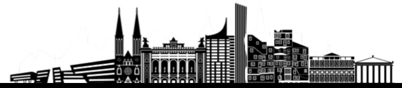
XXX International Symposium of Mechanical Ventilation of Albert Einstein Hospital
Albert Einstein Hospital, São Paolo, Brazil
August 16, 2023; 10:30–11:00 am BRT

Advances in Mechanical Ventilation

permissive *vs* aggressive ventilation






Disclosures

- until January 2021 Xenios/Fresenius, Germany
- until January 2023 Hamilton Medical AG, Switzerland

Agenda

- permissive *vs* aggressive ventilation
- low V_T ventilation
- lower or higher PEEP
- ΔP and MP
- prioritization of settings

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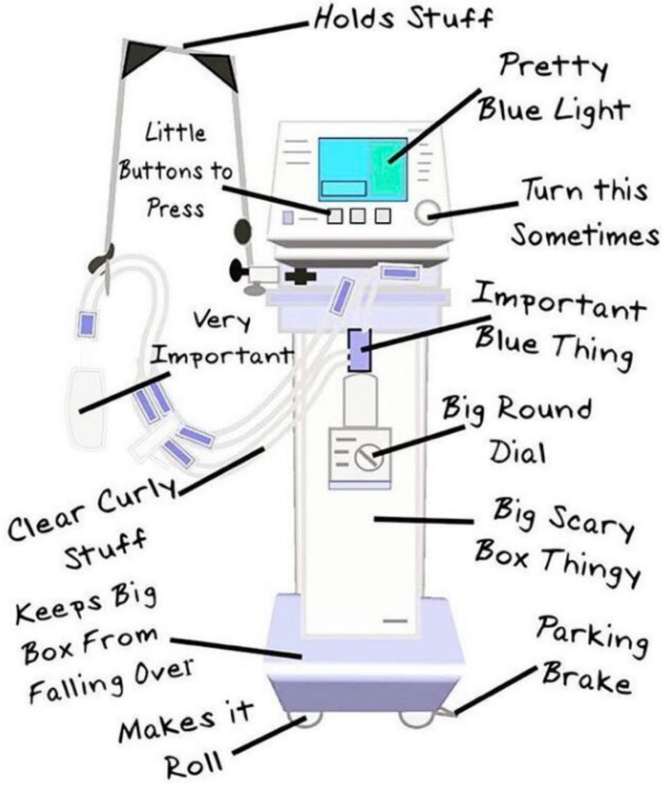
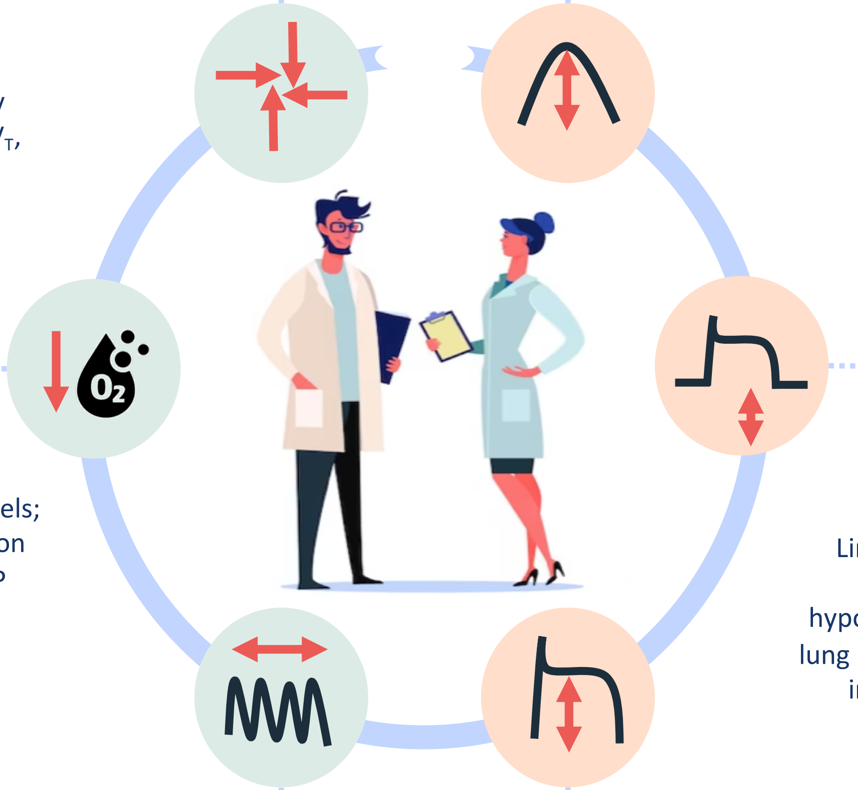


ventilator settings in critically ill patients—prioritize permissive over aggressive ventilation



Step 1

Use low V_T

Reduce the size of V_T; reductions might be more beneficial in patients with less compliant lungs.

Rational

Volutrauma

Randomized clinical trials and observational studies have shown benefit from low V_T; ventilation with low V_T might lead to hypoxemia; a compensatory increase in RR may be harmful.

Step 2

Do not use high PEEP by default

Limit use of high PEEP to patients with severe hypoxemia, and only when lung lesions are recruitable; instead, consider prone positioning.

Rational

Atelectrauma *vs* overdistension

Randomized clinical trials could not confirm benefit from high PEEP, and observational studies even suggested harm; in some patients high PEEP could lead to overdistension rather than recruitment.

Step 3

Check ΔP and MP

If high, consider reducing V_T further; consider a change in other ventilator settings, like higher PEEP when lung lesions may be recruitable, or a longer inspiration time.

Rational

Energytrauma

Meta–analyses showed associations of higher ΔP and MP with relevant clinical outcomes; even short periods with high ΔP or high MP could be detrimental.

Step 4

Reduce the RR

In an attempt to reduce MP, reduce RR; allow the CO_2 level to rise if MP remains high.

Rational

Permissive hypercapnia

RR is an important contributor to the amount of energy transferred to the lung; lowering RR reduces MP, but may induce hypercapnia.

Step 5

Use O_2 wisely

Do not target high O_2 levels; use high FiO_2 if a reduction in V_T and use of low PEEP results in hypoxemia.

Rational

Chemotrauma

Several studies have pointed at the side–effects of hyperoxia; some randomized clinical trials have shown benefit of restrictive O_2 use; a low O_2 target, though, might increase the risk of hypoxemia.

Step 6

Integrate

Refine settings further by incrementally adjusting V_T, PEEP, RR and FiO_2.

Rational

Combining the settings

Everchanging patient conditions mandate frequent refinements; automation could be helpful, also by reducing the ICU staff workloads associated with lung–protective ventilation.

V_T, tidal volume; PEEP, positive end–expiratory pressure; ΔP, driving pressure; MP, mechanical power of ventilation; RR, respiratory rate; FiO_2, fraction of inspired O_2

Infographic on ventilation management by **Marcus Schultz,** Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

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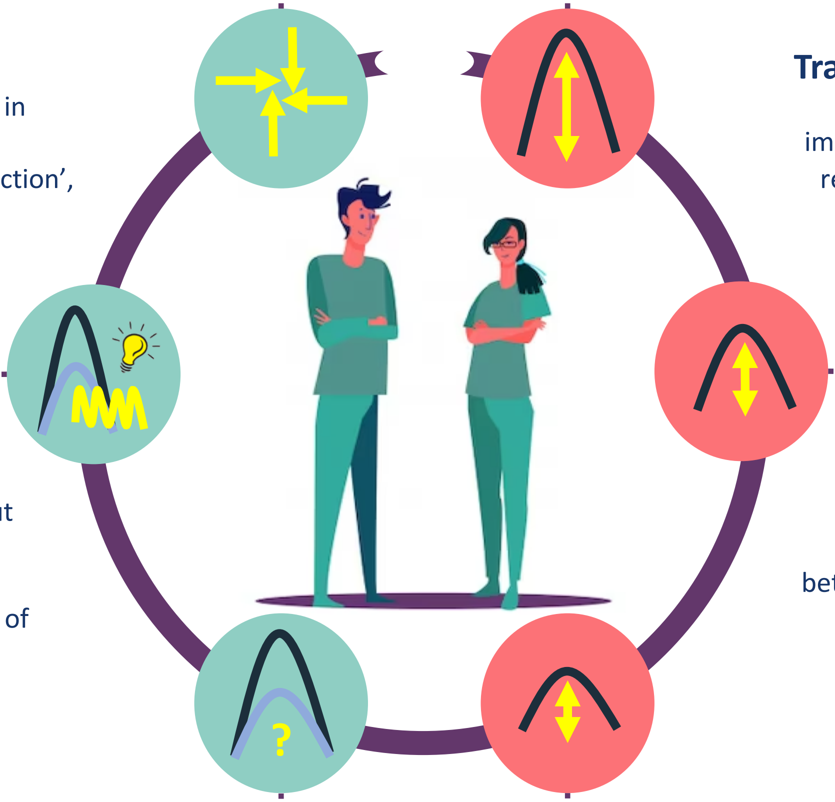
Infographic on ventilation management by **Marcus Schultz,** Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

titration of V_T in critically ill patients—there is no one–size–fits–all



Step 1

Traditionally–sized V_T

V_T of 10–15 ml/kg PBW improves oxygenation, and reduces the need for high RR.

Rational

In the early years of ICU

High V_T was traditionally used in the operating room to prevent hypoxemia, also because PEEP was hardly used in this setting; and with high V_T RR can stay low.

Step 2

Use low V_T

V_T of 10–15 ml/kg PBW clearly causes harm; it is better to use low V_T, of 6–8 ml/kg PBW, certainly in patients that are deeply sedated and paralyzed.

Rational

Low *vs* high V_T

Randomized clinical trials have shown benefit of low V_T; realize, though, that these studies were mostly conducted in deeply sedated and often paralyzed patients.

Step 3

Use even lower V_T in selected cases

A further reduction of V_T, to e.g., 4 ml/kg PBW, might be beneficial, for instance when ΔP and MP remain high, but it comes with a need for higher RR; extracorporeal removal of CO_2 might help to keep both V_T and RR low.

Rational

Ultralow V_T

Interest has moved into using even lower V_T; however, lower V_T leads to hypercapnia, and so far ultralow V_T has only been thoroughly tested under extracorporeal removal of CO_2.

Step 4

Keep V_T low in selected cases

Low V_T should be considered in deeply sedated and paralyzed patients, and in patients with a low C_{RS}, even those without ARDS; low V_T can decrease ΔP and MP in these patients as well.

Rational

Low V_T in non–ARDS patients?

One randomized clinical trial failed to show benefit of low V_T in non–ARDS patients; of note, most patients in this study were spontaneous breathing and had a relative normal C_{RS}.

Step 5

Keep an eye on RR

V_T should remain low, but not at any cost: an offsetting increase in RR could negate the benefit of low V_T, or worse.

Rational

Harm of low V_T?

Re–analysis of preceding studies suggest that low V_T could also be harmful; in patients with relative normal C_{RS} the use of low V_T could cause harm if it triggers the use of higher RR.

Step 6

Integrate

Refine the settings; keep in mind that the goal of ventilation is ‘lung–protection’, and not necessarily gas exchange.

Rational

Combining the settings

Low V_T effects both oxygenation and decarboxylation, and thus may require the use of higher FiO_2, perhaps even increases in PEEP, and adjustments in RR—but keep ΔP and MP low.

V_T, tidal volume; PBW, predicted body weight; PEEP, positive end–expiratory pressure; ΔP, driving pressure; MP, mechanical power of ventilation; C_{RS}, respiratory system compliance; RR, respiratory rate; FiO_2, fraction of inspired O_2

Infographic on V_T titrations by **Marcus Schultz**, Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

The NEW ENGLAND JOURNAL of MEDICINE

QUESTION Does the use of a lower tidal volume (V_T) with mechanical ventilation affect important clinical outcomes in ARDS patients?

CONCLUSION Ventilation with a lower V_T than is traditionally used results in decreased mortality and increases the number of days without ventilator use.

POPULATION

344 Women **516** Men

patients with ARDS

mean age: **52** years

LOCATION

ICUs in the USA

VENTILATION STRATEGIES

861 patients with mild, moderate or severe ARDS

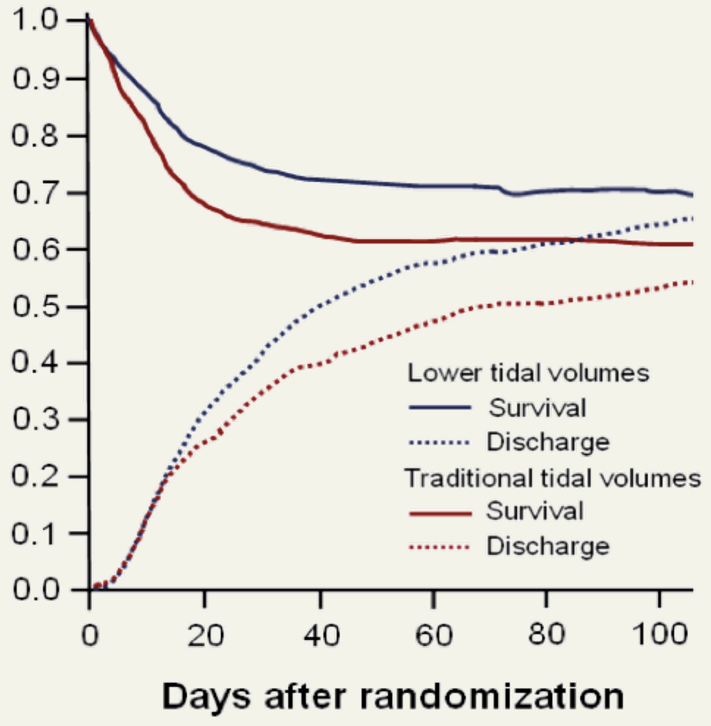
432 patients
lower V_T
(6 ml/kg)
[~ 400 to 500 ml]

429 patients
traditional V_T
(12 ml/kg)
[~1000 to 1200 ml]

(PRIMARY) OUTCOME

hospital mortality and duration of invasive ventilation

FINDINGS



ARDS Network investigators. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. [*New Eng J Med* 2000; **342**:1301 doi: 10.1056/NEJM200005043421801]

JAMA Network

QUESTION For patients in the ICU who are ventilated for reasons other than ARDS, is low tidal volume superior to intermediate tidal volume?

CONCLUSION Among ICU patients receiving invasive ventilation, a strategy with a low tidal volume was not superior to using intermediate tidal volume.

POPULATION

621 Men **340** Women

ICU patients without ARDS expected to be intubated for more than 24 hours

Median age: **68** years (IQR, 59-76)

LOCATIONS

6 ICUs in the Netherlands

INTERVENTIONS

961 Patients randomized

477 Randomized
475 Analyzed

Low tidal volume

Started at tidal volume of 6 mL/kg; tidal volume then decreased in steps of 1 mL/kg predicted body weight

484 Randomized
480 Analyzed

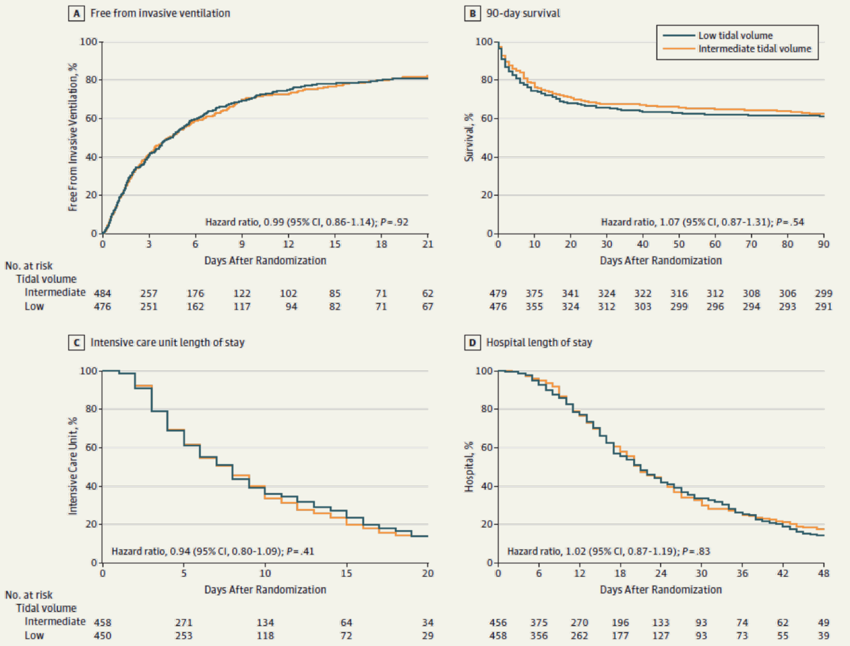
Intermediate tidal volume

Started at tidal volume of 10 mL/kg; if plateau pressure exceeded 25 cm H_2O, tidal volume was decreased in steps of 1 mL/kg predicted body weight

PRIMARY OUTCOME

Number of ventilator-free days and alive at day 28

FINDINGS



Writing Group for the PReVENT Investigators. Effect of a low vs intermediate tidal volume strategy on ventilator-free days in intensive care unit patients without ARDS: a randomized clinical trial [published online October 24, 2018]. *JAMA*. doi:10.1001/jama.2018.14280

ATS Journals

QUESTION What is the impact of mechanical power on mortality in patients with ARDS as compared with that of primary ventilator variables such as the ΔP, V_T, and RR?

CONCLUSION Mechanical power was associated with mortality during controlled mechanical ventilation in ARDS, but a simpler model using only the ΔP and RR was equivalent.

POPULATION

1728 Women **2821** Men

Patients with ARDS

Mean Age: **55** years

LOCATION

6 RCTs and **1** observational study

VENTILATION PARAMETERS

4549 patients with mild, moderate or severe ARDS

MP
0.32 J/min/kg

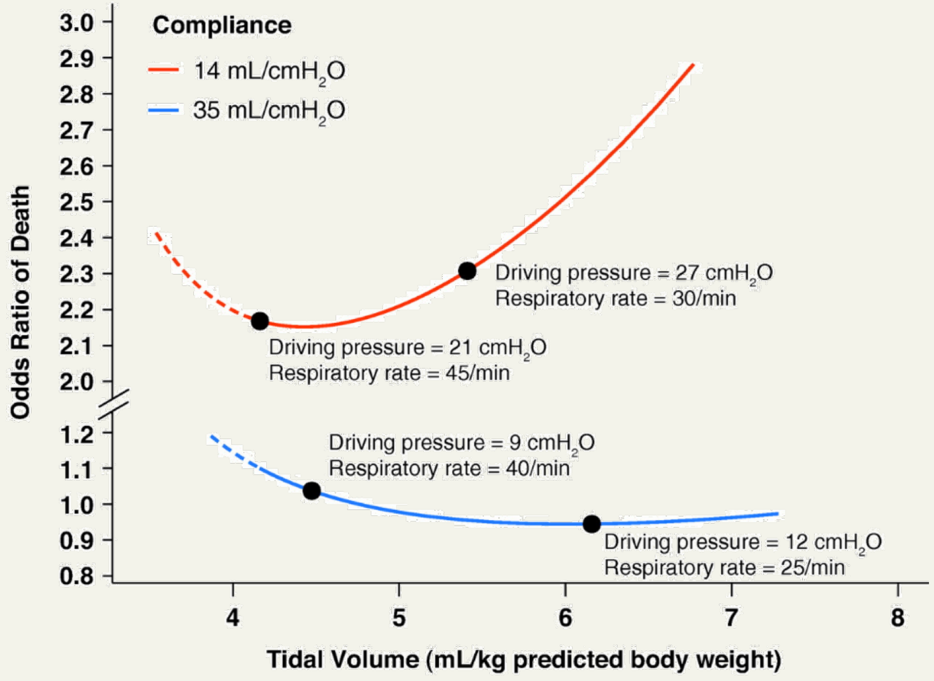
RR
26 breath/min

ΔP
15 cm H_2O

(PRIMARY) OUTCOME

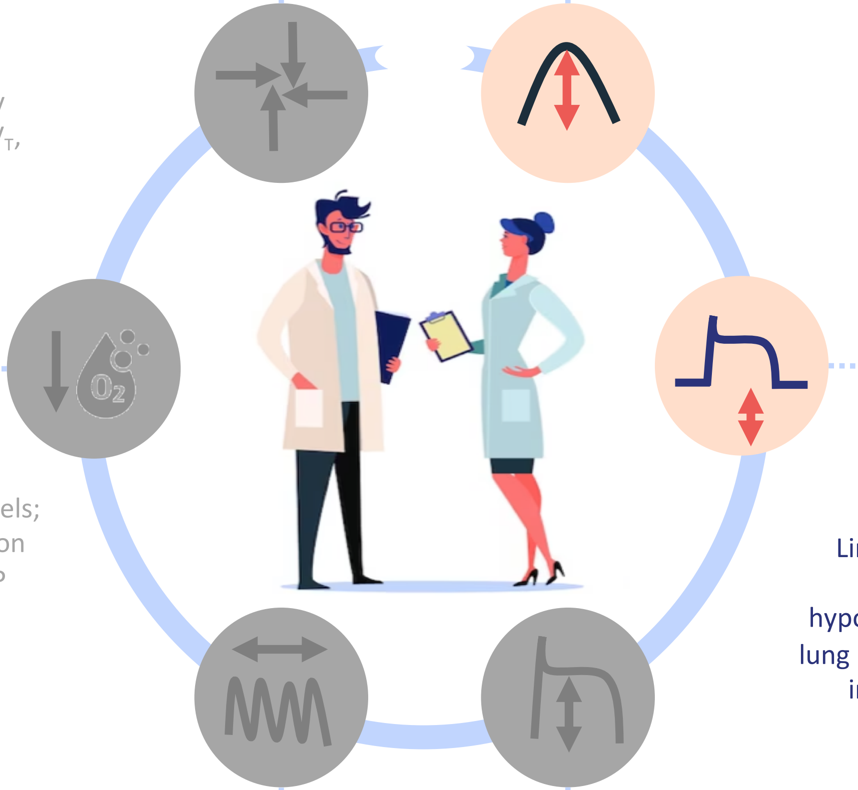
Mortality at 28 or 60 days

FINDINGS



Costa et al. Ventilatory Variables and Mechanical Power in Patients with the acute respiratory distress syndrome. [*American Journal of Respiratory and Critical Care Medicine* 2021; **204**:303 doi:10.1164/rccm.202009-3467OC]

ventilator settings in critically ill patients—prioritize permissive over aggressive ventilation



Step 1

Use low V_T

Reduce the size of V_T; reductions might be more beneficial in patients with less compliant lungs.

Rational

Volutrauma

Randomized clinical trials and observational studies have shown benefit from low V_T; ventilation with low V_T might lead to hypoxemia; a compensatory increase in RR may be harmful.

Step 2

Do not use high PEEP by default

Limit use of high PEEP to patients with severe hypoxemia, and only when lung lesions are recruitable; instead, consider prone positioning.

Rational

Atelectrauma *vs* overdistension

Randomized clinical trials could not confirm benefit from high PEEP, and observational studies even suggested harm; in some patients high PEEP could lead to overdistension rather than recruitment.

Step 3

Check ΔP and MP

If high, consider reducing V_T further; consider a change in other ventilator settings, like higher PEEP when lung lesions may be recruitable, or a longer inspiration time.

Rational

Energytrauma

Meta–analyses showed associations of higher ΔP and MP with relevant clinical outcomes; even short periods with high ΔP or high MP could be detrimental.

Step 6

Integrate

Refine settings further by incrementally adjusting V_T, PEEP, RR and FiO_2.

Rational

Combining the settings

Everchanging patient conditions mandate frequent refinements; automation could be helpful, also by reducing the ICU staff workloads associated with lung–protective ventilation.

Step 5

Use O_2 wisely

Do not target high O_2 levels; use high FiO_2 if a reduction in V_T and use of low PEEP results in hypoxemia.

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Chemotrauma

Several studies have pointed at the side–effects of hyperoxia; some randomized clinical trials have shown benefit of restrictive O_2 use; a low O_2 target, though, might increase the risk of hypoxemia.

Step 4

Reduce the RR

In an attempt to reduce MP, reduce RR; allow the CO_2 level to rise if MP remains high.

Rational

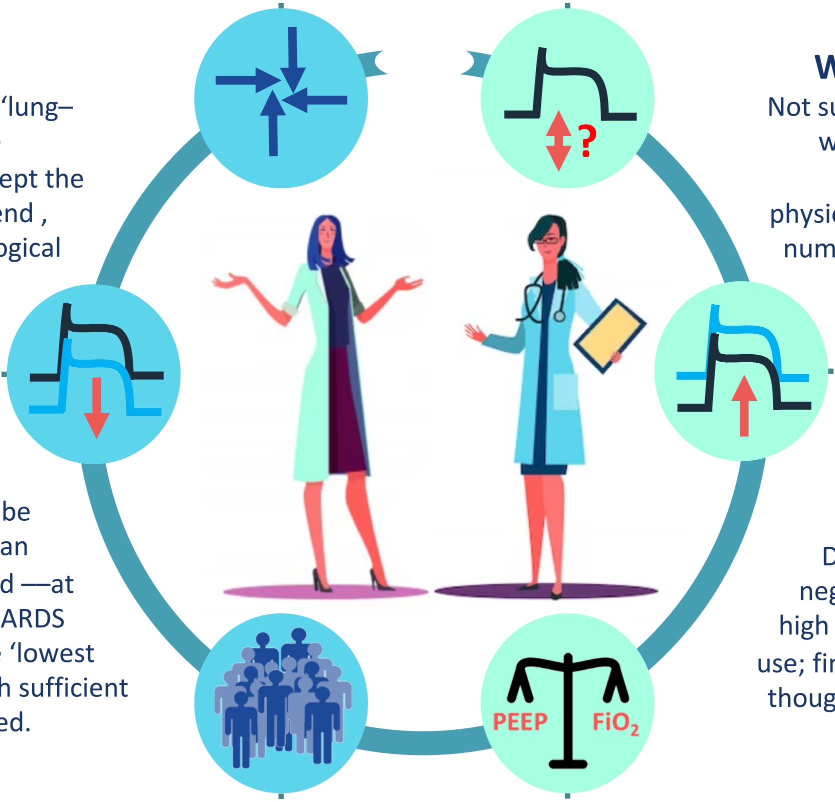
Permissive hypercapnia

RR is an important contributor to the amount of energy transferred to the lung; lowering RR reduces MP, but may induce hypercapnia.

V_T, tidal volume; PEEP, positive end–expiratory pressure; ΔP, driving pressure; MP, mechanical power of ventilation; RR, respiratory rate; FiO_2, fraction of inspired O_2

Infographic on ventilation management by **Marcus Schultz,** Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

titration of PEEP in critically ill patients—prioritize clinical benefit over physiology



Step 1

What is 'Low' PEEP?

Not sure – but ever wondered why the 'lowest' PEEP is 5 cmH_2O? There is no physiology behind this 'magic' number—it is the number of fingers on one hand.

Rational

'Physiology' of PEEP

PEEP can improve lung aeration; realize, though, that PEEP always causes lung overdistension as well.

Step 2

Do not use high PEEP by default

Despite neutral, and even negative findings in studies, high PEEP remains popular to use; findings of meta–analyses, though, strongly argue against the use of high PEEP.

Rational

High PEEP

Randomized clinical trials in patients with ARDS failed to show clinical benefit of high PEEP; one well–performed randomized clinical trial in patients with ARDS even showed harm of high PEEP.

Step 3

Use a table to set PEEP (and FiO_2)

Use a 'low PEEP/high FiO_2 table', as use of a 'high PEEP/low FiO_2 table' has no advantages—it could even be harmful to use; currently, there are no valid arguments to use P_{eso} outside of a research setting.

Rational

Titration of PEEP

One approach is to use PEEP/FiO_2 tables; another way is to use P_{eso}, but randomized clinical trials failed to show clinical benefit of this approach.

Step 4

Individualize (high) PEEP

High PEEP may still be beneficial, but probably only in ARDS patients with recruitable lung lesions, and only when the balance between recruitment and overdistension is acceptable. Monitoring changes in ΔP, and maybe also in MP, could be helpful herein.

Rational

Heterogeneity

There is heterogeneity of treatment effect; one Bayesian re–analysis suggest harm of high PEEP in patients with ARDS from pneumonia; one randomized clinical trial suggest harm from high PEEP if ARDS lesions are not recruitable.

Step 5

PEEP *vs* FiO_2

So the 'lowest' PEEP can be 0 cmH_2O, even if this mean that higher FiO_2 is needed —at least in patients without ARDS the best PEEP maybe the 'lowest possible PEEP' with which sufficient oxygenation in guaranteed.

Rational

Patients without ARDS

One randomized clinical trial showed low PEEP (to as low as 0 cmH_2O) to be non–inferior to fixed high PEEP (of 8 cmH_2O); as expected, more often hypoxemia occurred with low PEEP.

Step 6

Integrate

The goal of ventilation is 'lung–protection'; do not chase physiology—instead, accept the pathophysiology; in the end , ventilation is not physiological at all.

Rational

Combining the settings

Low PEEP may favor atelectases, but high PEEP increases the risk of overdistension; monitoring ΔP, and maybe also MP, could be helpful; note that (high) PEEP may have a negative effect on circulation.

PEEP, positive end–expiratory pressure; ARDS, acute respiratory distress syndrome; P_{eso} , esophagus pressure; ΔP, driving pressure; MP, mechanical power of ventilation; FiO_2, fraction of inspired O_2

Infographic on PEEP titrations by **Marcus Schultz**, Amsterdam UMC, Amsterdam, the Netherlands (1.1–260423)

JAMA Network

QUESTION What is the association of higher vs lower PEEP with patient-important outcomes in adults with ARDS who are receiving ventilation with low tidal volumes?

CONCLUSION Higher levels of PEEP were associated with improved survival among patients with moderate to severe ARDS.

POPULATION

892 Women **1407** Men

patients with mild, moderate or severe ARDS (IPD metanalysis)

Mean Age: **56** years

LOCATION

3 RCTs
in **4** countries

VENTILATION STRATEGIES

2299 patients with mild, moderate or severe ARDS

1136 patients
high PEEP
[> 15 cm H_2O] with RM

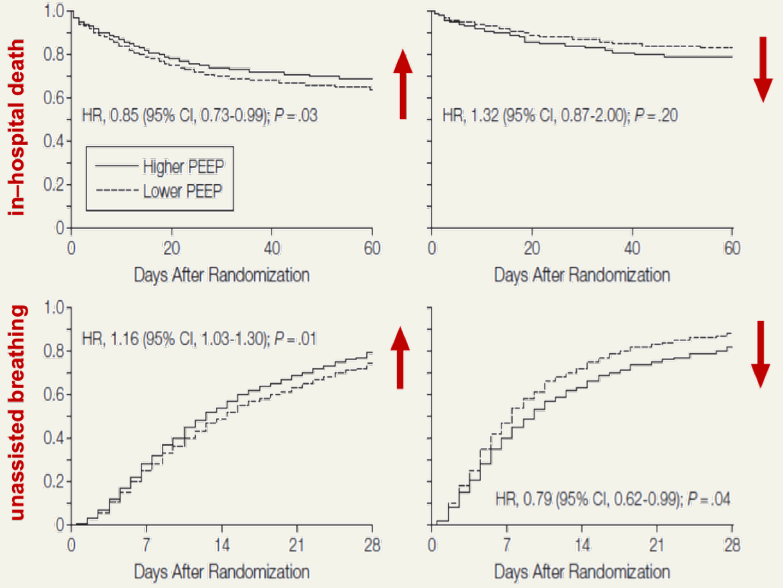
1163 patients
low PEEP
[< 12 cm H_2O] without RM

(PRIMARY) OUTCOME

28–day mortality; length of ICU and hospital stay; VFD28; pneumothorax requiring drainage or barotrauma within 7 days

FINDINGS

benefit in moderate to severe ARDS, harm in mild ARDS



Briel M *et al*. Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome – Systematic Review and Meta-analysis [*JAMA* 2010; **303**:865]

JAMA Network™

QUESTION Does use of a lung recruitment maneuver associated with PEEP titration according to the best respiratory-system compliance reduce 28-day mortality of patients with moderate to severe ARDS, compared with a conventional low–PEEP strategy?

CONCLUSION A strategy using a lung recruitment maneuver and titrated PEEP increased mortality of patients with moderate to severe ARDS.

POPULATION

379 Women **631** Men

consecutive patients with moderate to severe ARDS

Mean Age: **51** years

LOCATION

120 ICUs from **9** countries

VENTILATION STRATEGIES

1010 patients with moderate or severe ARDS

501 patients
titrated (high) PEEP [>15 cm H_2O] with RM

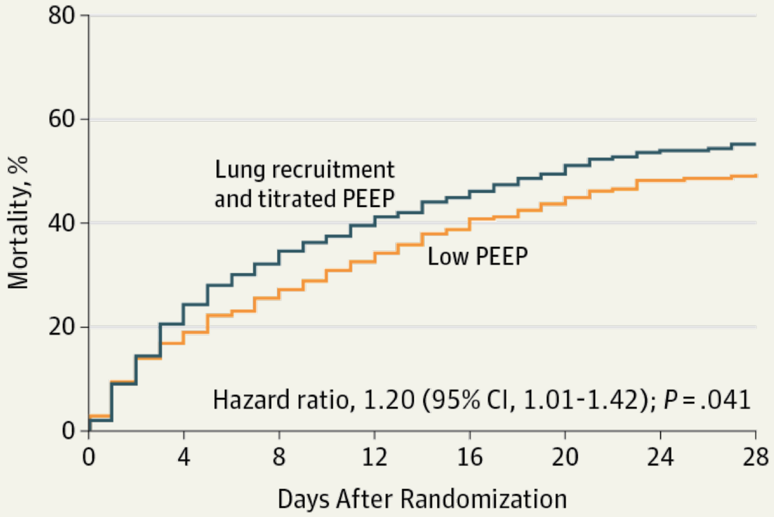
509 patients
standard (low) PEEP [< 12 cm H_2O] without RM

(PRIMARY) OUTCOME

28–day mortality; length of ICU and hospital stay; VFD28; pneumothorax requiring drainage or barotrauma within 7 days

FINDINGS

lower ΔP (!), but more pneumothorax and barotrauma with high PEEP + RM



Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators. Effect of Lung Recruitment and Titrated PEEP vs Low PEEP on Mortality in Patients With ARDS–A Randomized Clinical Trial [*JAMA* 2017; **318**:1335]

QUESTION Do ventilation strategies using higher PEEP and/or RMs decrease mortality in patients with ARDS ventilated with low tidal volumes?

CONCLUSION In patients ventilated with low tidal volumes, the routine use of higher PEEP and/or RMs does not reduce mortality in unselected patients with ARDS.

POPULATION

1482 Women **2388** Men

patients with moderate to severe ARDS (IPD metanalysis)

Mean Age: **56** years

LOCATION

16 RCTs worldwide

VENTILATION STRATEGIES

3870 patients moderate or severe ARDS

1377 patients **higher PEEP, no RM**

2383 patients **higher PEEP, RM**

110 patients **RM alone**

(PRIMARY) OUTCOME

28–day mortality; various other ICU and hospital outcomes

FINDINGS

Study	Intervention Events	Intervention Total	Control Events	Control Total	RR	95%–CI	Weight
Higher PEEP alone							
Brower 2004	76	276	68	273	1.11	[0.83; 1.46]	13.4%
Talmor 2008	5	30	12	31	0.43	[0.17; 1.07]	1.9%
Mercat 2008	107	385	119	382	0.89	[0.72; 1.11]	17.7%
Subgroup	**188**	**691**	**199**	**686**	**0.91**	**[0.68; 1.23]**	**33.1%**
Heterogeneity: $I^2 = 53\%$, $\tau^2 = 0.03$, $p = 0.12$							
Test for effect in subgroup: $z = -0.60$ ($p = 0.55$)							
Higher PEEP and recruitment manoeuvres							
Meade 2008	135	475	164	508	0.88	[0.73; 1.06]	20.2%
Huh 2009	12	30	9	27	1.20	[0.60; 2.39]	3.3%
Hodgson 2011	3	10	2	10	1.50	[0.32; 7.14]	0.7%
Kacmarek 2016	22	99	27	101	0.83	[0.51; 1.36]	5.9%
Cavalcanti 2017	277	501	251	509	1.12	[1.00; 1.26]	27.5%
Hodgson 2019	14	57	15	56	0.92	[0.49; 1.72]	3.9%
Subgroup	**463**	**1172**	**468**	**1211**	**1.01**	**[0.89; 1.16]**	**61.4%**
Heterogeneity: $I^2 = 17\%$, $\tau^2 = < 0.01$, $p = 0.30$							
Test for effect in subgroup: $z = 0.20$ ($p = 0.84$)							
Recruitment manoeuvres alone							
Xi 2010	16	55	24	55	0.67	[0.40; 1.11]	5.5%
Subgroup	**16**	**55**	**24**	**55**	**0.67**	**[0.40; 1.11]**	**5.5%**
Heterogeneity: not applicable							
Test for effect in subgroup: $z = -1.56$ ($p = 0.12$)							
Random effects model	**667**	**1918**	**691**	**1952**	**0.96**	**[0.84; 1.09]**	**100.0%**
Heterogeneity: $I^2 = 35\%$, $\tau^2 = 0.01$, $p = 0.12$							
Test for overall effect: $z = -0.68$ ($p = 0.50$)							
Test for subgroup differences: $\chi^2_2 = 2.65$, df = 2 ($p = 0.27$)							

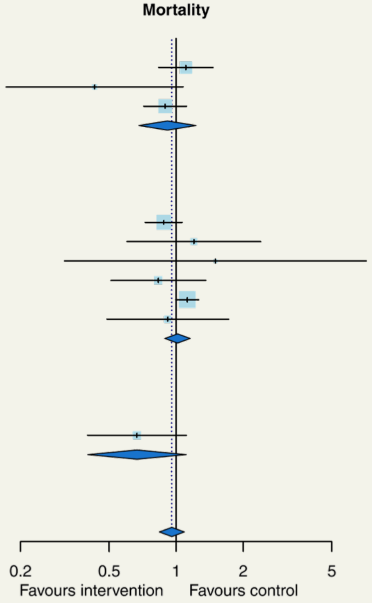


Fig. 2 Forest plot for mortality (collapsed at 28 days, ICU discharge, hospital discharge or 60–days). Studies are stratified according to whether higher PEEP and recruitment manoeuvres were used separately or as a bundle of interventions. ICU, intensive care unit; PEEP, positive end-expiratory pressure

Ball L *et al*. Effects of higher PEEP and recruitment maneuvers on mortality in patients with ARDS: a systematic review, meta-analysis, meta-regression and trial sequential analysis of randomized controlled trials [*ICMx* 2022; **205**:865]

ATS Journals

QUESTION What are the relative effects of different PEEP selection strategies on mortality in adult patients with moderate to severe Acute Respiratory Distress Syndrome?

CONCLUSION In adult patients with moderate to severe Acute Respiratory Distress Syndrome, higher PEEP without LRM is associated with a lower risk of death.

POPULATION

4646 Patients

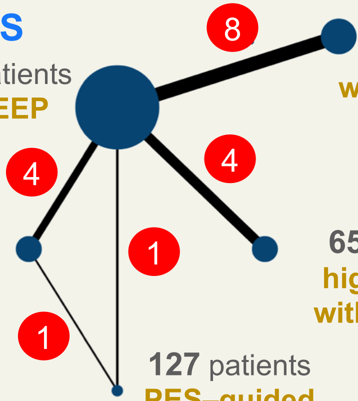
patients with moderate to severe ARDS (IPD metanalysis)

Mean Age: **60** years

LOCATION

18 RCTs worldwide

STRATEGIES



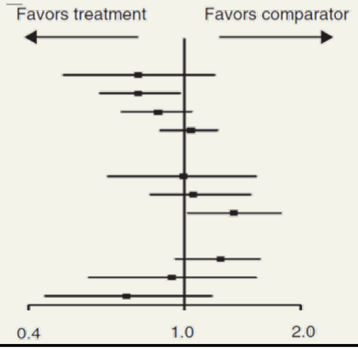
(PRIMARY) OUTCOME

28–day mortality;
various other ICU and hospital outcomes

[a network meta–analysis using a Bayesian framework]

FINDINGS

	Direct comparisons: Patients	Direct comparisons: Trials	Network Risk Ratio (95% CrI)	Absolute risk difference (95% CrI)	Posterior probabilities: RR < 1.0	Posterior probabilities: RR > 1.0	Posterior probabilities: ARR > 1%	Certainty
vs. Lower PEEP strategy								
Pes-guided	49	1	0.77 (0.48, 1.22)	−0.09 (−0.21, 0.09)	0.87	0.13	0.84	Moderate
Higher PEEP without LRM	1,162	4	0.77 (0.60, 0.96)	−0.09 (−0.16, −0.01)	0.99	0.01	0.98	High
Higher PEEP with brief LRM	1,335	4	0.83 (0.67, 1.02)	−0.07 (−0.13, 0.01)	0.96	0.04	0.94	Moderate
Higher PEEP with prolonged LRM	1,900	8	1.06 (0.89, 1.22)	0.02 (−0.04, 0.09)	0.23	0.77	0.15	Low
vs. Higher PEEP without LRM strategy								
Pes-guided	200	1	1.00 (0.65, 1.54)	0.00 (−0.11, 0.16)	0.50	0.50	0.44	Moderate
Higher PEEP with brief LRM	0	0	1.07 (0.79, 1.48)	0.02 (−0.08, 0.12)	0.32	0.68	0.25	Low
Higher PEEP with prolonged LRM	0	0	1.37 (1.04, 1.81)	0.11 (0.01, 0.21)	0.01	0.99	0.01	Moderate
Additional comparisons								
Higher PEEP with prolonged vs. brief LRM	0	0	1.27 (0.97, 1.64)	0.09 (−0.01, 0.18)	0.04	0.96	0.03	Low
Pes-guided vs. Higher PEEP with brief LRM	0	0	0.93 (0.55, 1.54)	−0.02 (−0.16, 0.17)	0.61	0.39	0.57	Low
Pes-guided vs. Higher PEEP with prolonged LRM	0	0	0.73 (0.45, 1.19)	−0.11 (−0.25, 0.08)	0.90	0.10	0.88	Low



Dianti J *et al*. Association of Positive End–Expiratory Pressure and Lung Recruitment Selection Strategies with Mortality in Acute Respiratory Distress Syndrome–a Systematic Review and Network Meta–Analysis [*Am J Resp Crit Care Med* 2022; **205**:865; doi:10.1164/rccm.202108-1972OC]

EJA European Journal of Anaesthesiology

QUESTION In patients with COVID–19–related ARDS, is a higher PEEP strategy superior to a lower PEEP strategy with regarding the number of ventilator–free days (VFDs)?

CONCLUSION In patients with C–ARDS, use of higher PEEP may be associated with a lower number of VFDs, and may increase the incidence of AKI and need for RRT.

PARTICIPANTS

318 Women **675** Men

studies in patients with C–ARDS

median age: **65** years

LOCATION

22 ICUs in the Netherlands

VENTILATION STRATEGIES

993 patients with moderate to severe ARDS

674 patients lower PEEP

259 patients higher PEEP

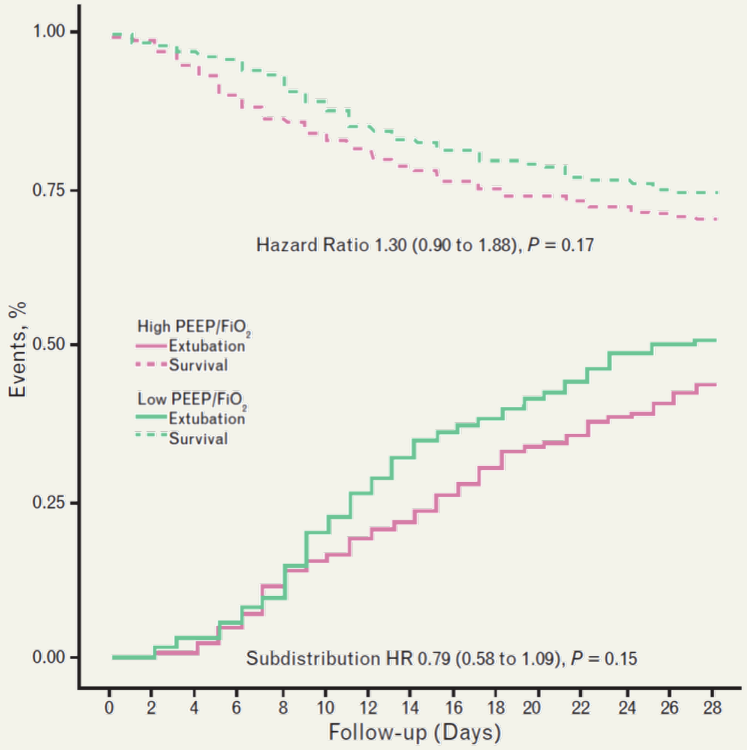
468 matched patients lower PEEP

234 matched patients higher PEEP

(PRIMARY) OUTCOME

number of VFDs, distant organ failures including AKI and use of RRT, and mortality

FINDINGS



PRoVENT–COVID–investigators. Association of early PEEP settings with ventilator–free days in patients with COVID–19 ARDS. [*Eur J Anaesth* 2021; **38**:1274]

BJA

QUESTION Is there heterogeneity in treatment effects in patients enrolled in the ART, using a machine learning approach?

CONCLUSION Recruitment maneuvers and titrated PEEP may be harmful in ARDS patients with pneumonia or requiring vasopressor support. Driving pressure appears to modulate the association between the ART study intervention, etiology of ARDS, and mortality.

POPULATION

379 Women **631** Men

consecutive patients with moderate to severe ARDS

Mean Age: **51** years

LOCATION

120 ICUs
from **9** countries

VENTILATION STRATEGIES

1010 patients with moderate or severe ARDS

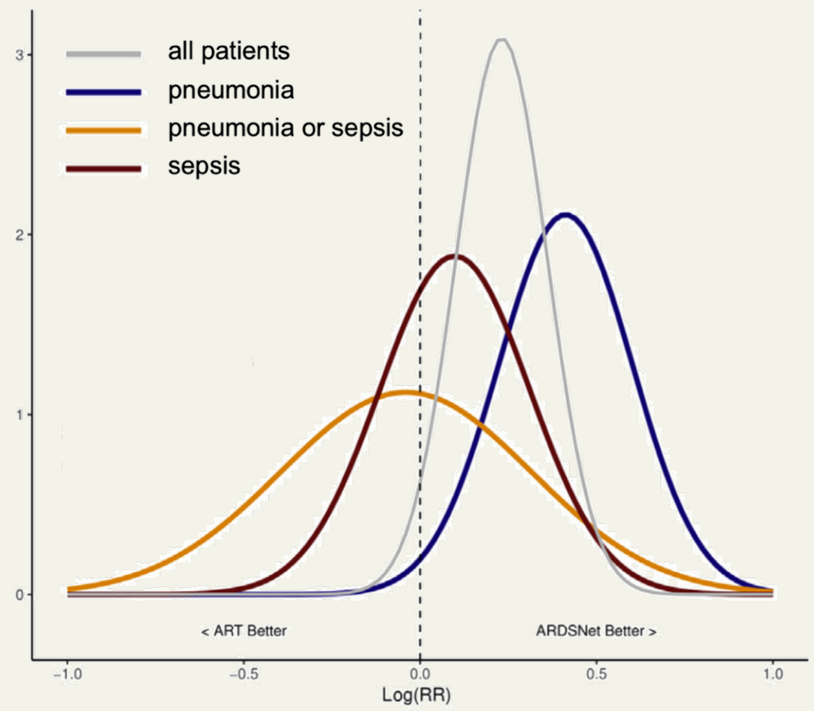
501 patients
titrated (high) PEEP
[>15 cm H_2O] with RM

509 patients
standard (low) PEEP
[< 12 cm H_2O] without RM

OUTCOME OF THE BAYESIAN ANALYSIS

28–day mortality

FINDINGS



Zampieri F for the ART Investigators. Heterogeneous effects of alveolar recruitment in acute respiratory distress syndrome: a machine learning reanalysis of the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial [*BJA* 2019; **123**:88; 10.1016/j.bja.2019.02.026]

THE LANCET
Respiratory Medicine

QUESTION Does a mechanical ventilation strategy that is personalized to individual patients' lung morphology improve the survival of patients with ARDS when compared with standard of care?

CONCLUSION Personalization of ventilation decreased mortality in patients with ARDS [in the posthoc analysis]; a ventilator strategy misaligned with lung morphology substantially increases mortality.

POPULATION

114 Women **286** Men

patients with ARDS for less than 12 hours

Median Age: **62** years

LOCATION

20 ICUs in France

INTERVENTION

400 patients with moderate to severe ARDS

204
standard care
V_T 6 ml/kg PBW
low PEEP

196
personalized care

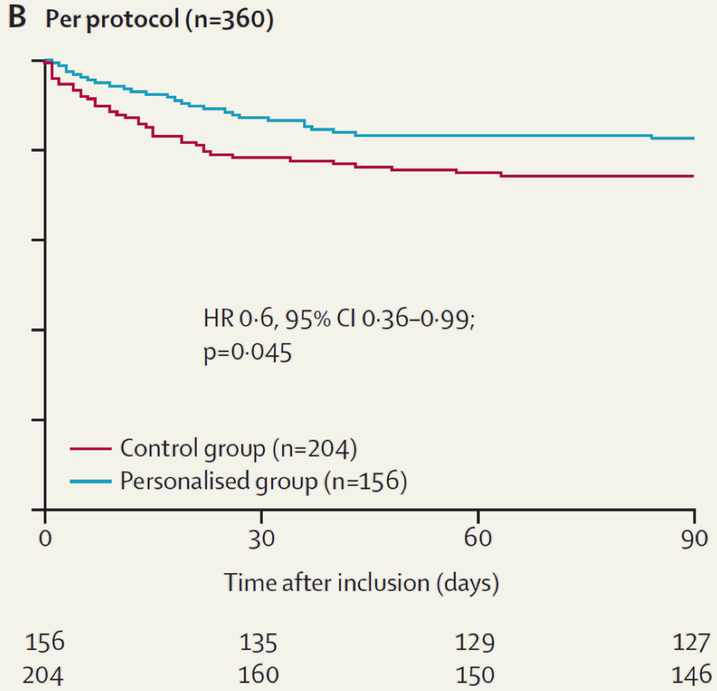
non–focal
V_T 6 ml/kg PBW
high PEEP
with RM

focal
V_T 8 ml/kg PBW
low PEEP and
prone positioning

(PRIMARY) OUTCOME

mortality at day 90; ventilator–free days, ARDS resolution; LOS in ICU; barotrauma

FINDINGS



LIVE–investigators. Personalized mechanical ventilation tailored to lung morphology versus low PEEP for patients with ARDS in France: a multicenter, single–blind, randomized clinical trial. [*Lancet Respir Med* 2019; **7**:870; doi:10.1016/S2213-2600(19)30138-9. Epub 2019 Aug 6]

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mortality at day 90; ventilator–free days, ARDS resolution; LOS in ICU; barotrauma

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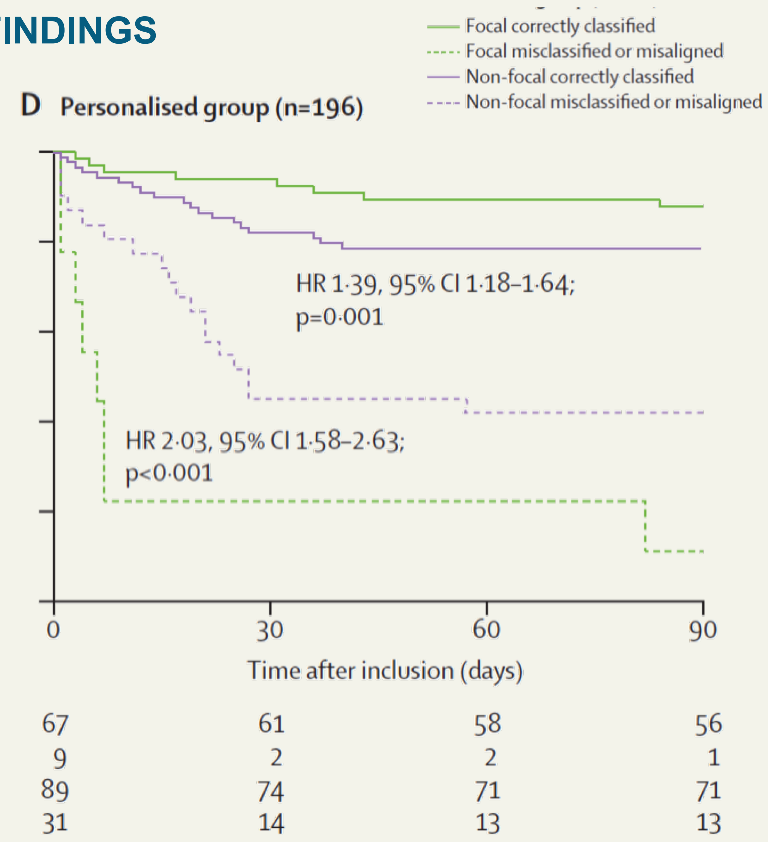

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JAMA Network™

QUESTION In ICU patients who received invasive ventilation for reasons other than acute respiratory distress syndrome (ARDS), is a strategy with lower positive end-expiratory pressure (PEEP) noninferior to higher PEEP with respect to ventilator-free days at day 28?

CONCLUSION This clinical trial found that among ICU patients receiving invasive ventilation, a strategy with lower PEEP was noninferior to a strategy using higher PEEP for the outcome of ventilator-free days, supporting the use of lower PEEP in patients without ARDS.

POPULATION

623 Men **346** Women

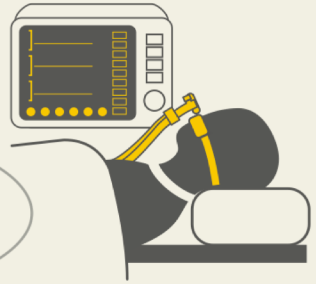
Adults without ARDS expected not to be extubated within 24 hours of intubation

Median age: **66** years

LOCATIONS

8 ICUs in the Netherlands

INTERVENTION



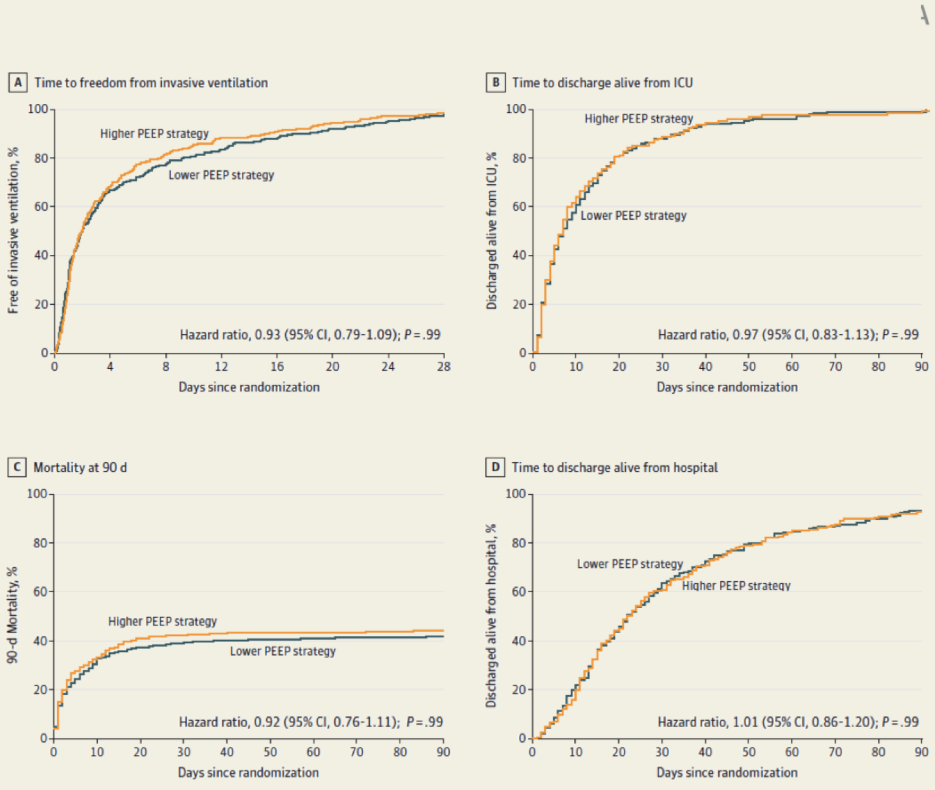
980 Patients randomized
969 Patients analyzed

476 **Lower PEEP strategy**
Lowest level between 0-5 cm H_2O

493 **Higher PEEP strategy**
Lowest level of 8 cm H_2O

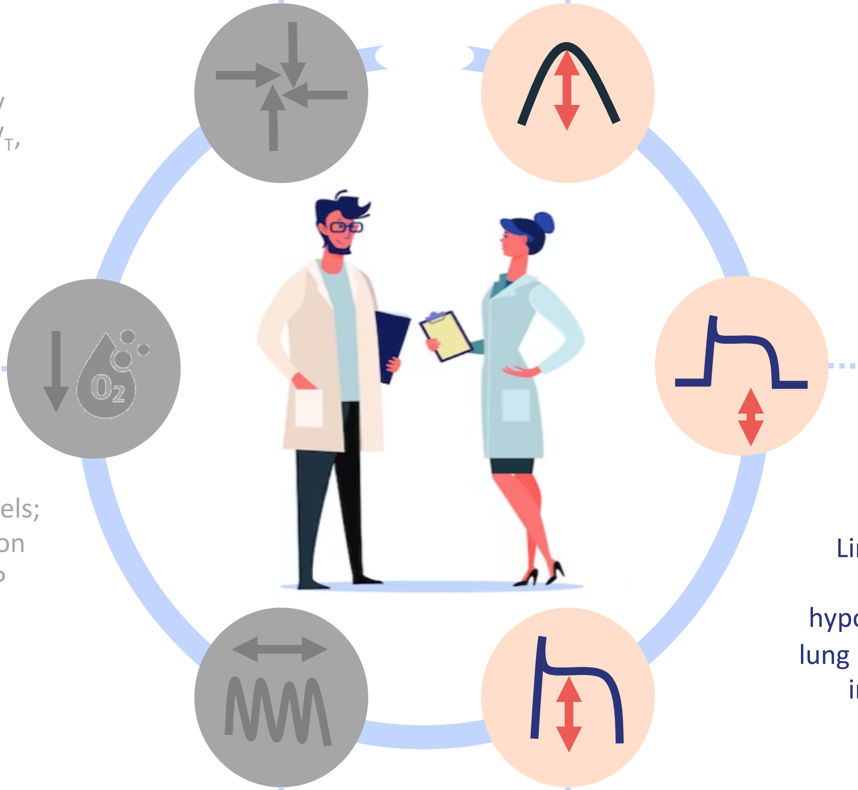
PRIMARY OUTCOME

Number of ventilator-free days by study day 28 (noninferiority margin of −10%)



Writing Committee for the RELAx Collaborative Group. Effect of a lower vs higher positive end-expiratory pressure strategy on ventilator-free days in ICU patients without ARDS: a randomized clinical trial. *JAMA*. Published online December 9, 2020. doi:10.1001/jama.2020.23517

ventilator settings in critically ill patients—prioritize permissive over aggressive ventilation



Step 1

Use low V_T

Reduce the size of V_T; reductions might be more beneficial in patients with less compliant lungs.

Rational

Volutrauma

Randomized clinical trials and observational studies have shown benefit from low V_T; ventilation with low V_T might lead to hypoxemia; a compensatory increase in RR may be harmful.

Step 2

Do not use high PEEP by default

Limit use of high PEEP to patients with severe hypoxemia, and only when lung lesions are recruitable; instead, consider prone positioning.

Rational

Atelectrauma *vs* overdistension

Randomized clinical trials could not confirm benefit from high PEEP, and observational studies even suggested harm; in some patients high PEEP could lead to overdistension rather than recruitment.

Step 3

Check ΔP and MP

If high, consider reducing V_T further; consider a change in other ventilator settings, like higher PEEP when lung lesions may be recruitable, or a longer inspiration time.

Rational

Energytrauma

Meta–analyses showed associations of higher ΔP and MP with relevant clinical outcomes; even short periods with high ΔP or high MP could be detrimental.

Step 4

Reduce the RR

In an attempt to reduce MP, reduce RR; allow the CO_2 level to rise if MP remains high.

Rational

Permissive hypercapnia

RR is an important contributor to the amount of energy transferred to the lung; lowering RR reduces MP, but may induce hypercapnia.

Step 5

Use O_2 wisely

Do not target high O_2 levels; use high FiO_2 if a reduction in V_T and use of low PEEP results in hypoxemia.

Rational

Chemotrauma

Several studies have pointed at the side–effects of hyperoxia; some randomized clinical trials have shown benefit of restrictive O_2 use; a low O_2 target, though, might increase the risk of hypoxemia.

Step 6

Integrate

Refine settings further by incrementally adjusting V_T, PEEP, RR and FiO_2.

Rational

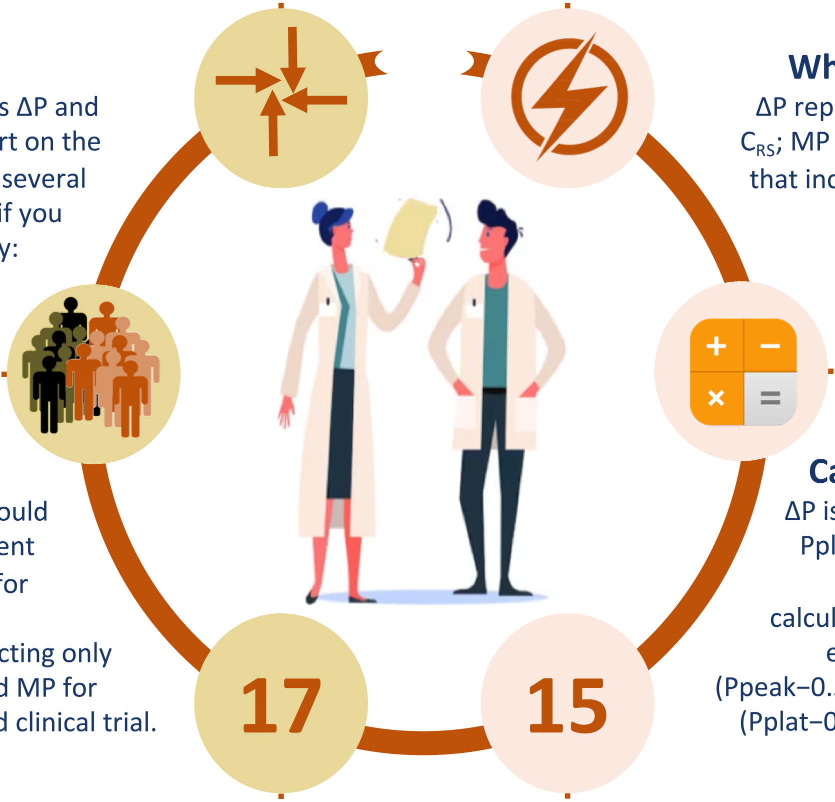
Combining the settings

Everchanging patient conditions mandate frequent refinements; automation could be helpful, also by reducing the ICU staff workloads associated with lung–protective ventilation.

V_T, tidal volume; PEEP, positive end–expiratory pressure; ΔP, driving pressure; MP, mechanical power of ventilation; RR, respiratory rate; FiO_2, fraction of inspired O_2

Infographic on ventilation management by **Marcus Schultz,** Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

driving pressure and mechanical power in critically ill patients—associations or causal relations?



Step 1 — Rational

What are ΔP and MP?

ΔP represents the ratio of V_T to C_{RS}; MP is a summary parameter that includes V_T, RR, and airway pressures including ΔP.

Associations

Meta–analyses have shown associations of higher ΔP and MP with worse clinical outcomes, in patients with ARDS and also in patients without ARDS; even short periods with high ΔP or MP could be harmful.

Step 2 — Rational

Calculate ΔP and MP

ΔP is the difference between Pplat (or Pmax) and PEEP in VCV (or PCV); MP can be calculated using simple power equations: $0.098*V_T*RR*(Ppeak-0.5*ΔP)$ (or $0.098*V_T*RR*(Pplat-0.5*ΔP)$) in VCV (or PCV).

Causal relations?

Despite the appealing associations of ΔP and MP with worse clinical outcomes, we should realize that there have been no randomized clinical trials yet that tested whether a ventilation strategy that targets either lower ΔP or less MP leads to better outcomes.

Step 3 — Rational

How to achieve low ΔP

A first logical and pragmatic step is to reduce V_T, higher PEEP may also decrease ΔP if it reduces atelectases; note that in one randomized clinical trial in patients with ARDS, high PEEP resulted in a lower ΔP but also higher mortality.

Safety cutoffs for ΔP

It is uncertain what is a safe ΔP; meta–analyses suggest, or use, 15 cmH_2O but it remains uncertain whether this is correct and useful in all patients categories.

Step 4 — Rational

How to achieve low MP

This is where the pain starts; which ventilation parameter to prioritize?; adjusting one setting that may lower MP may require a change in another setting that actually may rise MP—e.g., a decrease in V_T may require an increase in RR, but higher RR will increase MP.

Safety cutoffs for MP

The same is true for MP, it is uncertain what is a safe MP; meta–analyses suggest, or use, 17 J/min but it remains uncertain whether this is correct and useful in all patients categories.

Step 5 — Rational

Enrichment

In this way, ΔP and MP could be used to compare patient cohorts, or maybe even for prognostic or predictive enrichment, e.g., by selecting only patients with high ΔP and MP for inclusion in a randomized clinical trial.

Again, associations?

There is a discussion ongoing whether these two parameters are not just 'biomarkers'; this may also explain the associations with outcomes—the sicker the lung, the higher ΔP and MP, but also the higher the chance of dying.

Step 6 — Rational

Integrate

The summary parameters ΔP and MP are dependent, in part on the way the ventilator is set; several settings can be adjusted if you want to lower the energy: V_T, RR, and PEEP.

Combining the settings

It may be advisable to regularly check ΔP and MP, and changes thereof over time; whether ventilation strategies that target low ΔP or MP really improve outcomes, however, still need to be studied.

ΔP, driving pressure; MP, mechanical power of ventilation; V_T, tidal volume; C_{RS}, compliance; RR, respiratory rate; V(P)CV, volume (pressure) controlled ventilation; PEEP, positive end–expiratory pressure; ARDS, acute respiratory distress syndrome

Infographic on energytrauma by **Marcus Schultz**, Amsterdam UMC, Amsterdam, the Netherlands (1.0–260423)

The NEW ENGLAND JOURNAL of MEDICINE

QUESTION Is ΔP an index more strongly associated with survival than V_T or PEEP in patients who are not actively breathing?

CONCLUSION ΔP is the ventilation variable that best stratified risk; decreases in ΔP owing to changes in ventilator settings may be strongly associated with increased survival.

POPULATION

~40% Women **~60%** Men

patients with ARDS included in RCTs

Mean Age: from **34** to **60** years

SOURCE

9 trials worldwide

METHODS

multilevel mediation analysis of individual patient data from **3562** patients

prediction model
univariate
multivariate

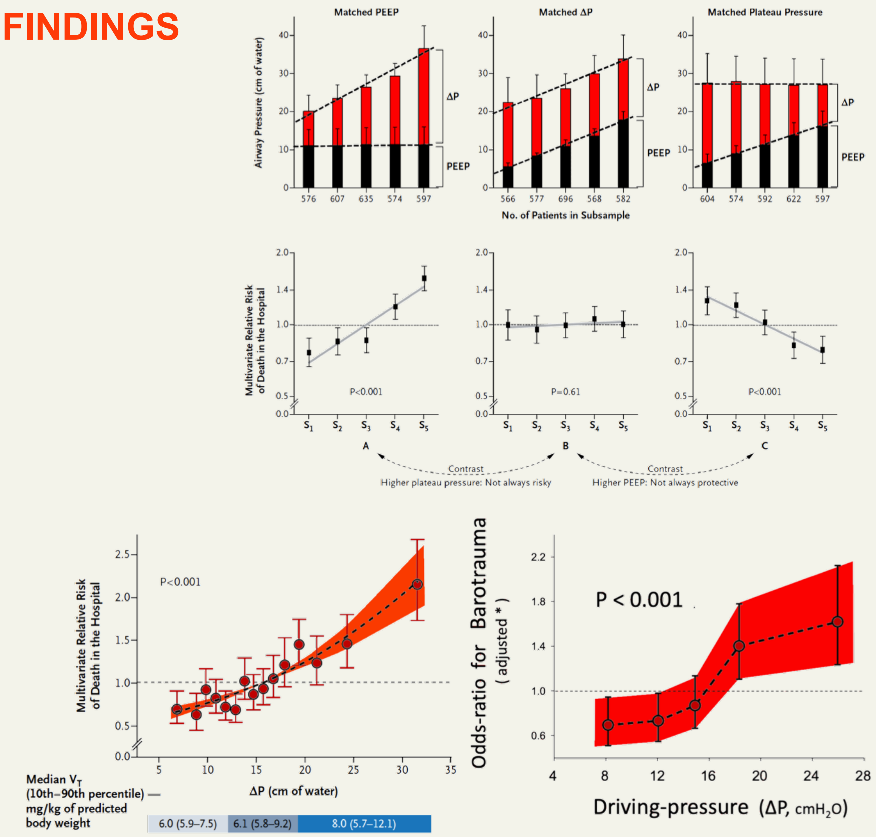
mediation analysis

risk priority
of ΔP, V_T and PEEP

(PRIMARY) OUTCOME

60–day mortality

FINDINGS



Amato M. Driving Pressure and Survival in the Acute Respiratory Distress Syndrome. [*New Eng J Med* 2015; **372**:747; doi:10.1056/NEJMsa1410639]

QUESTION What is the association between mechanical power (MP) and mortality in critically ill patients receiving invasive ventilation for at least 48 hours?

CONCLUSION High MP of ventilation is independently associated with higher in-hospital mortality and several other outcomes in ICU patients receiving invasive ventilation for at least 48 hours.

POPULATION

3614 Women **4593** Men

patients with data stored in the databases of the MIMIC–III and eICU

Median Age: **63** years

LOCATION

2 databases from US

CLASSIFICATION

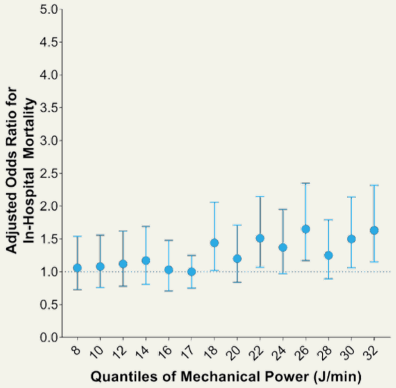
individual patient data from **8207** patients

3846 MIMIC–III database

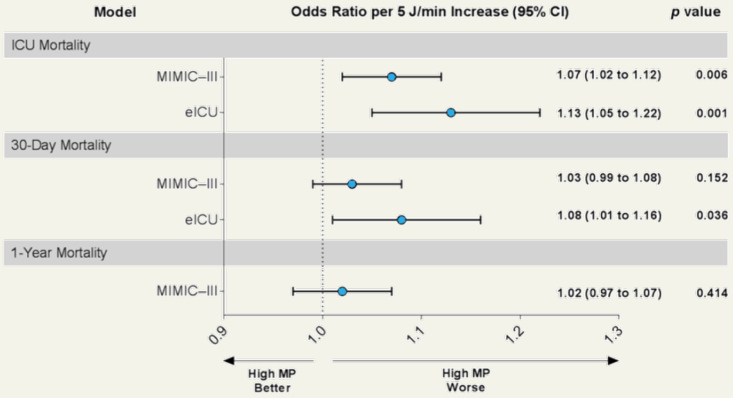
4361 eICU database

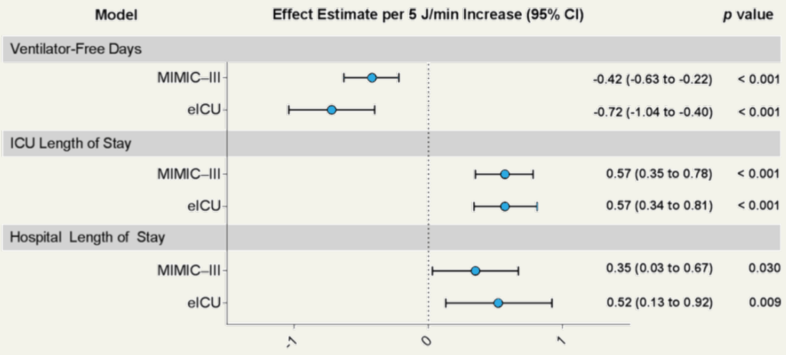
(PRIMARY) OUTCOME

in–hospital mortality; MP in first 48 hours



FINDINGS





Serpa Neto A. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. [*Intensive Care Med* 2018; **44**:1914; doi:10.1007/s00134-018-5375-6]

THE LANCET
Respiratory Medicine

QUESTION What is the association between exposure to different intensities of mechanical ventilation over time and intensive care unit (ICU) mortality in patients with acute respiratory failure?

CONCLUSION Cumulative exposure to higher intensities of mechanical ventilation was harmful, even for short durations.

POPULATION

5141 Women **8267** Men

patients receiving ventilation for 4 hours or more

Median Age: **62** years

LOCATION

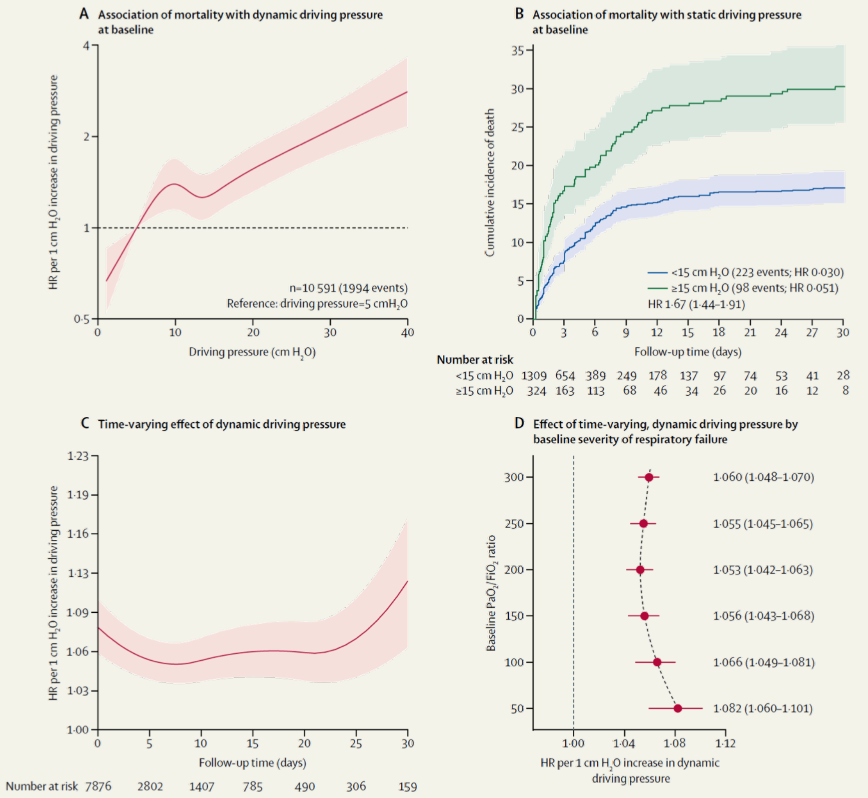
9 ICUs in Toronto, Canada

FINDINGS

	Exposure to high driving pressure		Exposure to high mechanical power	
	HR estimate (95% CrI)	p value	HR estimate (95% CrI)	p value
Baseline variables				
PaO_2/FiO_2, mm Hg	0·945 (0·896–0·994)	0·026	0·977 (0·930–1·031)	0·38
Age, years	1·108 (1·048–1·160)	<0·0001	1·128 (1·080–1·182)	<0·0001
APACHE III score	1·602 (1·526–1·680)	<0·0001	1·591 (1·524–1·669)	<0·0001
APACHE pH	0·832 (0·809–0·859)	<0·0001	0·840 (0·820–0·864)	<0·0001
Time-varying variables				
Days with driving pressure ≥15 cm H_2O	1·049 (1·023–1·076)	<0·0001	..	..
Days with mechanical power ≥17 J/min	..	..	1·069 (1·047–1·092)	<0·0001

1622 (20·6%) of 7876 patients died; 64 281 daily observations were recorded. HRs were the adjusted HRs associated with a 1-SD increment in the given variable. Values higher than 1 indicate increased mortality. The values used for SDs were as follows: PaO_2/FiO_2 ratio 119; pH 0·11; age 17 years; and APACHE III score 29. The effects of the number of days with either driving pressure greater than or equal to 15 cm H_2O or mechanical power greater than or equal to 17 J/min were estimated using Quasi-Poisson models in the joint model analyses. HR=hazard ratio. CrI=credible interval. PaO_2=partial pressure of oxygen. FiO_2=fraction of inspired oxygen. APACHE=Acute Physiology and Chronic Health Evaluation.

Table 3: **Cumulative effect on HRs of exposure to high intensities of mechanical ventilation for 7876 patients with available data**



Urner M. Time-varying intensity of mechanical ventilation and mortality in patients with acute respiratory failure: a registry-based, prospective cohort study. [*Lancet Resp Med* 2020; **8**:905; doi: 10.1016/S2213-2600(20)30325-8]

EJA European Journal of Anaesthesiology

QUESTION Does the intensity of ventilation, reflected by the mechanical power of ventilation (MP), has an association with outcome in invasively ventilated patients without ARDS.

CONCLUSION In ICU patients without ARDS, MP has an independent association with mortality. This finding suggest that MP holds an added predictive value over its individual components, making MP an attractive parameter to monitor and target in these patients.

POPULATION

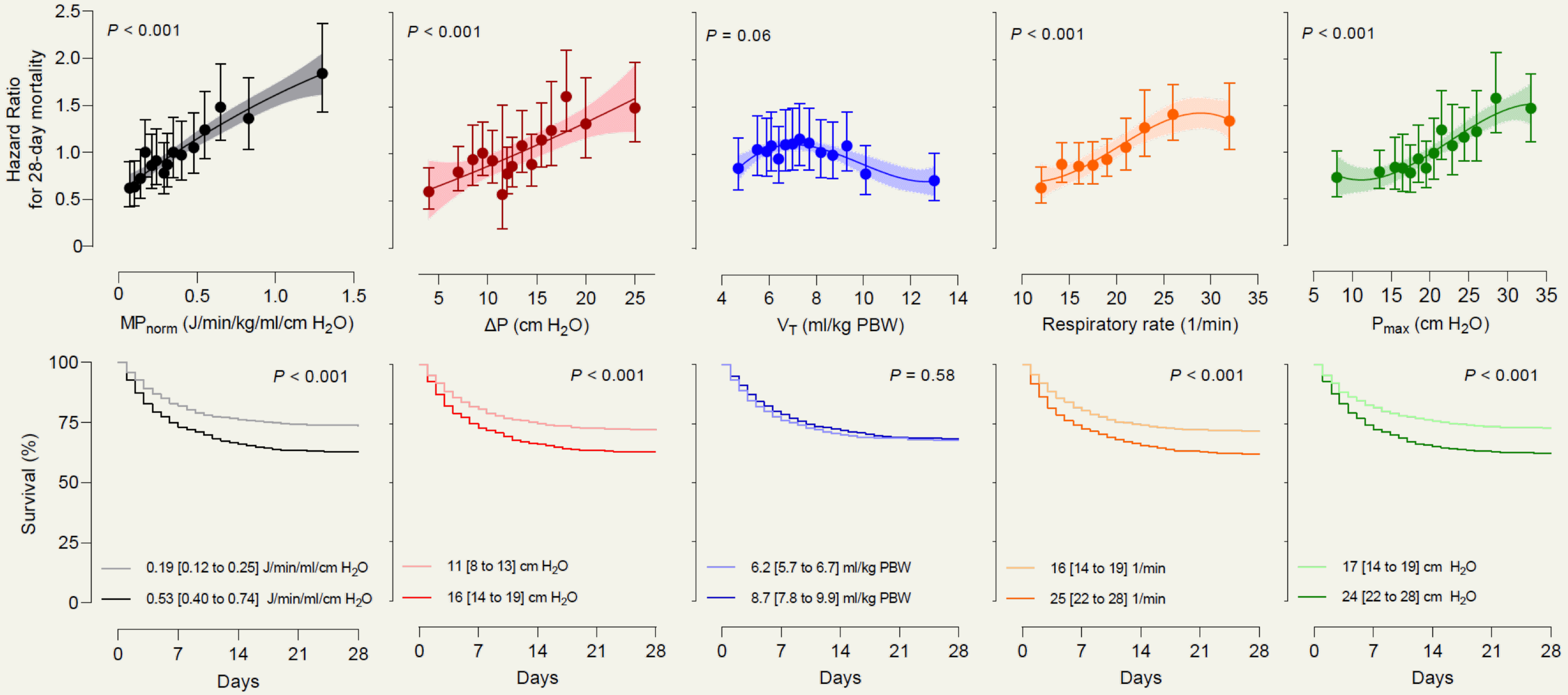
1962 Patients

ICU patients without ARDS, expected to need invasive ventilation > 24 hours

Median Age: **67** years

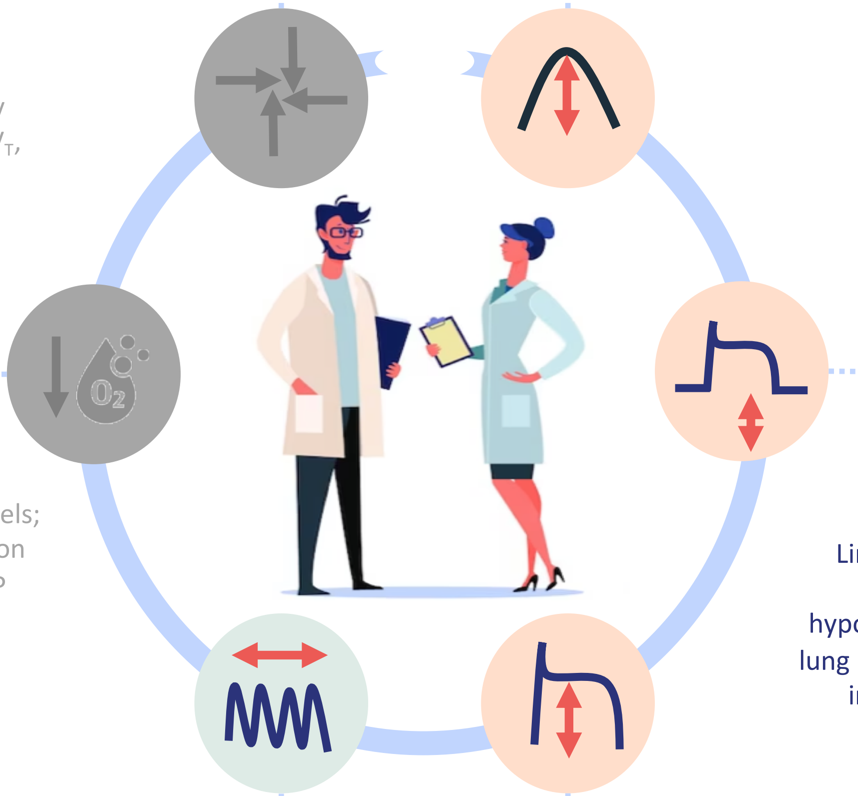
LOCATION

8 ICUs in the Netherlands



van Meenen D, for the NEBULAE–, PReVENT– and RELAx–investigators. Effect of Intensity of Ventilation on Outcome in Invasively Ventilated ICU patients without ARDS—An IPD–analysis of Three Randomized Clinical Trials. [*Eur J Anaesth* 2022; Nov 21; doi:10.1097/EJA.0000000000001778]

ventilator settings in critically ill patients—prioritize permissive over aggressive ventilation



Step 1

Use low V_T

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Rational

Volutrauma

Randomized clinical trials and observational studies have shown benefit from low V_T; ventilation with low V_T might lead to hypoxemia; a compensatory increase in RR may be harmful.

Step 2

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Limit use of high PEEP to patients with severe hypoxemia, and only when lung lesions are recruitable; instead, consider prone positioning.

Rational

Atelectrauma *vs* overdistension

Randomized clinical trials could not confirm benefit from high PEEP, and observational studies even suggested harm; in some patients high PEEP could lead to overdistension rather than recruitment.

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V_T, tidal volume; PEEP, positive end–expiratory pressure; ΔP, driving pressure; MP, mechanical power of ventilation; RR, respiratory rate; FiO_2, fraction of inspired O_2

Infographic on ventilation management by **Marcus Schultz,** Amsterdam UMC, Amsterdam, the Netherlands (1.1–240423)

ATS Journals

QUESTION What is the impact of mechanical power on mortality in patients with ARDS as compared with that of primary ventilator variables such as the ΔP, V_T, and RR?

CONCLUSION Mechanical power was associated with mortality during controlled mechanical ventilation in ARDS, but a simpler model using only the ΔP and RR was equivalent.

POPULATION

1728 Women **2821** Men

Patients with ARDS

Mean Age: **55** years

LOCATION

6 RCTs and **1** observational study

VENTILATION PARAMETERS

4549 patients with mild, moderate or severe ARDS

MP
0.32 J/min/kg

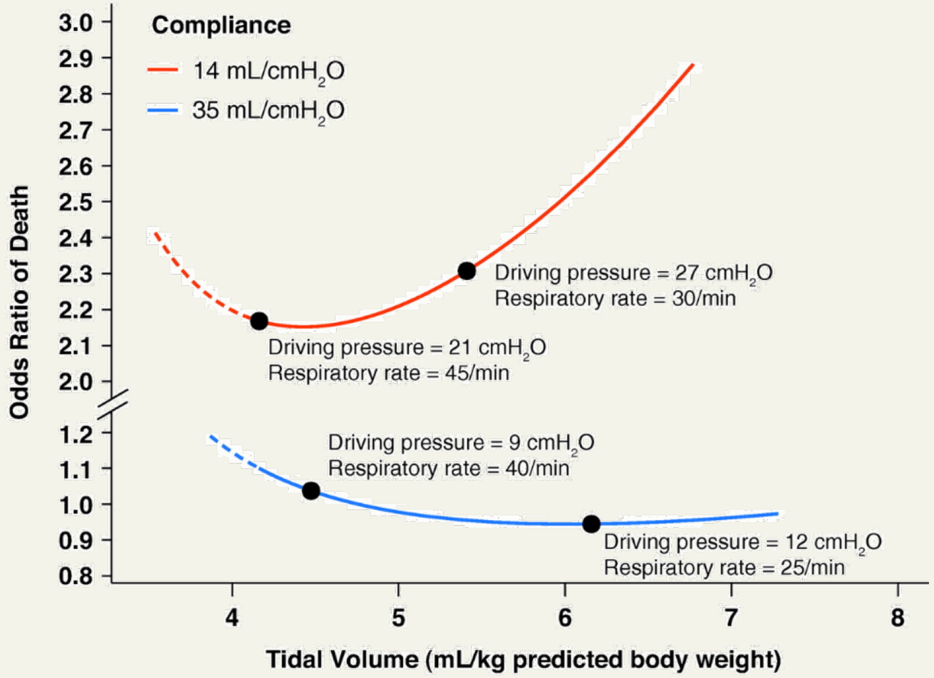
ΔP
15 cm H_2O

RR
26 breath/min

(PRIMARY) OUTCOME

Mortality at 28 or 60 days

FINDINGS



Costa et al. Ventilatory Variables and Mechanical Power in Patients with the acute respiratory distress syndrome. [*American Journal of Respiratory and Critical Care Medicine* 2021; **204**:303 doi:10.1164/rccm.202009-3467OC]

Critical Care Explorations

Society of Critical Care Medicine
The Intensive Care Professionals

QUESTION Is the amount of mechanical power of ventilation (MP) under adaptive support ventilation (ASV) different from that under nonautomated pressure–controlled ventilation?

CONCLUSION This study suggests ASV may have benefits compared with pressure–controlled ventilation with respect to the MP transferred from the ventilator to the respiratory system in passive invasively ventilated critically ill patients.

POPULATION

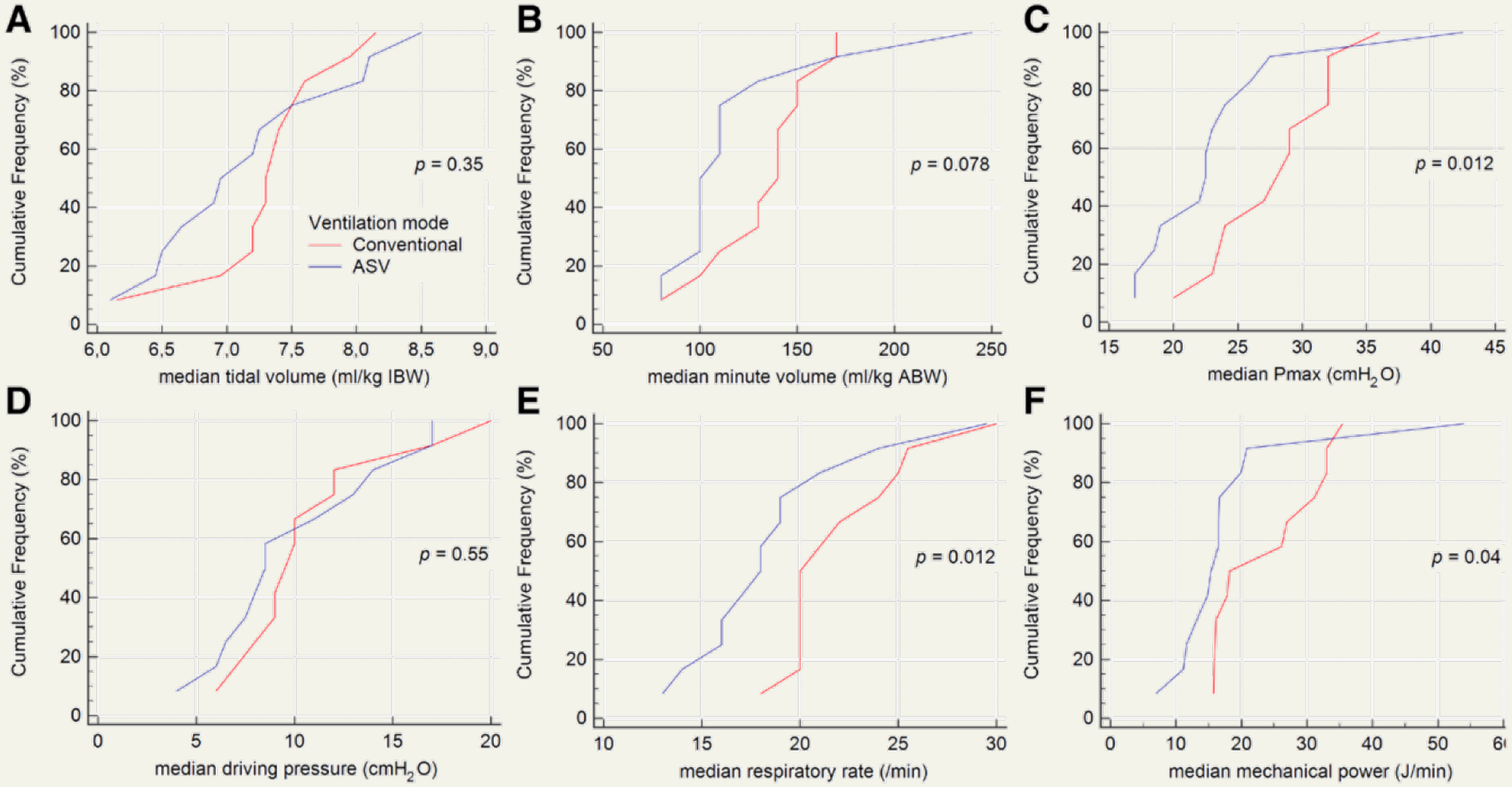
7 Women **15** Men

patients expected to nee invasive ventilation for the next 24 hours

Median Age: **67** years

LOCATION

1 ICUs in The Netherlands



Buiteman–Kruizinga L. Comparison of Mechanical Power During Adaptive Support Ventilation Versus Nonautomated Pressure–Controlled Ventilation—A Pilot Study. [*Crit Care Explorations* 2021; **3**:e0335. doi: 10.1097/CCE.0000000000000335]

Journal of
Clinical Medicine

QUESTION In COVID–19 patients with ARDS, does INTELLiVENT–ASV reduce the driving pressure and mechanical power of ventilation compared with conventional ventilation?

CONCLUSION INTELLiVENT–ASV reduces the intensity of ventilation in COVID–19 patients with ARDS.

POPULATION

12 Women **39** Men

COVID–19 with moderate to severe ARDS

Median Age: **63** years

LOCATION

2 ICUs in the Netherlands

INTERVENTION

51 patients intubated in the ICU for acute hypoxemia

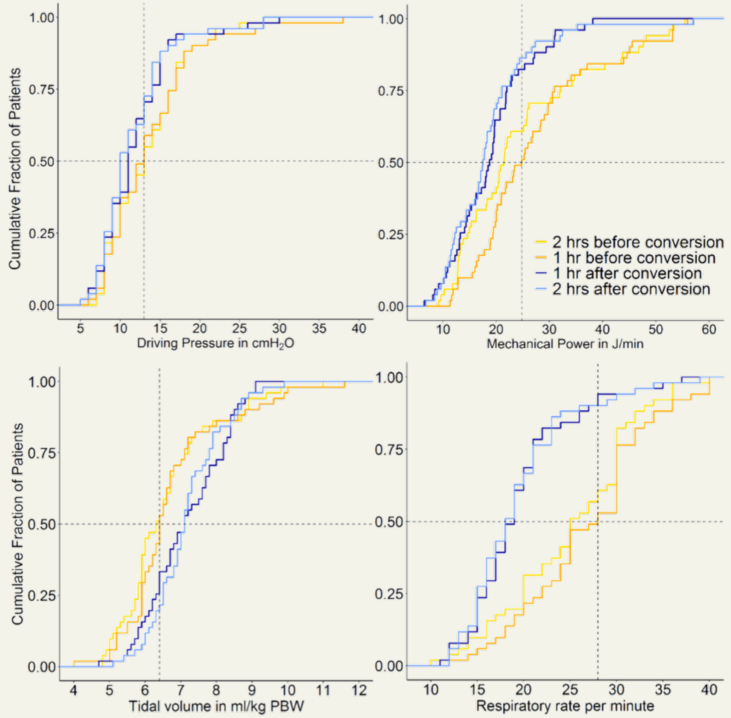
conventional ventilation → **automated ventilation**

crossover

(PRIMARY) OUTCOME

ΔP and MP before and after converting from conventional ventilation to INTELLiVENT–ASV

FINDINGS



Buiteman–Kruizinga L. Effect of INTELLiVENT-ASV versus Conventional Ventilation on Ventilation Intensity in Patients with COVID-19 ARDS—An Observational Study. [*J Clin Med* 2021; 10:5409]

under review

QUESTION Does INTELLiVENT–Adaptive Support Ventilation (ASV) reduce respiratory system and pulmonary driving pressure (ΔP_{RS} vs. ΔP_{TP}) and mechanical power of ventilation (MP_{RS} vs. MP_{TP}) in patients with moderate–to–severe ARDS that receive lung–protective ventilation?

CONCLUSION INTELLiVENT–ASV reduces ΔP_{TP} and MP_{TP}, in patients with moderate–to–severe ARDS that receive lung–protective ventilation.

POPULATION

13 passive patients

ICU patients with moderate to severe ARDS with a Peso *in situ*

Median Age: **67** years

LOCATION

1 ICU
in the
Netherlands

INTERVENTION

13 patients under invasive ventilation + Peso

randomized

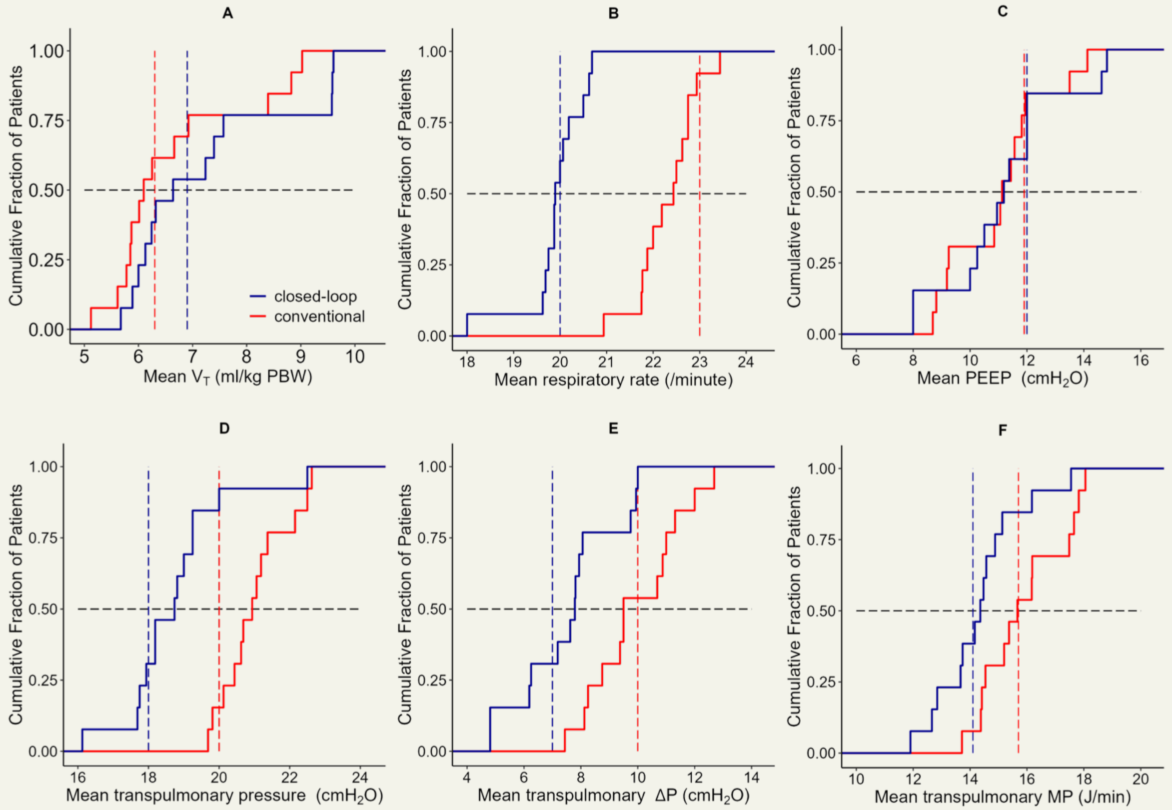
4 hours conventional ventilation *or* closed–loop

crossover

4 hours conventional ventilation *or* closed–loop

(PRIMARY) OUTCOME

ΔP_{TP}, ΔP_{RS}, V_T, RR, PEEP, PIP_{TP}, MP_{TP} and MP_{RS}



Buiteman–Kruizinga L, for the AiRDRoP–investigators. Does Automated closed–loop ventilation Reduce DRiving Pressure levels in patients with ARDS ('AiRDRoP') [2017; NCT03211494 at clinicaltrials.gov]

The NEW ENGLAND JOURNAL of MEDICINE

QUESTION Does a ventilatory strategy designed to minimize lung injuries reduce not only pulmonary complications but also mortality at 28 days in patients with ARDS?

CONCLUSION As compared with conventional ventilation, the protective strategy was associated with improved survival at 28 days, a higher rate of weaning, and a lower rate of barotrauma in patients with ARDS.

POPULATION

53 patients

patients with early (moderate to severe) ARDS

mean age: **35** years

LOCATION

2 ICUs in Brazil

VENTILATION STRATEGIES

53 patients with early (moderate to severe) ARDS

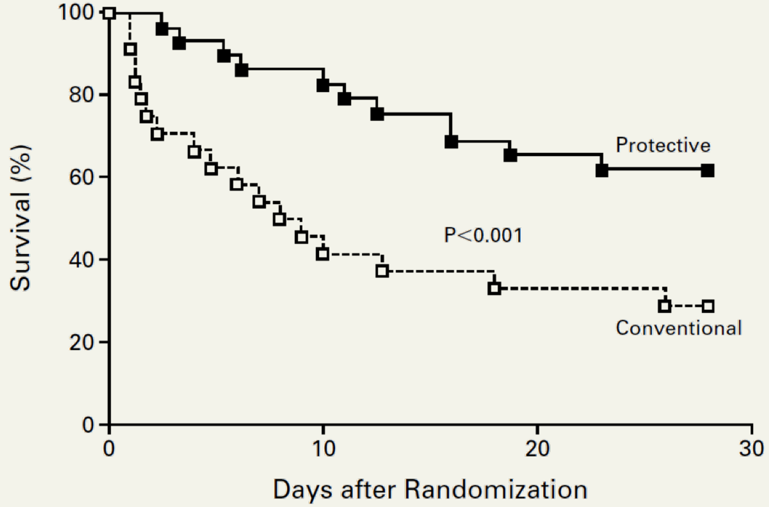
29 patients
'protective'
low V_T (6 ml/kg) + permissive hypercapnia (CO_2 up to 80 mmHg [10.7 kPa]) + P_{flex} for PEEP

24 patients
'conservative'
high V_T (12 ml/kg) + normocapnia (CO_2 up to 25 mmHg [3.3 kPa]) + incremental PEEP

(PRIMARY) OUTCOME

Survival at day 28 (primary); duration of ventilation, barotrauma

FINDINGS



No. at Risk	0	10	20	30
Protective	29	25	20	18
Conventional	24	11	9	7

Amato M. Effect of a protective–ventilation strategy on mortality in the acute respiratory distress syndrome. [*New Eng J Med* 1998; **338**:347 doi:10.1056/NEJM199802053380602]

QUESTION Which ventilator variable to prioritize when striving to achieve reduced MP levels?

CONCLUSION Increasing Pplat and increasing RR are most associated with a higher risk of high MP. When striving to achieve a lower MP, the RR seems to be the most attractive ventilator variable to adjust.

POPULATION

2885 Patients

ICU patients without ARDS, expected to need invasive ventilation > 24 hours

Median Age: **67** years

LOCATION

8 ICUs in the Netherlands

2885 patients randomized in the pooled dataset

1153 patients excluded
- **557** with spontaneous breathing activity
- **474** missing data for calculating MP
  - **64** extubation before data collection
  - **25** loss to follow-up
  - **19** ARDS at start of ventilation
  - **14** withdrew informed consent

1732 fully analyzable patients

NEBULAE–, PReVENT–, and RELAx–investigators (WIzARDS). Associations of Mechanical Power of Ventilation with Separate Ventilation Variables in Patients without ARDS. *In preparation.*

QUESTION Which ventilator variable to prioritize when striving to achieve reduced MP levels?

CONCLUSION Increasing Pplat and increasing RR are most associated with a higher risk of high MP. When striving to achieve a lower MP, the RR seems to be the most attractive ventilator variable to adjust.

POPULATION

2885 Patients

ICU patients without ARDS, expected to need invasive ventilation > 24 hours

Median Age: **67** years

LOCATION

8 ICUs in the Netherlands

NEBULAE–, PReVENT–, and RELAx–investigators (WIzARDS). Associations of Mechanical Power of Ventilation with Separate Ventilation Variables in Patients without ARDS. *In preparation.*

QUESTION Which ventilator variable to prioritize when striving to achieve reduced MP levels?

CONCLUSION Increasing Ppeak and increasing RR are most associated with a higher risk of high MP. When striving to achieve a lower MP, the RR seems to be the most attractive ventilator variable to adjust.

POPULATION

2885 Patients

ICU patients without ARDS, expected to need invasive ventilation > 24 hours

Median Age: **67** years

LOCATION

8 ICUs in the Netherlands

NEBULAE–, PReVENT–, and RELAx–investigators (WIzARDS). Associations of Mechanical Power of Ventilation with Separate Ventilation Variables in Patients without ARDS. *In preparation.*

Conclusions

- from (too) aggressive to permissive
- from single variables to parameters
- from simple to complex settings
- ΔP and MP —— V_T, minute volume, RR, and maybe PEEP
- automation