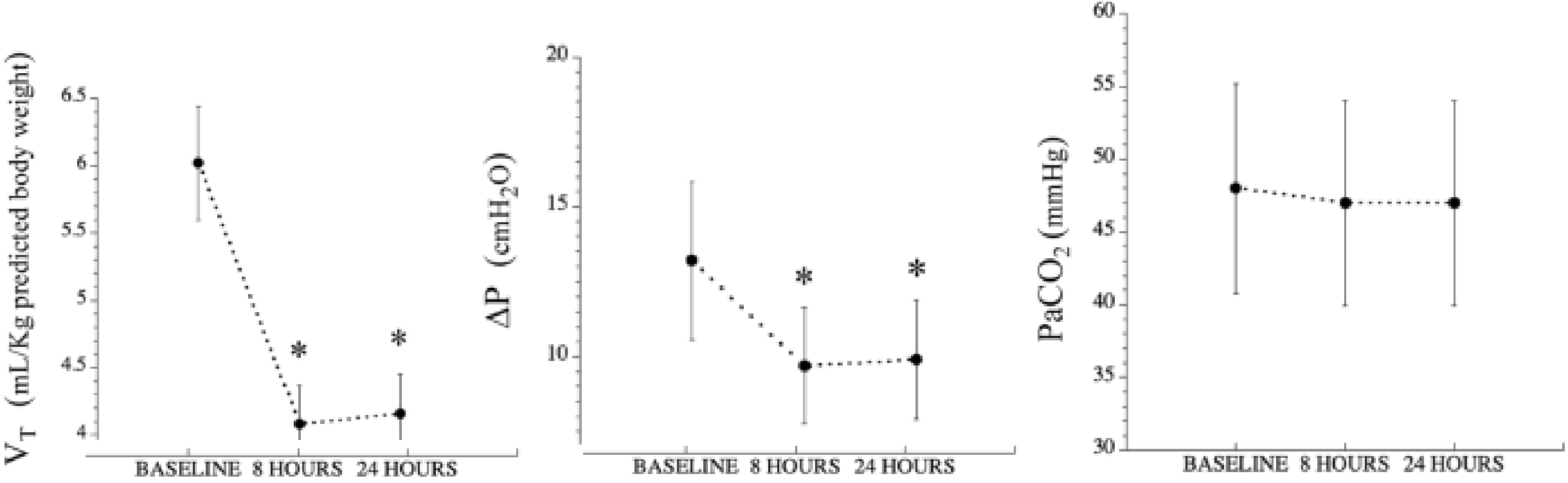
1970-2000	2000-2010	2010-2020	2020-beyond?
Development and refinement of the technology (University of Michigan experience, ELSO) Failure of early RCTs to demonstrate efficacy in severe adult respiratory failure (Zapol et al., Morris et al.)	Re-emergence of VV ECMO for life-threatening refractory hypoxemia (H1N1 Pandemic, CESAR Trial)	Establishment of early VV ECMO for severe ARDS (EOLIA, Bayesian Analysis, Meta-Analyses) Development and refinement of $ECCO_2R$ in less severe forms of acute respiratory failure (moderate ARDS, AECOPD)	?Prevention of patient-self-inflicted lung injury (P-SILI) ?$ECCO_2R$ to facilitate lung and diaphragm protective ventilation (REST) ?VV ECMO as a primary support modality in ARDS



Intensive Care Med (2019) 45:1451–1453
BMJ 2012;344:e2124

SUPERNOVA Pilot Study

- Phase 2 study to assessed feasibility and safety of $ECCO_2R$ to facilitate ultra-protective ventilation (V_T 4 mL/kg and P_{plat} ≤ 25 cmH2O) in patients with **moderate ARDS (n=95)**.



Intensive Care Med (2019) 45:592–600

REST Trial

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lower Tidal Volume Ventilation Facilitated by Extracorporeal Carbon Dioxide Removal vs Standard Care Ventilation on 90-Day Mortality in Patients With Acute Hypoxemic Respiratory Failure
The REST Randomized Clinical Trial

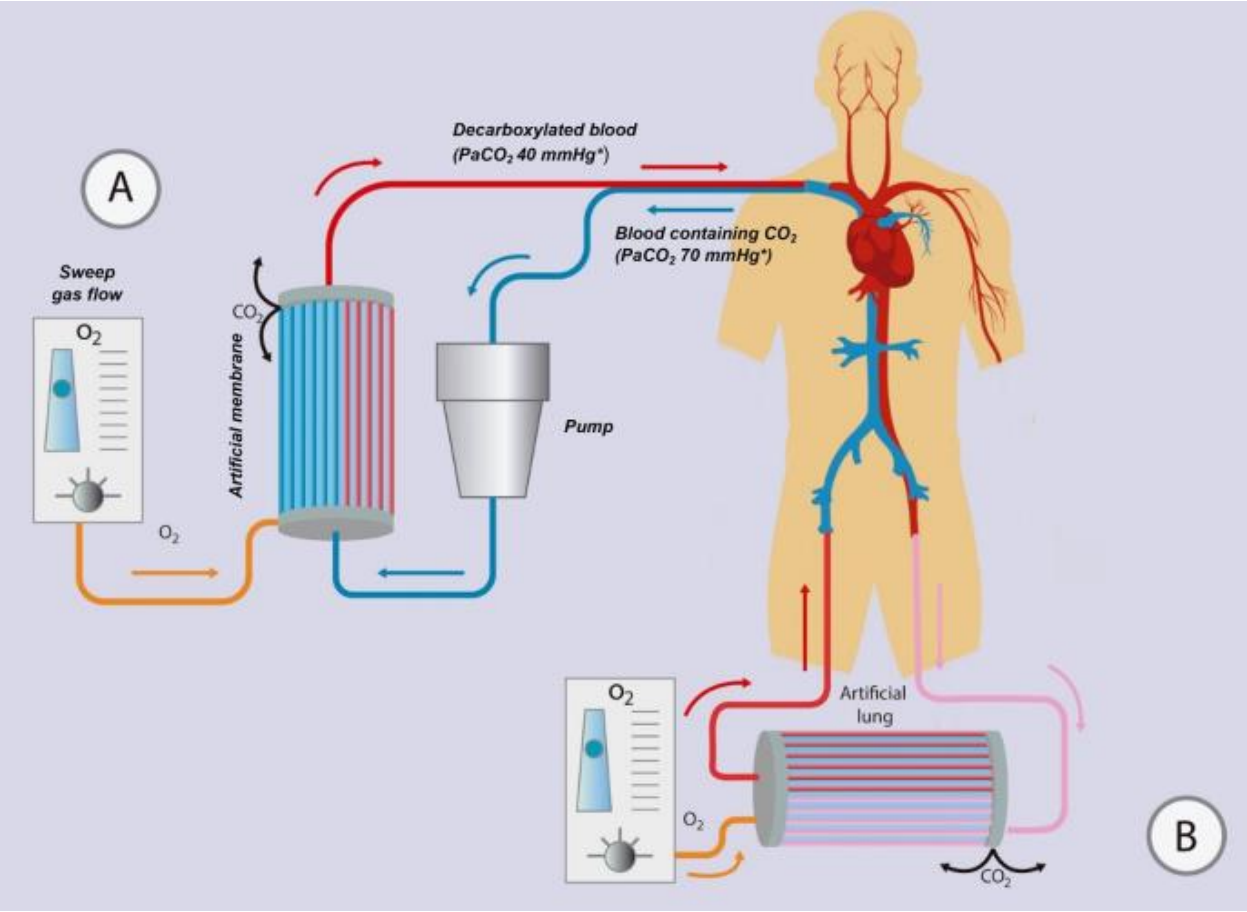
James J. McNamee, MB, ChB; Michael A. Gillies, MD; Nicholas A. Barrett, MB, ChB; Gavin D. Perkins, MD; William Tunnicliffe, MSc; Duncan Young, DM; Andrew Bentley, MD; David A. Harrison, PhD; Daniel Brodie, MD; Andrew J. Boyle, MB, ChB; Jonathan E. Millar, PhD; Tamas Szakmany, PhD; Jonathan Bannard-Smith, MB, ChB; Redmond P. Tully, MBBS; Ashley Agus, PhD; Cliona McDowell, MSc; Colette Jackson; Daniel F. McAuley, MD; for the REST Investigators

- Design: multicenter, randomized, open-label, pragmatic clinical trial
- Population: 405 ARDS (time from onset of hypoxemia ≤ 48hrs, P/F < 150) from 51 ICUs in the UK
- Period: May 2016 ~ Dec 2019
- Intervention vs. control: LTV ventilation facilitated by $ECCO_2R$ vs standard care with conventional LTV ventilation
- Primary outcome: 90d-mortality

JAMA. 2021 Sep 21;326(11):1013-1023

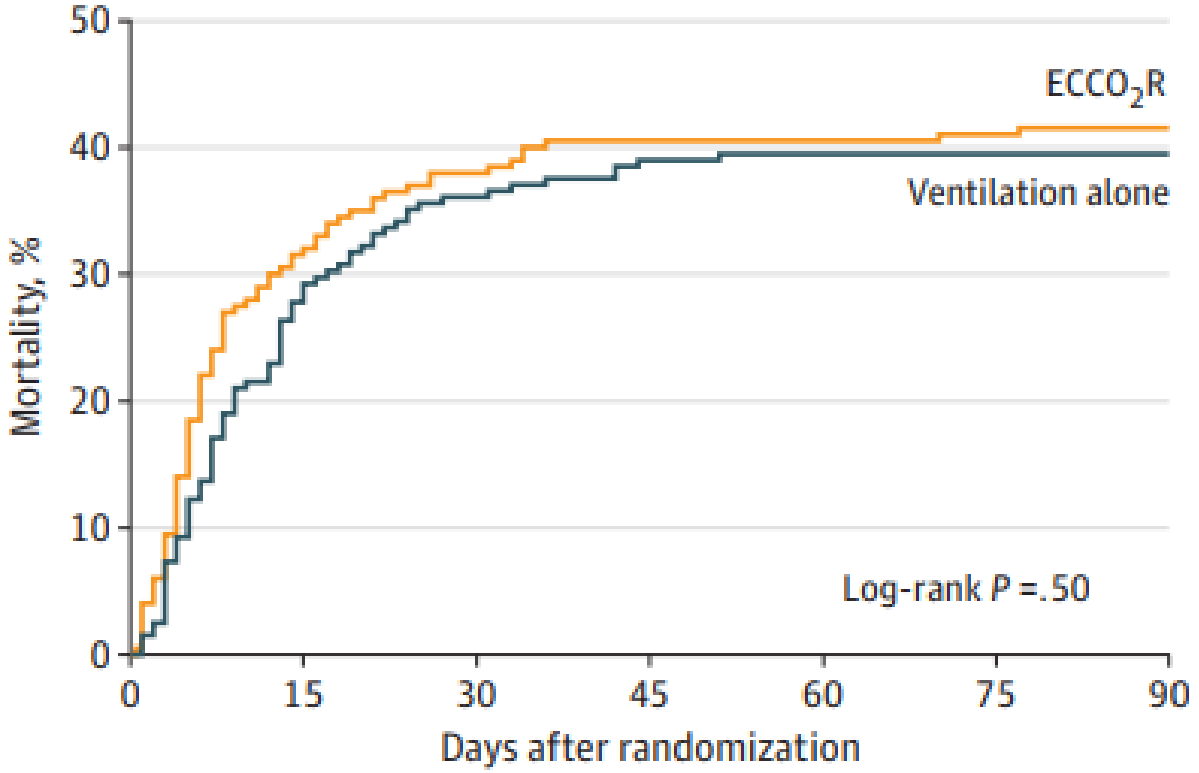
Interventions

- VenovenousECCO$_2$R
  - **TV ≤ 3ml/kg PBW**
  - P_{plat} < 25cmH2O
  - Sweep gas 10, blood flow 350~450ml/min
  - RR < 35/min
  - pH > 7.20
  - PaO2 7~10kPa (SpO2 88~95%)
  - The intervention was continued for at least 48 hours
- Standard care
  - TV 6 mL/kg PBW
  - PEEP set based on the ARDSNetwork trial



J Intensive Care Soc. 2017 May;18(2):159-169
Ann Intensive Care. 2019 Jul 2;9(1):79

No difference in mortality between $ECCO_2R$ and ventilator alone



No. at risk							
$ECCO_2R$	200	137	124	119	119	118	117
Ventilation alone	205	148	131	125	124	124	124

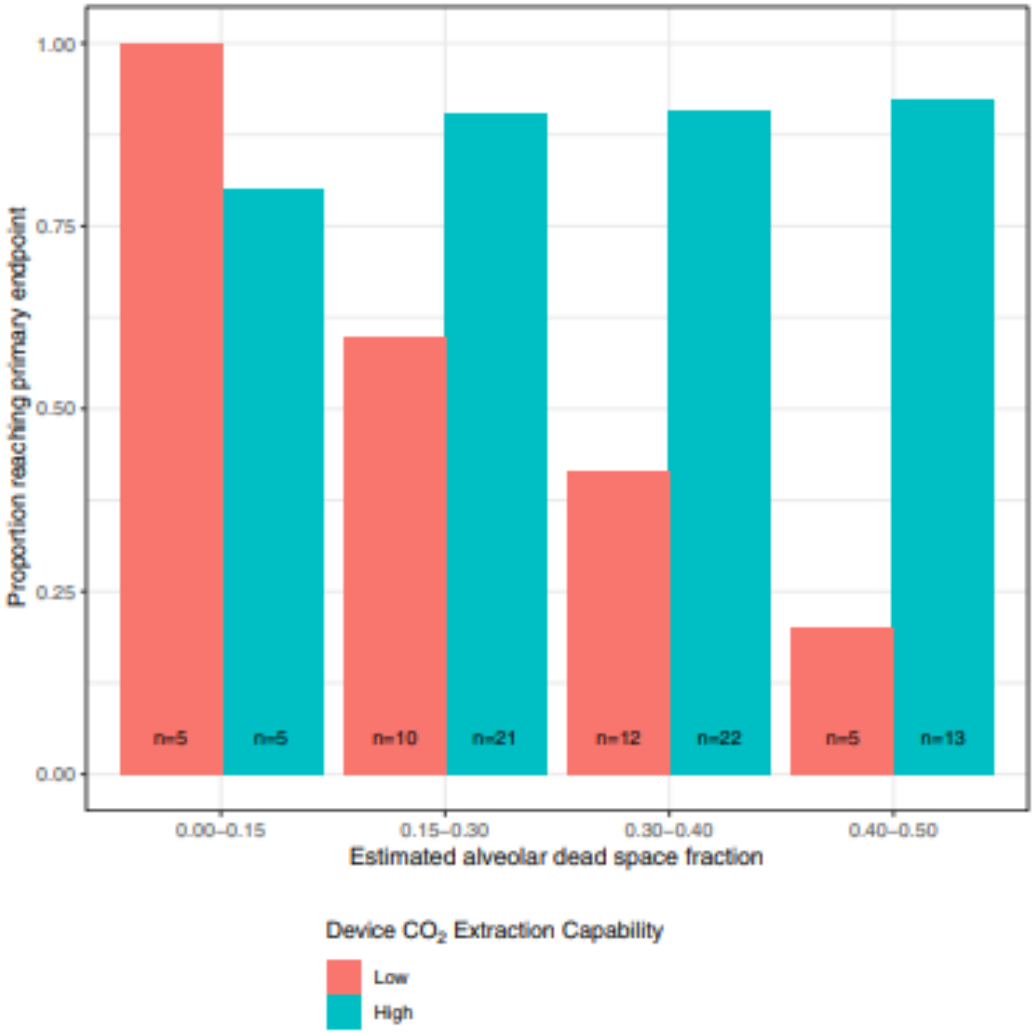
90d mortality 41.5% vs 39.5%
RR 1.05 (95% CI 0.83 to 1.33); p=0.68

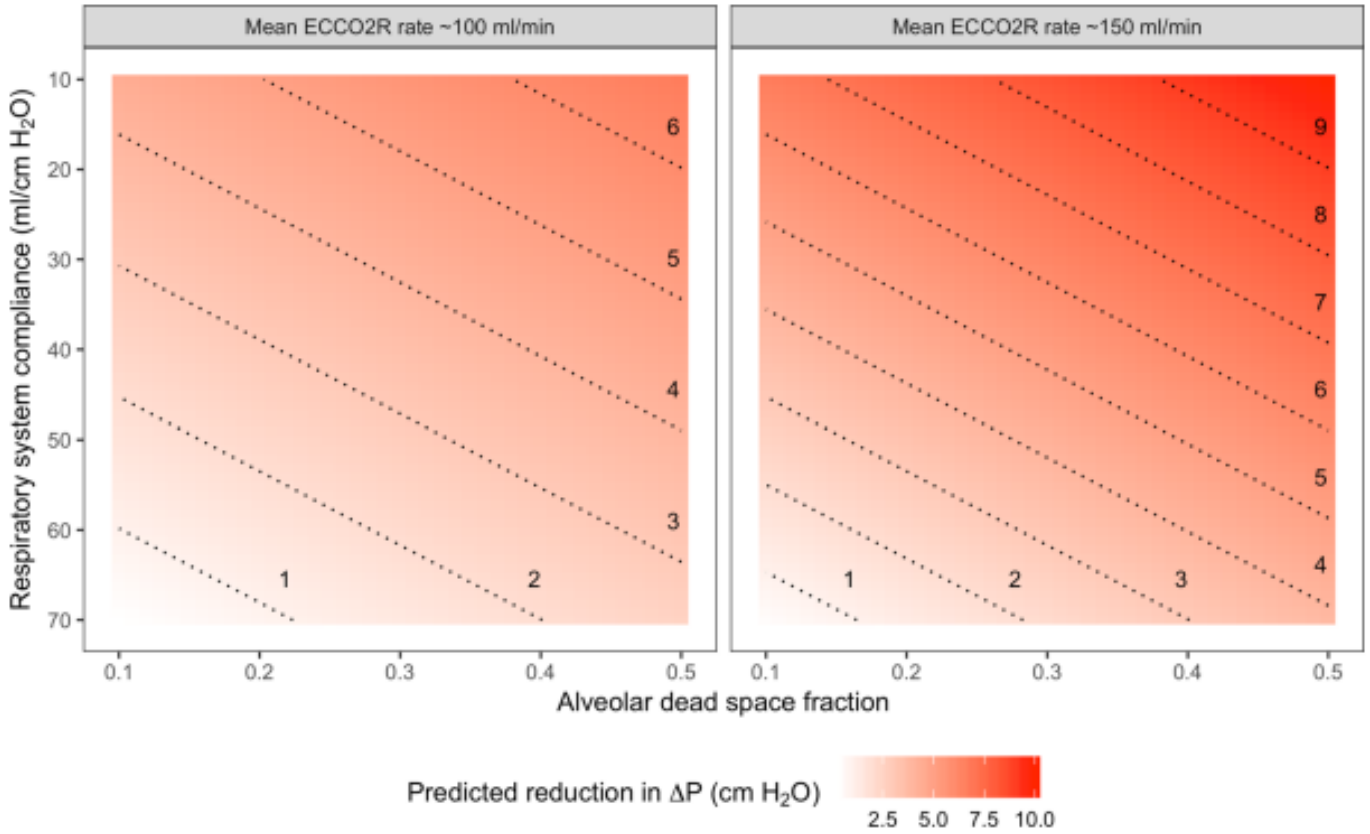
VFDs 7.1 vs 9.2 days
MD −2.1days (−3.8 to 0.3); p=0.02

Increased adverse events with use of an ECCO2R device

Adverse event	$ECCO_2R$ (n = 202)		Ventilation alone (n = 210)	
	No. of events	No. (%) of patients	No. of events	No. (%) of patients
Adverse events[a]	168	106 (52.5)	61	48 (22.9)
Related to study intervention[a,b]	65	51 (25.3)	0	0
Serious adverse events[c,d]	70	62 (30.7)	20	18 (8.6)
Related to study intervention[b]	22	21 (10.4)	0	0
Adverse events of specific interest				
Bleeding at other site (excluding intracranial hemorrhage)	18	17 (8.4)	3	3 (1.4)
Intracranial hemorrhage	10	10 (5.0)	2	2 (1.0)
Device failure causing adverse event	9	9 (4.5)	0	0
Bleeding at cannula site	8	8 (4.0)	0	0
Infectious complications[e]	7	7 (3.5)	1	1 (0.5)
Heparin-induced thrombocytopenia	4	4 (2.0)	0	0
Hemolysis	3	3 (1.5)	0	0
Ischemic stroke	1	1 (0.5)	3	3 (1.4)
Serious adverse events of specific interest[f]				
Bleeding at other site (excluding intracranial hemorrhage)	6	6 (3.0)	1	1 (0.5)
Intracranial hemorrhage	9	9 (4.5)	0	0
Infectious complications[e]	5	5 (2.5)	0	0
Device failure causing serious adverse event	2	2 (1.0)	0	0
Heparin-induced thrombocytopenia	1	1 (0.5)	0	0
Ischemic stroke	1	1 (0.5)	3	3 (1.4)

Determinants of the effect of extracorporeal carbon dioxide removal in the SUPERNOVA trial





Intensive Care Med (2019) 45:1219–1230

Ventilatory Variables and mechanical power

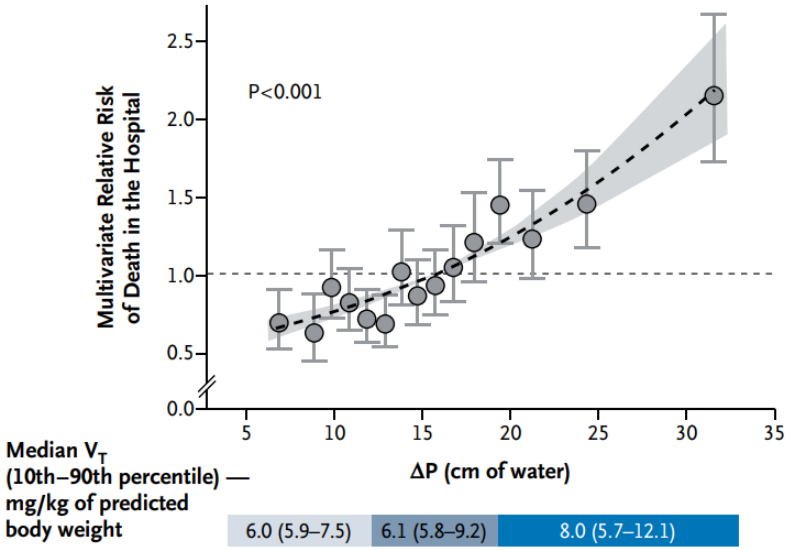
AJRCCM. 2021 Aug 1;204(3):303-311

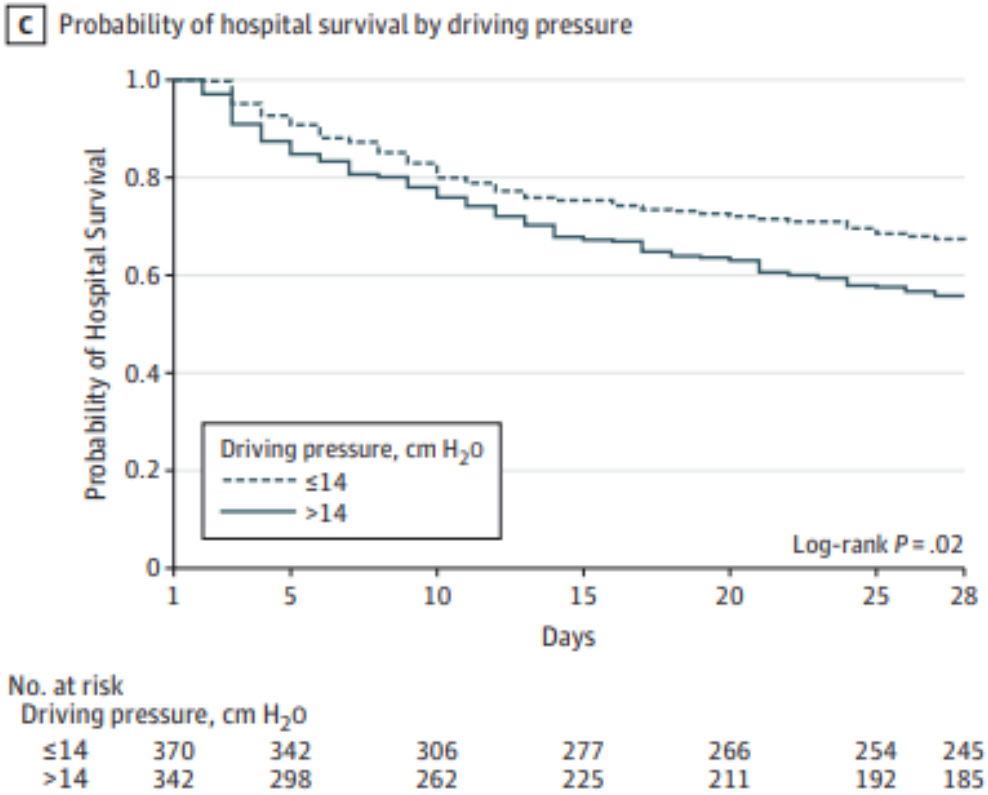
Driving pressure

SPECIAL ARTICLE

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.





NEJM 2015 Feb 19;372(8):747-55
JAMA. 2016 Feb 23;315(8):788-800

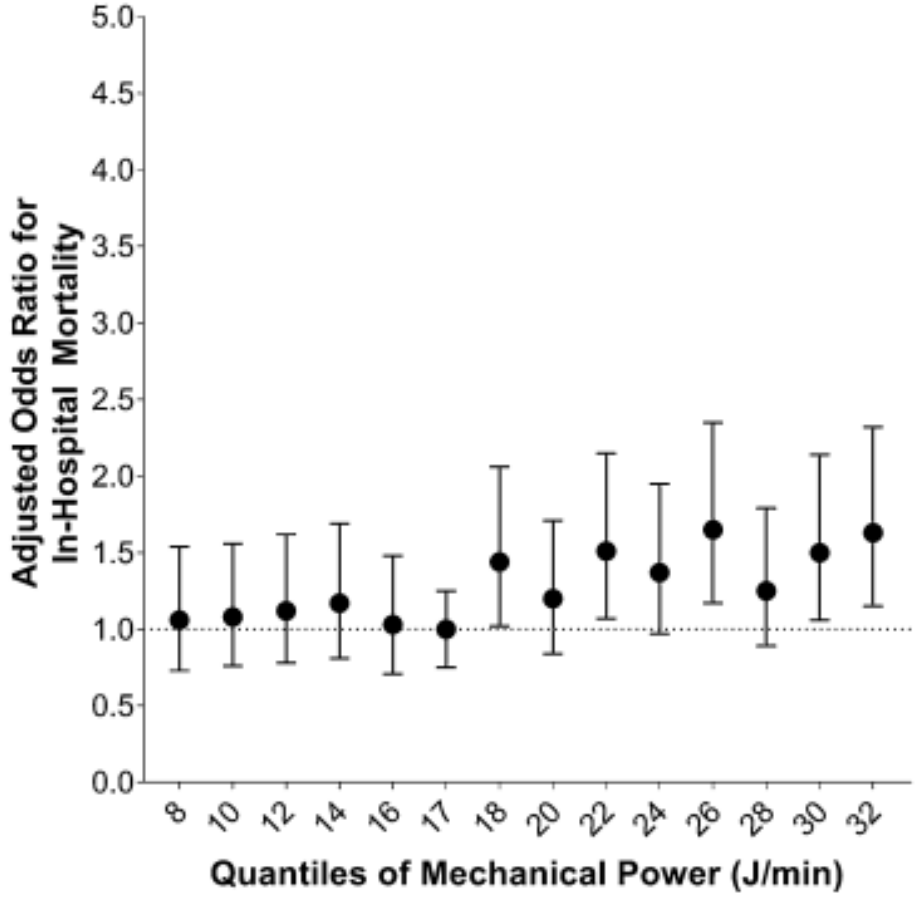
Mechanical power

ORIGINAL

Ventilator-related causes of lung injury: the mechanical power

L. Gattinoni[1*], T. Tonetti[1], M. Cressoni[2], P. Cadringher[3], P. Herrmann[1], O. Moerer[1], A. Protti[3], M. Gotti[2], C. Chiurazzi[2], E. Carlesso[2], D. Chiumello[4] and M. Quintel[1]

$$\text{Power}_{rs} = \text{RR} \cdot \left\{ \Delta V^2 \cdot \left[\frac{1}{2} \cdot \text{EL}_{rs} + \text{RR} \cdot \frac{(1 + I:E)}{60 \cdot I:E} \cdot R_{aw} \right] + \Delta V \cdot \text{PEEP} \right\}$$



Intensive Care Med. 2016 Oct;42(10):1567-1575
Intensive Care Med. 2018 Nov;44(11):1914-1922

The impact of the specific components of mechanical power on mortality

SNUH 분당서울대학교병원 SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

ORIGINAL ARTICLE

Ventilatory Variables and Mechanical Power in Patients with Acute Respiratory Distress Syndrome

Eduardo L. V. Costa[1,2], Arthur S. Slutsky[3,4], Laurent J. Brochard[3,4*], Roy Brower[5], Ary Serpa-Neto[6], Alexandre B. Cavalcanti[7], Alain Mercat[8], Maureen Meade[9], Caio C. A. Morais[1], Ewan Goligher[3,10,11], Carlos R. R. Carvalho[1], and Marcelo B. P. Amato[1]

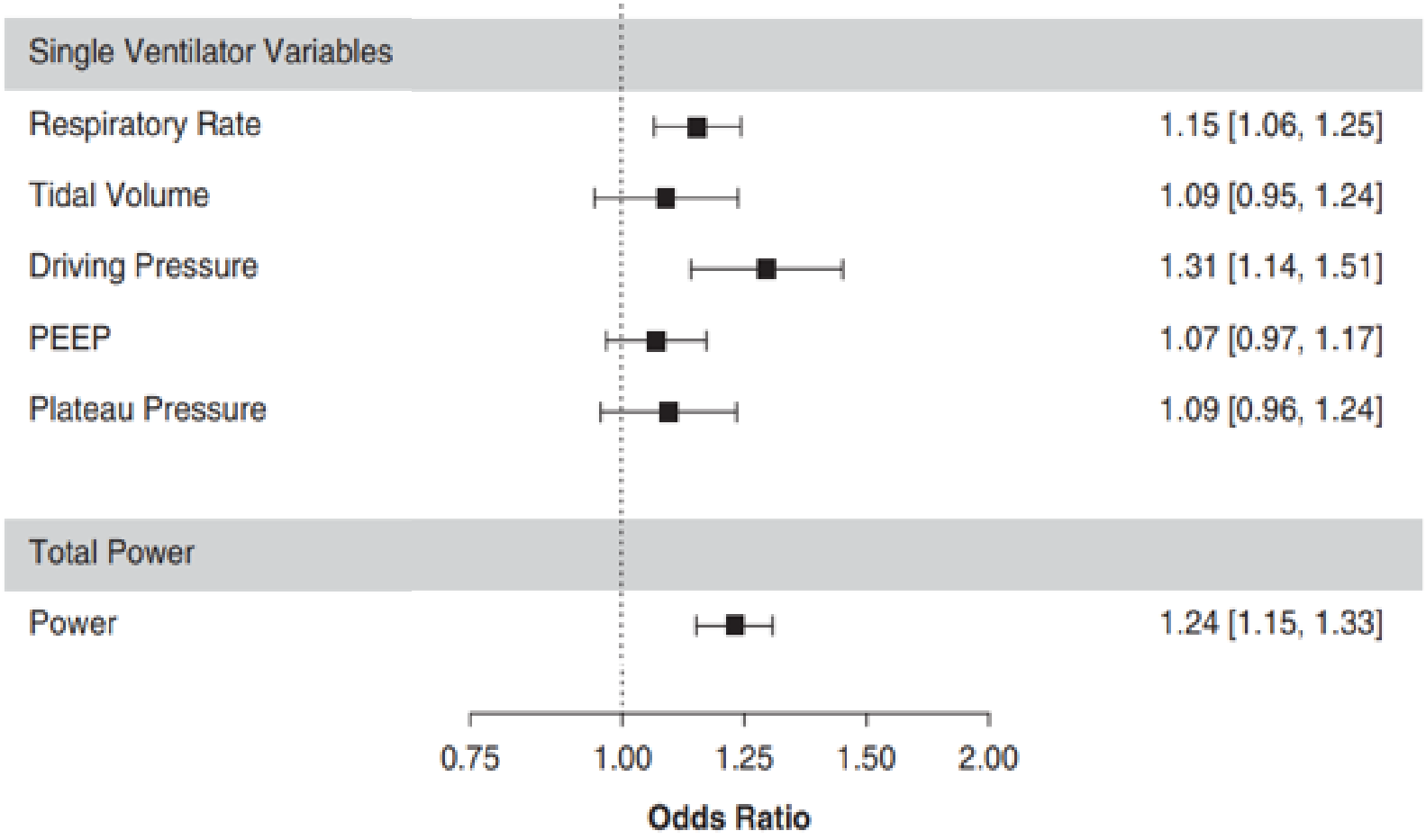
[1]Laboratório de Pneumologia, Laboratório de Investigação Médica 09, Disciplina de Pneumologia, Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, São Paulo, Brazil; [2]Instituto de Ensino e Pesquisa, Hospital Sírio-Libanes, São Paulo, São Paulo, Brazil; [3]Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada; [4]Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada; [5]Division of Pulmonary and Critical Care Medicine, School of Medicine, Johns Hopkins University, Baltimore, Maryland; [6]Hospital Israelita Albert Einstein, São Paulo, São Paulo, Brazil; [7]Instituto de Pesquisas Hospital do Coração–Hospital do Coração, São Paulo, São Paulo, Brazil; [8]Département de Médecine Intensive–Réanimation, Centre Hospitalier Universitaire d'Angers, Université d'Angers, Angers, France; [9]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [10]Division of Respirology, Department of Medicine, University Health Network and Sinai Health System, Toronto, Ontario, Canada; and [11]Toronto General Hospital Research Institute, Toronto General Hospital, Toronto, Ontario, Canada

ORCID IDs: 0000-0002-6941-3626 (E.L.V.C.); 0000-0002-0990-6701 (E.G.).

- Patient-level data of 4,549 patients, obtained from MIMIC-III database and from six RCTs on protective mechanical ventilation.
- Only patients under controlled mechanical ventilation were included.

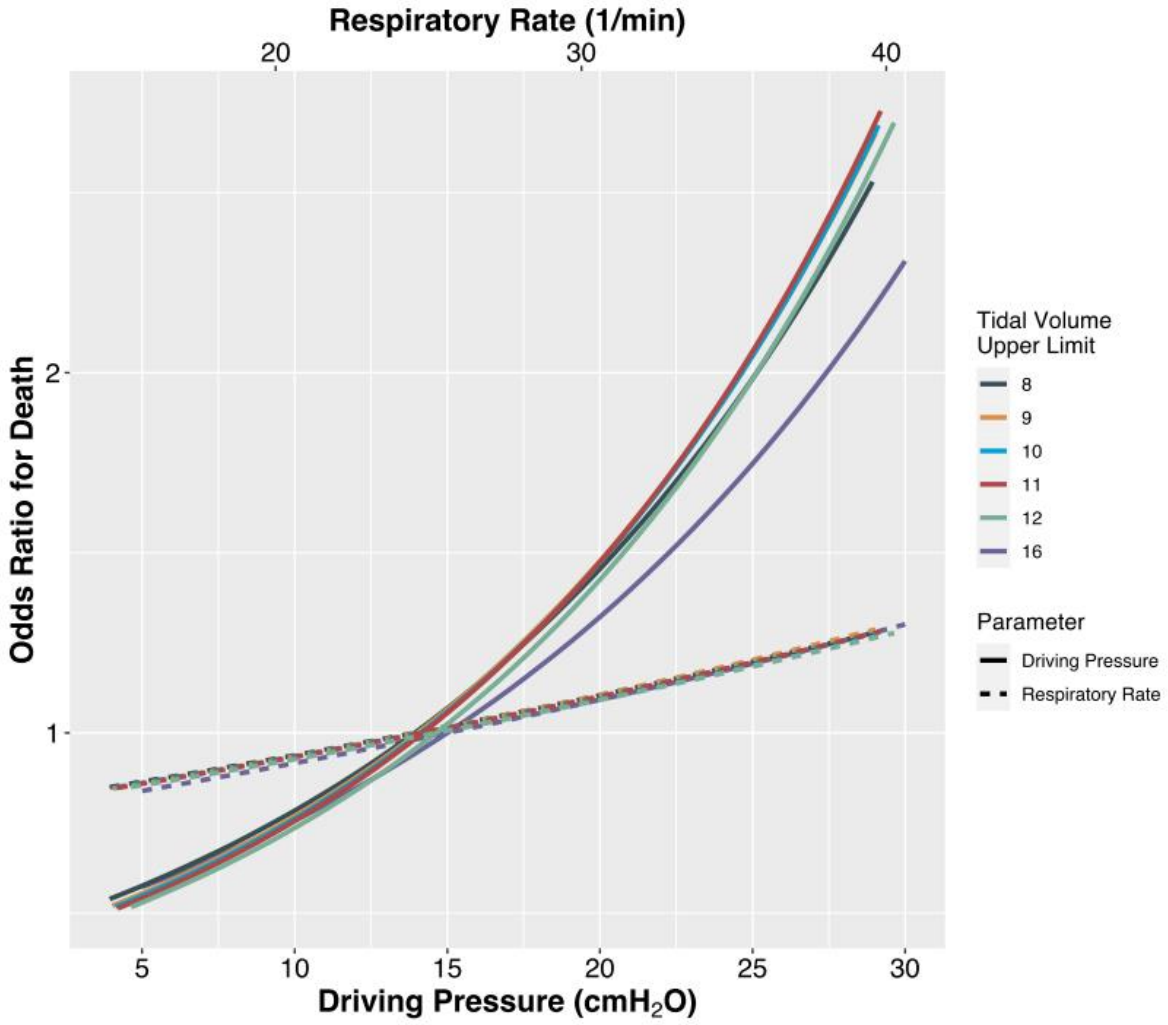
AJRCCM. 2021 Aug 1;204(3):303-311

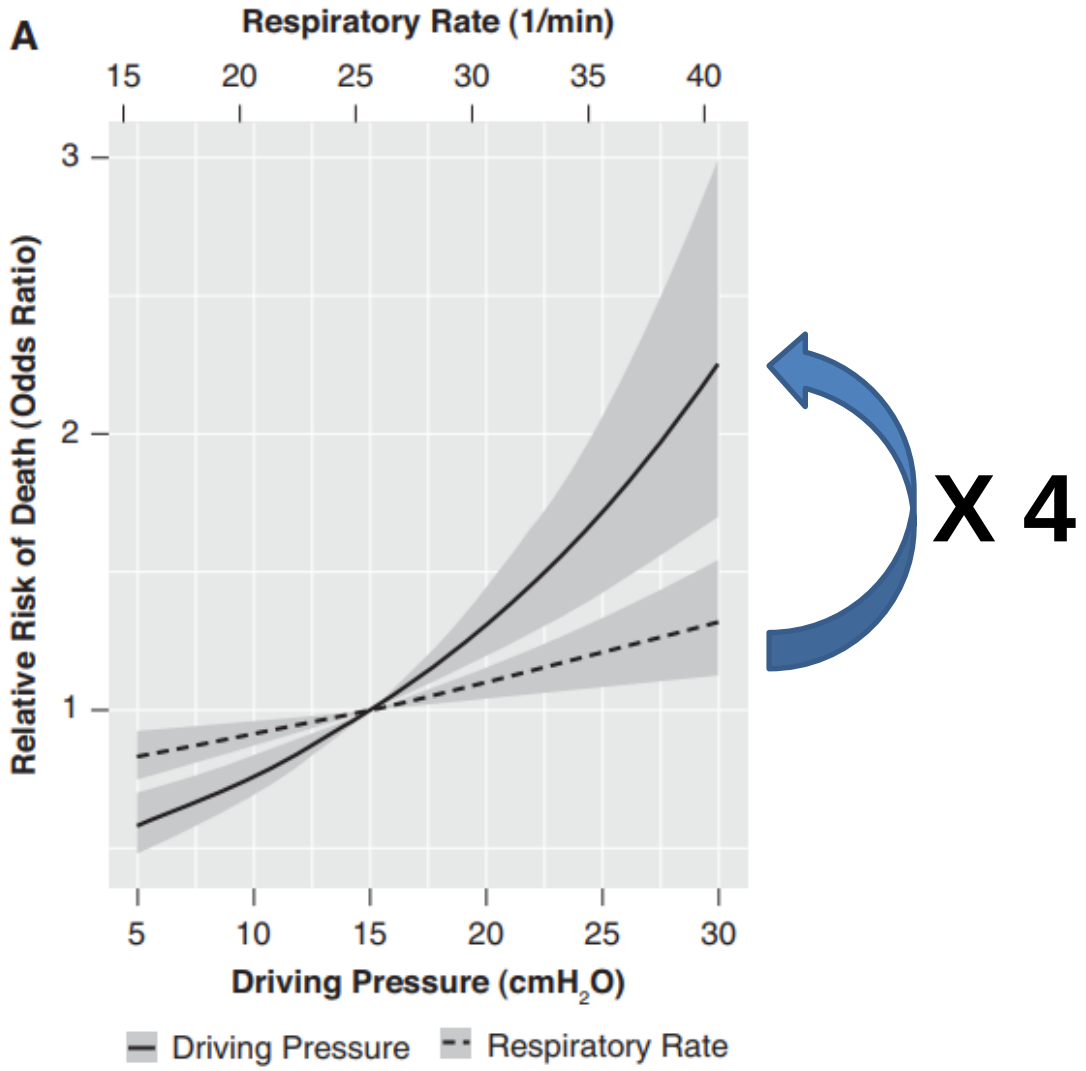
Logistic regression for mortality



Covariates commonly used over the Models : trial, study arm, respiratory system compliance, ventilatory ratio, arterial pH, $PaCO_2$, PaO_2/FIO_2

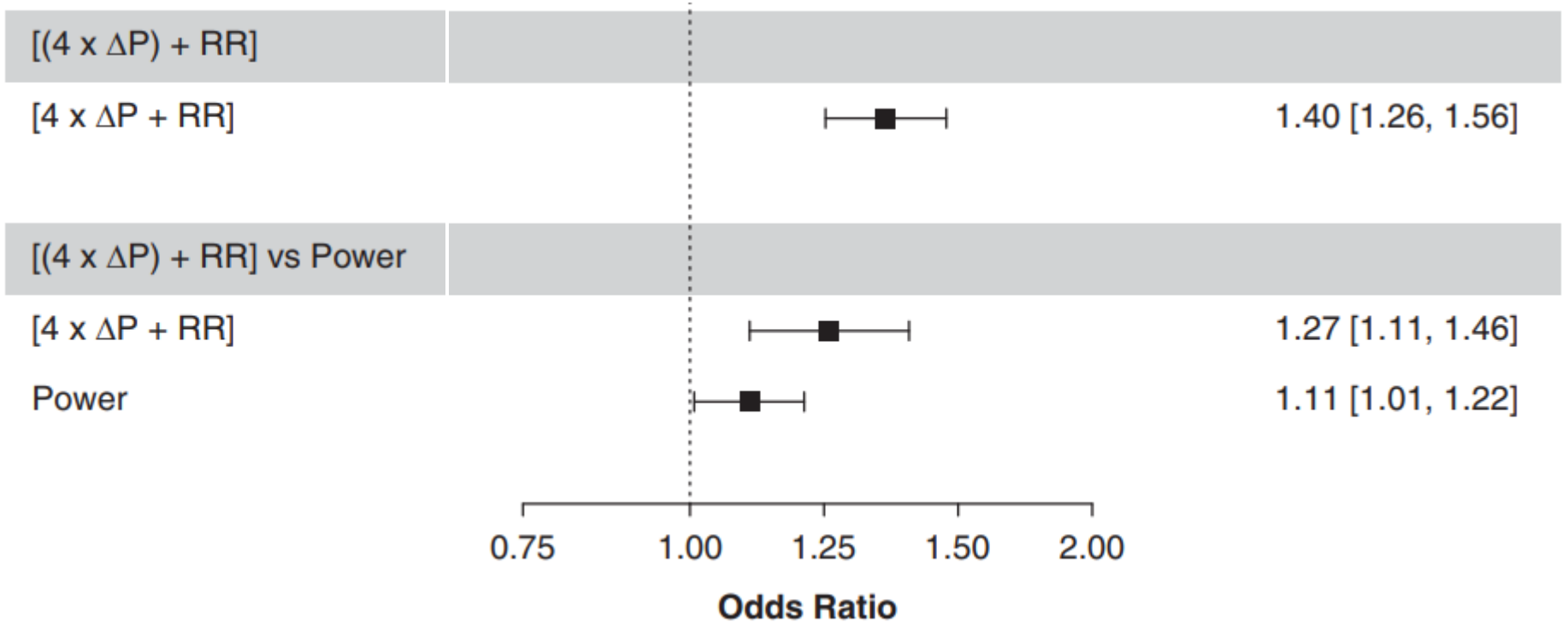
Modeled OR for death according to either △P or RR





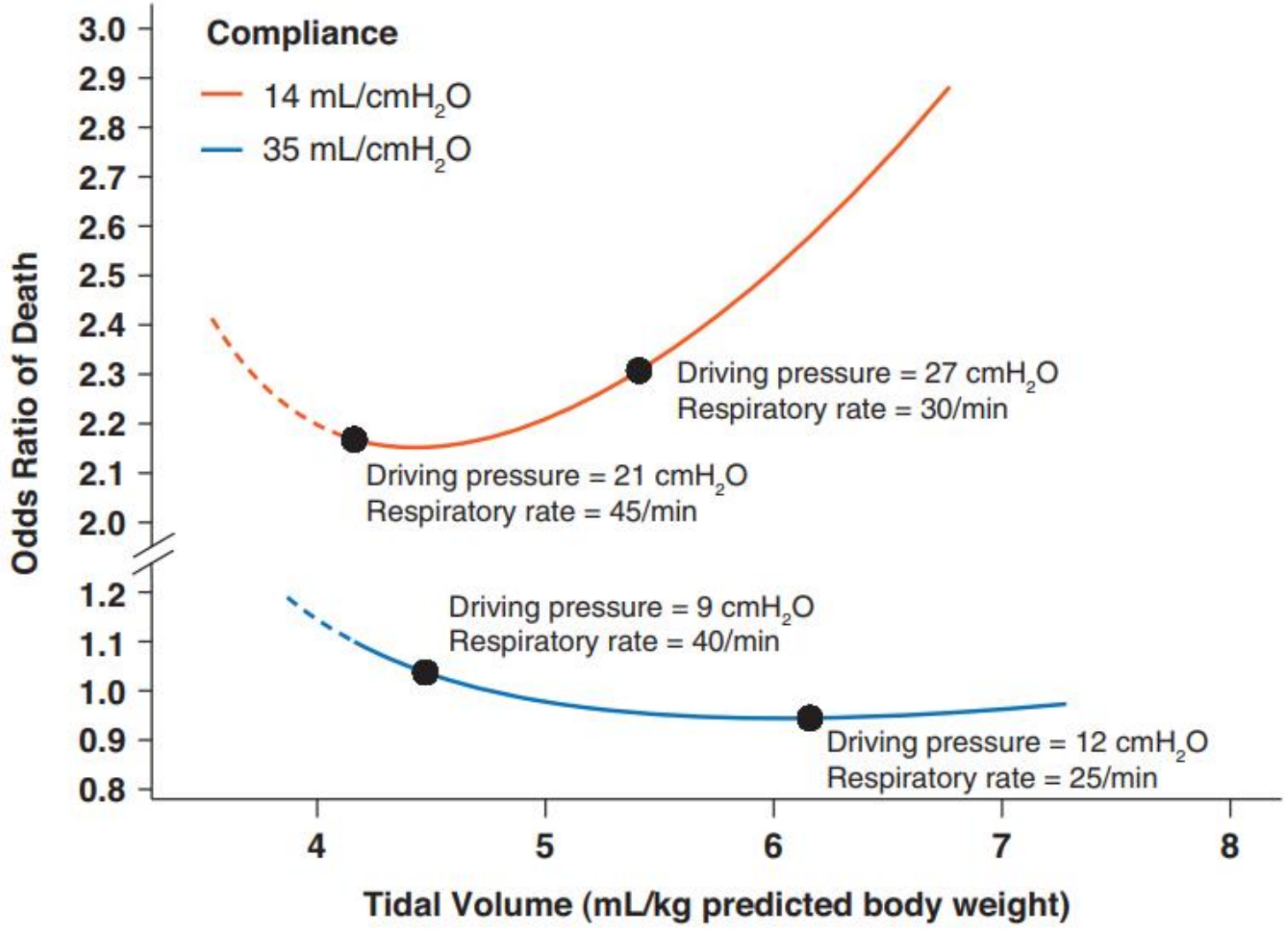
Logistic regression for mortality

4DPRR



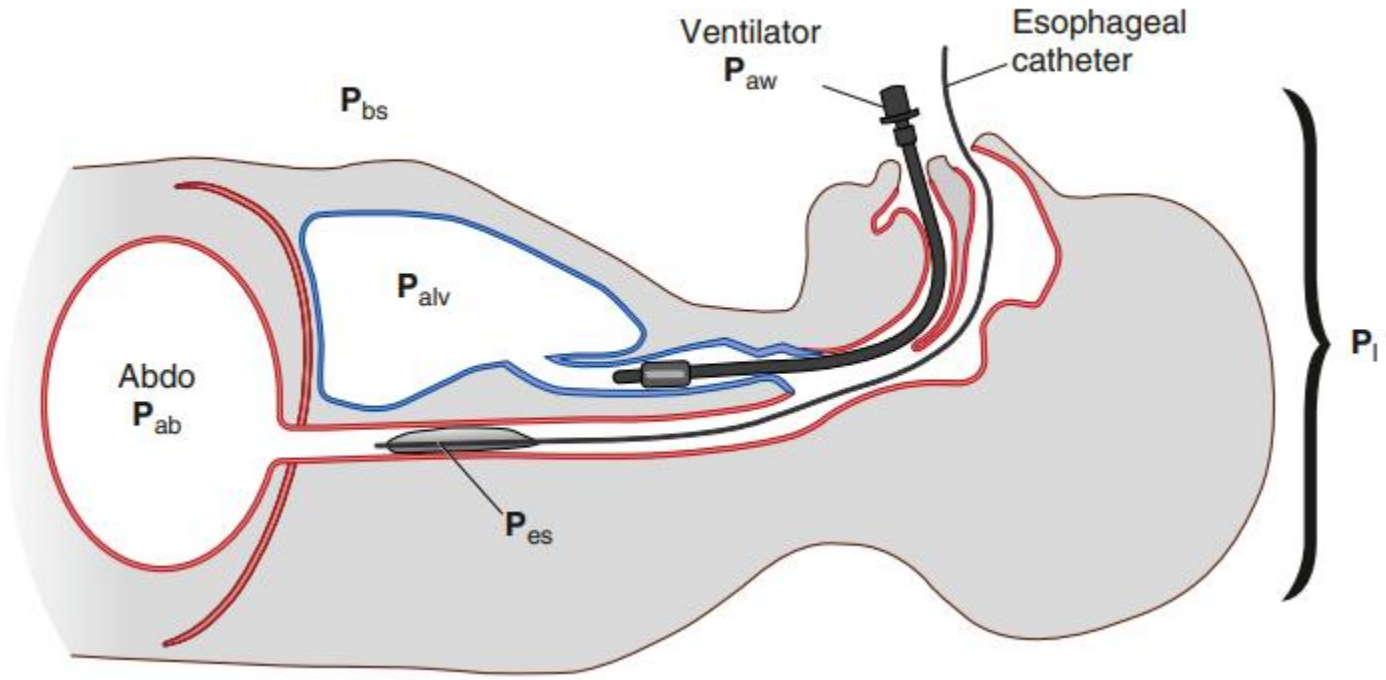
Covariates commonly used over the Models : trial, study arm, respiratory system compliance, ventilatory ratio, arterial pH, PaCO2, PaO2/FIO2

Isocapnic Curves



Esophageal pressure guided PEEP

AJRCCM. 2021 Nov 15;204(10):1153-1163



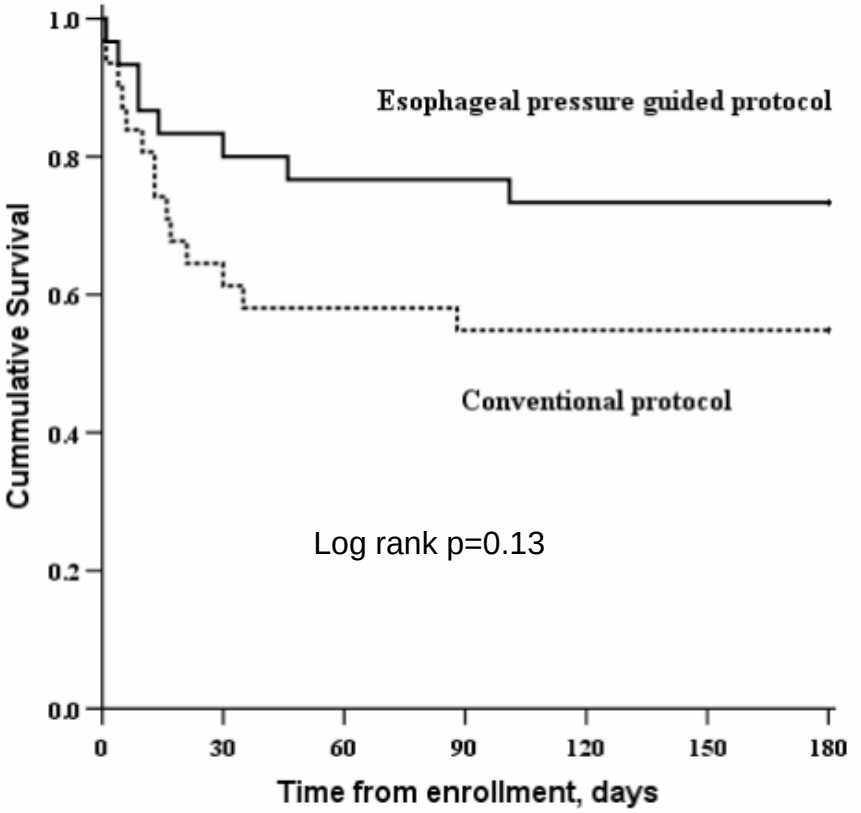
EPVent Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 13, 2008 VOL. 359 NO. 20

Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury

Daniel Talmor, M.D., M.P.H., Todd Sarge, M.D., Atul Malhotra, M.D., Carl R. O'Donnell, Sc.D., M.P.H., Ray Ritz, R.R.T., Alan Lisbon, M.D., Victor Novack, M.D., Ph.D., and Stephen H. Loring, M.D.



P_{ES}-guided PEEP vs empiric low PEEP

Esophageal-Pressure–Guided Group

FiO_2	0.4	0.5	0.5	0.6	0.6	0.7	0.7	0.8	0.8	0.9	0.9	1.0
P_{Lexp}	0	0	2	2	4	4	6	6	8	8	10	10

Control Group

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

Difference in 28-day mortality adjusting for APACHEII: RR 0.46 (95%CI 0.19–1.0); p=0.049

NEJM. 2008 Nov 13;359(20):2095-104

EPVent-2 Trial

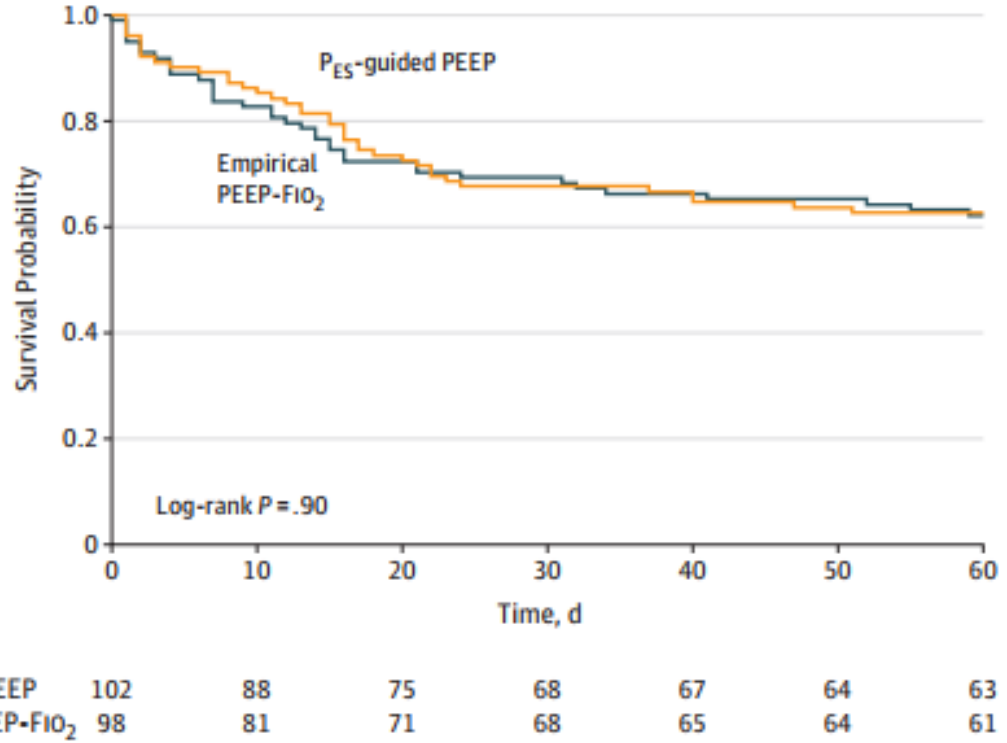
Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure–Guided Strategy vs an Empirical High PEEP-FIO_2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Jeremy R. Beitler, MD, MPH; Todd Sarge, MD; Valerie M. Banner-Goodspeed, MPH; Michelle N. Gong, MD, MSc; Deborah Cook, MD; Victor Novack, MD, PhD; Stephen H. Loring, MD; Daniel Talmor, MD, MPH; for the EPVent-2 Study Group



P_{ES}-guided PEEP vs empiric high PEEP

Control FiO2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
EPVent	5	5-8	8-10	10	10-14	14	14-18	20-24
EPVent-2	5-10	10-18	18-20	20	20	20-22	22	22-24

JAMA. 2019 Mar 5;321(9):846-857

The *post hoc* reanalysis of the EPVent-2 trial

SNUH 분당서울대학교병원 SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

ORIGINAL ARTICLE

Effect of Esophageal Pressure–guided Positive End-Expiratory Pressure on Survival from Acute Respiratory Distress Syndrome

A Risk-based and Mechanistic Reanalysis of the EPVent-2 Trial

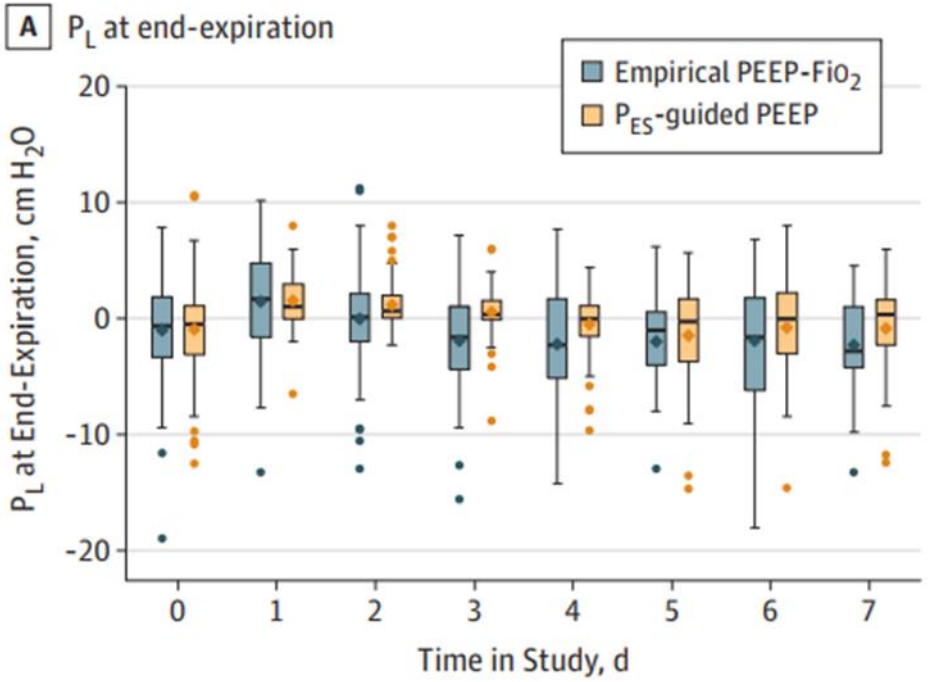
Todd Sarge[1], Elias Baedorf-Kassis[2], Valerie Banner-Goodspeed[1], Victor Novack[3], Stephen H. Loring[1], Michelle N. Gong[4], Deborah Cook[5], Daniel Talmor[1], and Jeremy R. Beitler[6]; for the EPVent-2 Study Group

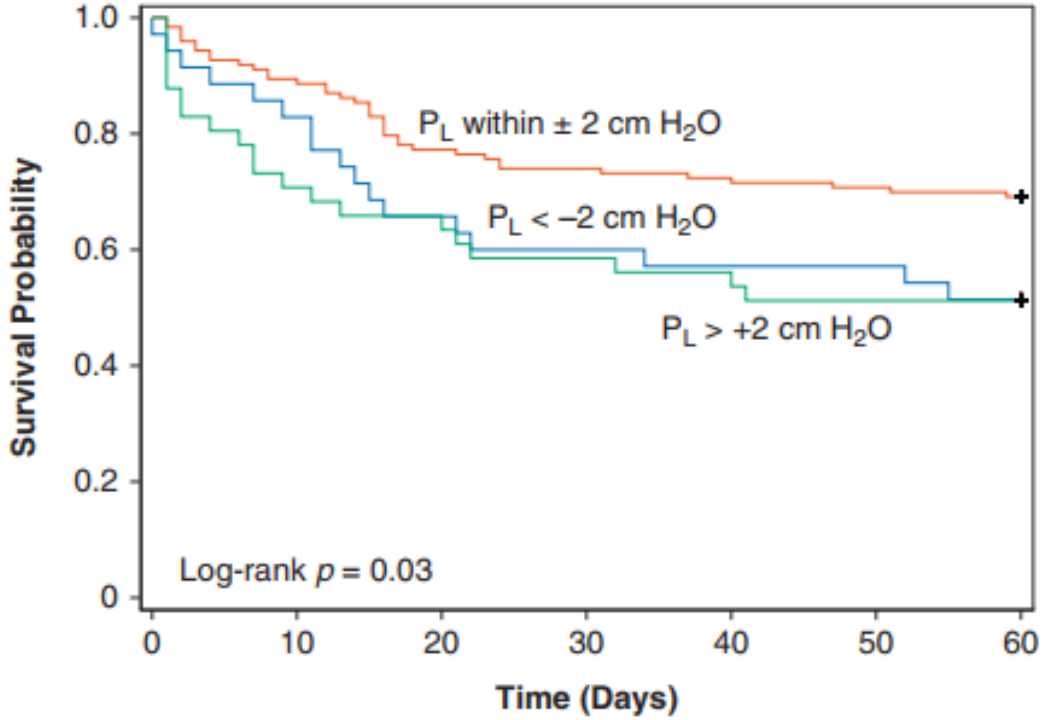
[1]Department of Anesthesia, Critical Care, and Pain Medicine and [2]Division of Pulmonary and Critical Care Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; [3]Soroka Clinical Research Center, Soroka University Medical Center, Beer-Sheva, Israel; [4]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York; [5]St. Joseph's Hospital, McMaster University, Hamilton, Ontario, Canada; and [6]Center for Acute Respiratory Failure, Division of Pulmonary, Allergy, and Critical Care Medicine, NewYork-Presbyterian Hospital, College of Physicians and Surgeons, Columbia University, New York, New York

ORCID ID: 0000-0003-0797-2374 (J.R.B.).

AJRCCM. 2021 Nov 15;204(10):1153-1163

Survival analysis by end-expiratory transpulmonary pressure



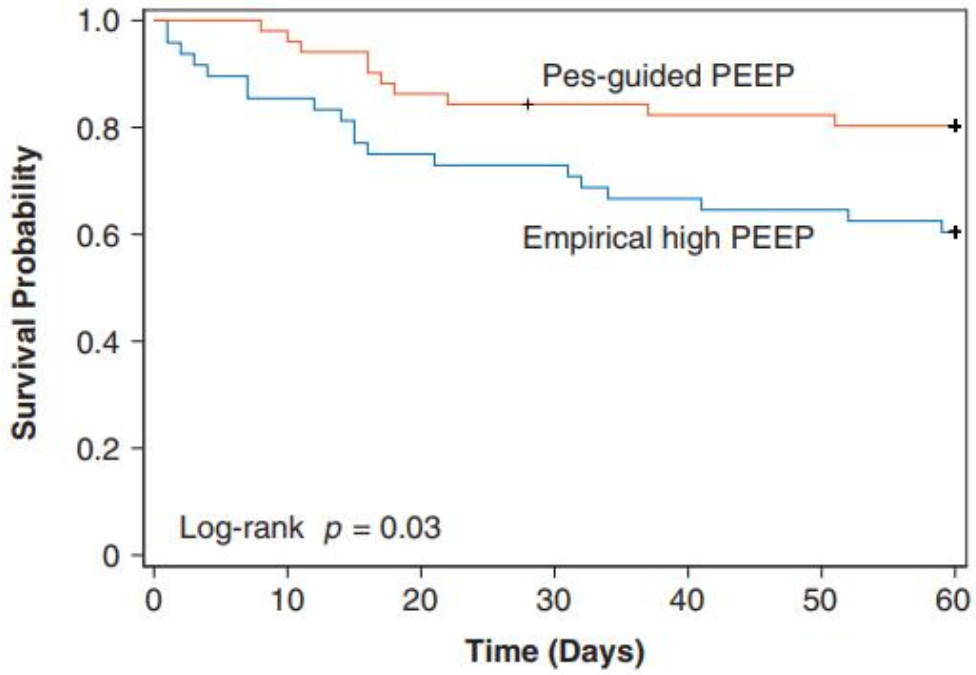


No. at Risk

P_L within ± 2 cm H_2O	123	110	95	91	89	87	85
P_L < –2 cm H_2O	35	29	23	21	20	20	18
P_L > +2 cm H_2O	41	29	27	24	23	21	21

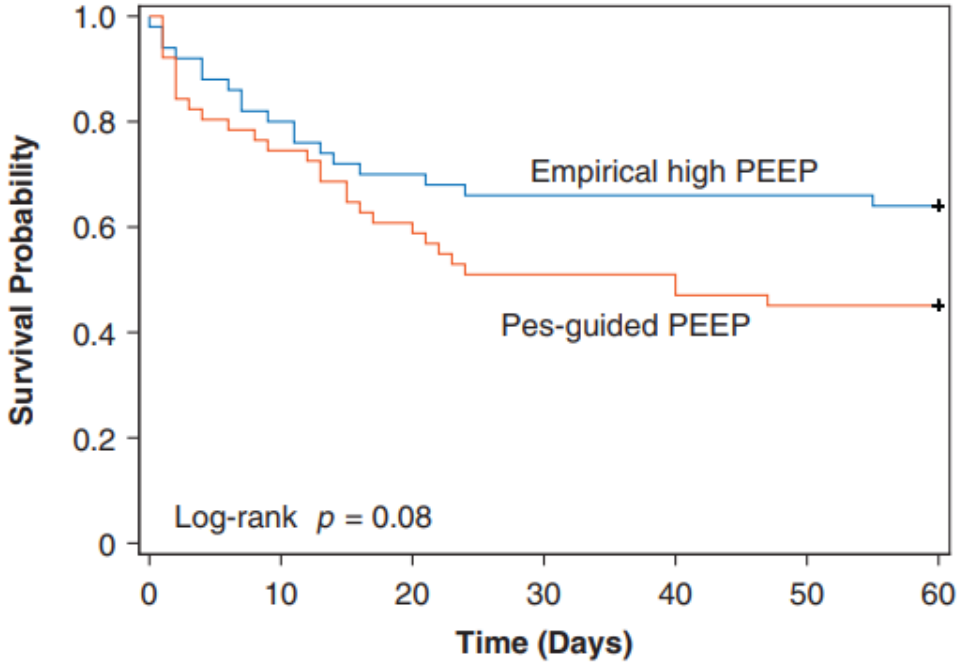
Treatment effects by APACHE II score

A Low APACHE-II



No. at Risk							
Pes-guided PEEP	51	50	44	42	41	41	40
Empirical high PEEP	48	41	36	35	32	31	29

B High APACHE-II



No. at Risk							
Pes-guided PEEP	51	38	31	26	26	23	23
Empirical high PEEP	50	40	35	33	33	33	32

Summary

- 1. Temperature control after cardiac arrest
  - Active fever control, BT <37.7 °C
- 2. Fluid in ICU
  - Balanced solution = Normal saline
- 3. Oxygen therapy in ICU
  - Low-normal PaO2 target = High-normal PaO2 target
- 4. ARDS
  - $ECCO_2R$ in Hypoxemic respiratory failure
    - $ECCO_2R$ < Conventional LTV
  - Ventilatory Variables and mechanical power
    - “Driving pressure” and “RR” are all that matters.
  - Pes-guided PEEP
    - Beneficial in patients with less multiorgan dysfunction
    - Set PEEP to titrate “End-expiratory PL” close to 0 cmH_2O

Thank You