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18 NOVEMBRE 2023

CONGRÈS 2023

# Ventilation Mécanique Protectrice
## Pourquoi et Comment ?

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UNIVERSITÉ Clermont Auvergne
FACULTÉ DE MÉDECINE

- Déclaration / **Liens d'intérets**
  - **Consultant** : Dräger Medical, GE Healthcare
  - **Intervenant (congrès)** : Fisher & Paykel Healthcare, GE Healthcare, Dräger Medical, Baxter, Getinge
  - **Support technique** : Draeger Medical, GE Healthcare

# Ventilation Mécanique Protectrice

**Objectif :**

**Limiter ou, idéalement prévenir, les lésions pulmonaires induites par la ventilation mécanique (VILI, Ventilator-Induced Lung Injury)**

# Ventilator-induced Lung Injury (VILI)

Lung injury affecting the airways and parenchyma caused by (or exacerbated by) mechanical ventilation:

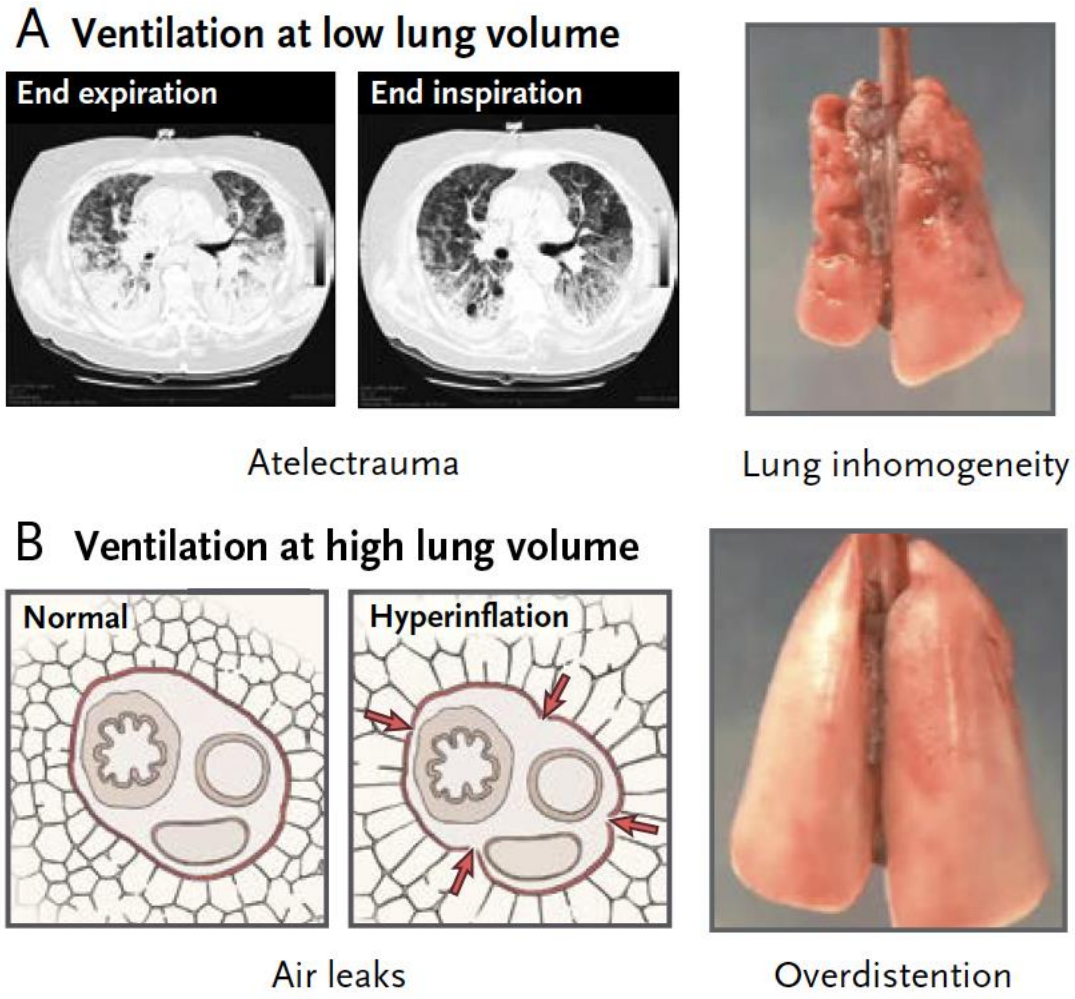
- **Volotrauma (tidal overdistention)**
  - Excessive end-inspiratory lung volume
- **Atelectrauma**
  - Shear forces resulting from cyclic opening and collapse of atelectatic but recruitable lung units
- **Barotrauma**
  - Alveolar rupture due to elevated transalveolar pressure (pneumothorax)
- **Biotrauma**
  - Translocation of mediators, bacteria, or lipopolysaccharide from the airspaces into the systemic circulation

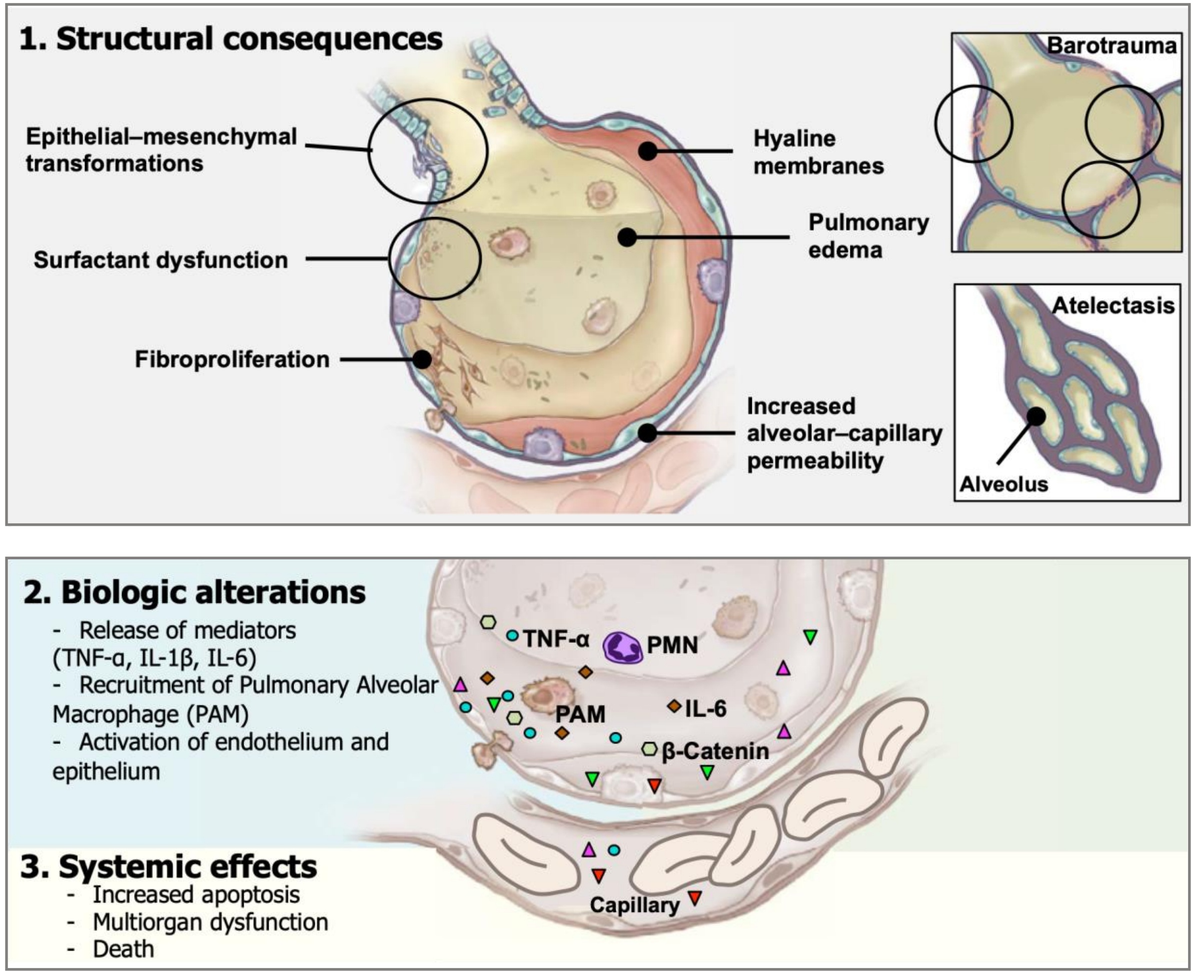
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

# Ventilator-Induced Lung Injury

Arthur S. Slutsky, M.D., and V. Marco Ranieri, M.D.



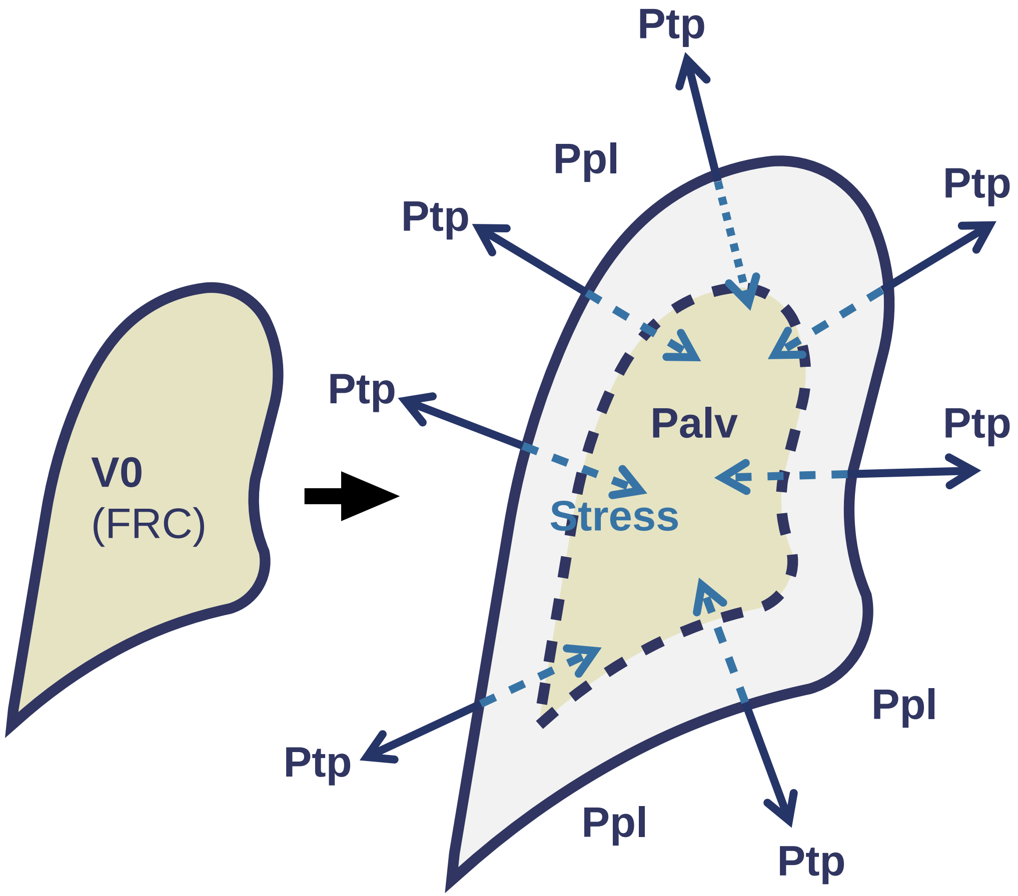

Slutsky AS, Ranieri VM. N Engl J Med 2013;369:2126-2136

# **Stress** and **Strain**

- **Stress**: force/area
- **Strain**: change in the dimension of a structure from its original dimension
Volumetric strain: volume change (ΔV) relative to resting (initial) lung volume (functional residual capacity, FRC)

**Strain** = ΔV / V0 = **ΔV / FRC**
= **(VT + ΔVPEP / FRC)**

**Stress = k × Strain**
(k: specific elastance)




**Stress = transpulmonary pressure (Ptp)**
**= Palv - Ppl**

# **Stress** and **Strain**

## (**Stress** = k × **Strain**)

(k: specific elastance)

- ↓ EELV: ↑ **Strain**
- ↓ VT: ↓ **Strain**

$$\textbf{Strain} = \frac{VT}{EELV}$$

- **VT alone does not determine risk of lung injury**
  (because it does not take into account the starting volume of the lung to which it is applied)
- **Low VT ventilation may lead to derecruitment and atelectasis**
- **Restoring EELV is critical to preventing lung injury**

VOLUME 342 MAY 4, 2000 NUMBER 18

# VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

## ARMA trial

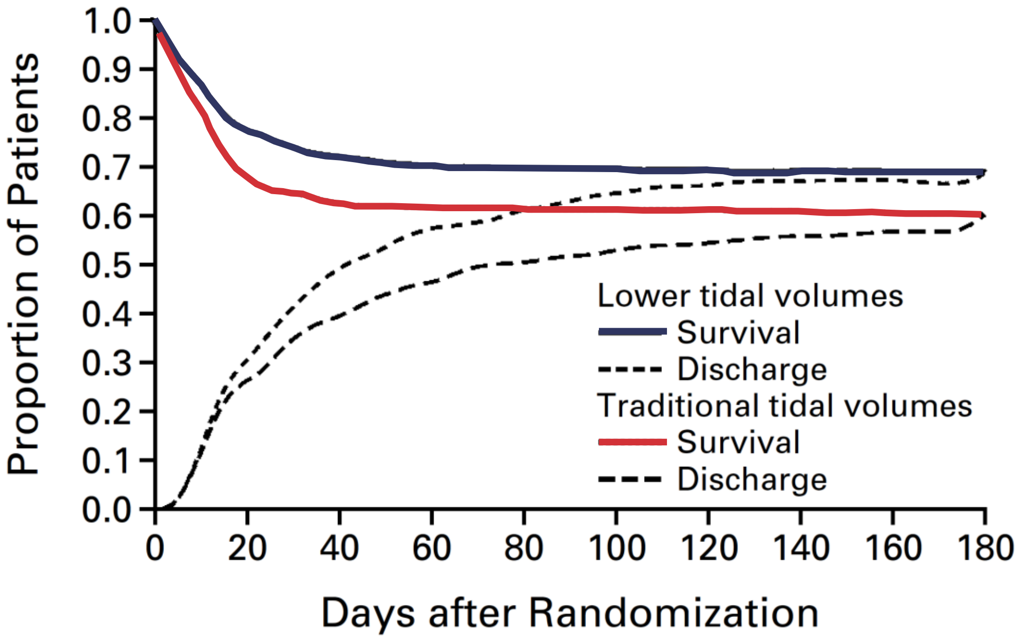
N=861 ARDS patients

Trial stopped after the fourth interim analysis

**TABLE 1.** SUMMARY OF VENTILATOR PROCEDURES.*

| VARIABLE | GROUP RECEIVING TRADITIONAL TIDAL VOLUMES | GROUP RECEIVING LOWER TIDAL VOLUMES |
|---|---|---|
| Ventilator mode | Volume assist–control | Volume assist–control |
| Initial tidal volume (ml/kg of predicted body weight)† | 12 | 6 |
| Plateau pressure (cm of water) | ≤50 | ≤30 |
| Ventilator rate setting needed to achieve a pH goal of 7.3 to 7.45 (breaths/min) | 6–35 | 6–35 |
| Ratio of the duration of inspiration to the duration of expiration | 1:1–1:3 | 1:1–1:3 |
| | Oxygenation goal $PaO_2$, 55–80 mm Hg, or $SpO_2$, 88–95% | |
| | Allowable combinations of $FiO_2$ and PEEP | |

**Figure 1.** Probability of Survival and of Being Discharged Home and Breathing without Assistance during the First 180 Days after Randomization



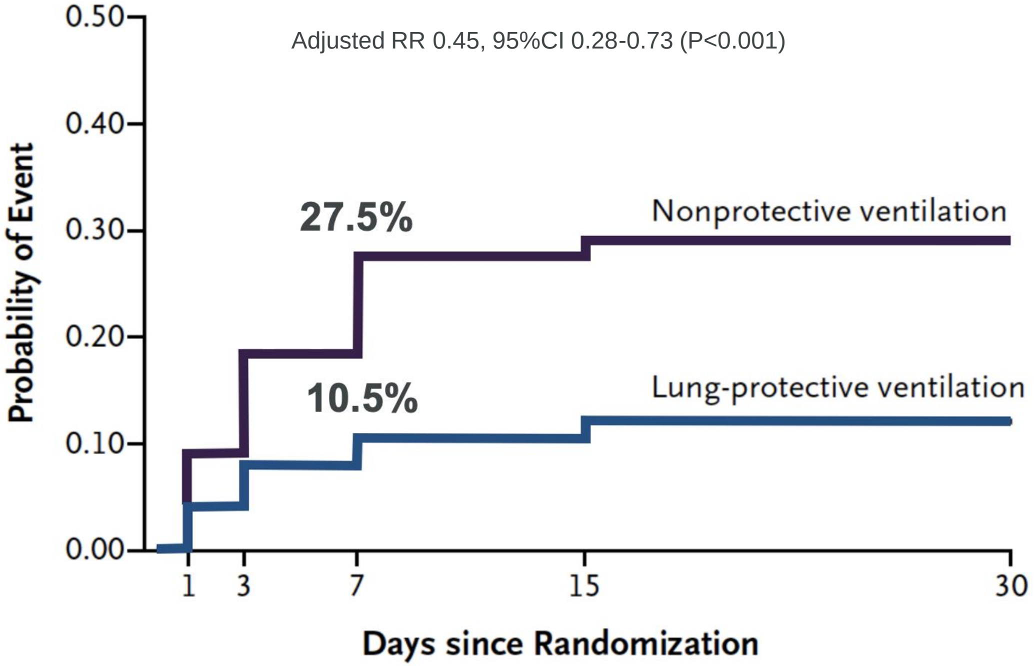
ORIGINAL ARTICLE

# A Trial of Intraoperative Low-Tidal-Volume Ventilation in Abdominal Surgery

Emmanuel Futier, M.D., Jean-Michel Constantin, M.D., Ph.D., Catherine Paugam-Burtz, M.D., Ph.D., Julien Pascal, M.D., Mathilde Eurin, M.D., Arthur Neuschwander, M.D., Emmanuel Marret, M.D., Marc Beaussier, M.D., Ph.D., Christophe Gutton, M.D., Jean-Yves Lefrant, M.D., Ph.D., Bernard Allaouchiche, M.D., Ph.D., Daniel Verzilli, M.D., Marc Leone, M.D., Ph.D., Audrey De Jong, M.D., Jean-Etienne Bazin, M.D., Ph.D., Bruno Pereira, Ph.D., and Samir Jaber, M.D., Ph.D., for the IMPROVE Study Group*

## IMPROVE trial

- N=400 abdominal surgery patients
- Intervention:
  - **- Non-protective ventilation**
    VT 10-12 ml/kg PBW, no PEEP, no RM
  - **- Lung-protective ventilation**
    VT 6-8 ml/kg PBW, PEEP 6-8 $cmH_2O$, repeated RM
- **Primary outcome**: Composite of pulmonary and non-pulmonary complications within 7 days after surgery




N Engl J Med 2013;369:428-37

2013 — 2014 — 2019 — 2020

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTI[CLE]

A Trial of Intraoperative L[ow-Tidal-Volume] Ventilation in Abdom[inal Surgery]

Emmanuel Futier, M.D., Jean-Michel C[...], Catherine Paugam-Burtz, M.D., Ph.D. [...], Mathilde Eurin, M.D., Arthur Neuschwander, M[...], Marc Beaussier, M.D., Ph.D., Christophe Gutton, M[...], Bernard Allaouchiche, M.D., Ph.D., Daniel Verzilli [...], Audrey De Jong, M.D., Jean-Etienne Bazin, M.D. [...], and Samir Jaber, M.D., Ph.D., for the IM[PROVE Study Group]*

ABSTRACT

BACKGROUND

Lung-protective ventilation with the use of low [...] expiratory pressure is considered best practice [...] patients. However, its role in anesthetized patie[nts ...] not known.

METHODS

In this multicenter, double-blind, parallel-group [...] adults at intermediate to high risk of pulmonar[y ...] dominal surgery to either nonprotective mecha[nical ventilation or] lung-protective ventilation. The primary outcom[e ...] monary and extrapulmonary complications occu[rring ...] surgery.

RESULTS

The two intervention groups had similar charact[eristics ...] The two intervention groups had similar charact[eristics ...] tion-to-treat analysis, the primary outcome occur[red ...] assigned to lung-protective ventilation, as compare[d ...] to nonprotective ventilation (relative risk, 0.40; 9[5% CI ...] to 0.68; P=0.001). Over the 7-day postoperative pe[riod ...] to lung-protective ventilation required noninvas[ive ...] acute respiratory failure, as compared with 34 ([...] ventilation (relative risk, 0.29; 95% CI, 0.14 to 0.61; [...] tal stay was shorter among patients receiving lung-[...] those receiving nonprotective ventilation (mean [...] −4.17 to −0.72; P=0.006).

CONCLUSIONS

As compared with a practice of nonprotective m[echanical ventilation ...] a lung-protective ventilation strategy in interme[diate ...] undergoing major abdominal surgery was associ[ated ...] comes and reduced health care utilization. (IMP[ROVE ...] NCT01282996.)

From the Département d'Anesthésie et Réanimation, Hôpital Estaing (E.F., J.-M.C., J.P., J.-E.B.), Université de Clermont-Ferrand, Retinoids, Reproduction, and Developmental Diseases Unit, Equipe Accueil 7281 (E.F., J.-M.C.), and the Biostatistics Unit, Direction de la Recherche Clinique (B.P.), Centre Hospitalier Universitaire (CHU) de Clermont-Ferrand, Clermont-Ferrand; Assistance Publique–Hôpitaux de Paris (AP-HP), Département d'Anesthésie et Réanimation, Hôpital Beaujon, Hôpitaux Universitaires Paris Nord Val de Seine and Université Paris Diderot, Sorbonne Paris Cité (C.P.-B., M.E., A.N.), Département d'Anesthésie et Réanimation, Hôpital Tenon (E.M.), and AP-HP, Département d'Anesthésie et Réanimation, Hôpital Saint-Antoine (M.B., C.G.), Paris; CHU de Nîmes, Section d'Anesthésie and Département d'Anesthésie et Réanimation, Nîmes (J.-Y.L.); CHU de Lyon, Département d'Anesthésie et Réanimation, Hôpital Edouard Herriot, Lyon (B.A.); CHU de Montpellier, Département d'Anesthésie et Réanimation B, Hôpital Saint-Eloi, and INSERM Unité 1046 and Université Montpellier 1, Montpellier (D.V., A.D.J., S.J.); and Assistance Publique–Hôpital de Marseille, Département d'Anesthésie et Réanimation, Hôpital Nord, Marseille (M.L.) — all in France. Address reprint requests to Dr. Jaber at the Département d'Anesthésie et Réanimation B (DAR B), 80 Ave. Augustin Fliche, 34295 Montpellier, France, or at s-jaber@chu-montpellier.fr.

*Additional investigators in the Intraoperative Protective Ventilation (IMPROVE) Study Group are listed in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2013;369:428-37.
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428 N ENGL J MED 369;5 NEJM.ORG AUGUST 1, 2013

High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVH[IO] trial): a multicentre randomised controlled trial

The PROVE Network Investigators* for the Clinical Trial Network of the European Society of Anaesthesiology

Summary

Background The role of positive end-expiratory pressure in mechanical ventilation during general anaest[hesia for] surgery remains uncertain. Levels of pressure higher than 0 cm $H_2O$ might protect against postoperative pu[lmonary] complications but could also cause intraoperative circulatory depression and lung injury from overdis[tension.] We tested the hypothesis that a high level of positive end-expiratory pressure with recruitment manoeuvres [protects] against postoperative pulmonary complications in patients at risk of complications who are receiving me[chanical] ventilation with low tidal volumes during general anaesthesia for open abdominal surgery.

Methods In this randomised controlled trial at 30 centres in Europe and North and South America, we [...] 900 patients at risk for postoperative pulmonary complications who were planned for open abdominal surge[ry ...] general anaesthesia and ventilation at tidal volumes of 8 mL/kg. We randomly allocated patients to either a h[igh level] of positive end-expiratory pressure (12 cm $H_2O$) with recruitment manoeuvres (higher PEEP group) or a low [level of] pressure (≤2 cm $H_2O$) without recruitment manoeuvres (lower PEEP group). We used a centralised c[...] generated randomisation system. Patients and outcome assessors were masked to the intervention. Primary [...] was a composite of postoperative pulmonary complications by postoperative day 5. Analysis was by intention[-to-treat.] The study is registered at Controlled-Trials.com, number ISRCTN70332574.

Findings From February, 2011, to January, 2013, 447 patients were randomly allocated to the higher PEE[P group] and 453 to the lower PEEP group. Six patients were excluded from the analysis, four because they withdrew [...] and two for violation of inclusion criteria. Median levels of positive end-expiratory pressure were 12 [...] (IQR 12–12) in the higher PEEP group and 2 cm $H_2O$ (0–2) in the lower PEEP group. Postoperative pu[lmonary] complications were reported in 174 (40%) of 445 patients in the higher PEEP group versus 172 (39%) of 449 in the lower PEEP group (relative risk 1·01; 95% CI 0·86–1·20; p=0·86). Compared with patients in the low[er PEEP] group, those in the higher PEEP group developed intraoperative hypotension and needed more vasoactive d[rugs.]

Interpretation A strategy with a high level of positive end-expiratory pressure and recruitment manoeuvre[s during] open abdominal surgery does not protect against postoperative pulmonary complications. An intraoperative p[rotective] ventilation strategy should include a low tidal volume and low positive end-expiratory pressure, without rec[ruitment] manoeuvres.

Funding Academic Medical Center (Amsterdam, Netherlands), European Society of Anaesthesiology.

Introduction

About 234 million major surgical procedures are undertaken worldwide every year. Of these interventions, around 2·6 million represent high-risk procedures, with 1·3 million patients developing complications that result in 315 000 in-hospital deaths.[1] Postoperative pulmonary complications are at least as frequent as cardiac complications during non-cardiac surgery[2] and are associated with increased risk of in-hospital death, particularly after open abdominal surgery.[3,4] Mechanical ventilation might affect the incidence of postoperative pulmonary complications[5] and, possibly, distal organ dysfunction.[6] Different mechanisms have been proposed to account for the injurious effects of ventilation. Both hyperinflation and repetitive tidal recruitment of lung units can induce the release of proinflammatory mediators, leading to lung and distal organ injury.[7]

Prevention of hyperinflation by use of low tidal [...] reduces mortality in patients with acute re[spiratory] distress syndrome.[8] Mortality can also be d[...] in individuals with severe acute respir[atory ...] syndrome by avoiding repetitive tidal recr[uitment] with high levels of positive end-expiratory p[ressure.] Furthermore, use of low tidal volumes in patients [...] lung injury under general anaesthesia might als[o ...] the incidence of postoperative pulmonary compli[cations.] This hypothesis was proven in a single-centre [...] national multicentre trial.[11] However, in both stu[dies ...] of lower tidal volumes was combined with high [...] of positive end-expiratory pressure; thus, did b[...] effects come from prevention of hyperinfla[tion ...] avoidance of repetitive tidal recruitment? Use of [...] levels of positive end-expiratory pressure could [...] atelectasis with ventilation strategies that inc[...]

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Intraoperative High Positive E[nd-Expiratory Pressure] (PEEP) With Recruitment Maneuvers v[s Low PEEP] on Postoperative Pulmonary Complicat[ions in Obese Patients]
A Randomized Clinical Trial

Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network for the Clinical Trial Network of the European Society of Anaesthesiology

IMPORTANCE An intraoperative higher level of positive end-expiratory positive pr[essure] (PEEP) with alveolar recruitment maneuvers improves respiratory function in obe[se patients] undergoing surgery, but the effect on clinical outcomes is uncertain.

OBJECTIVE To determine whether a higher level of PEEP with alveolar recruitmen[t] maneuvers decreases postoperative pulmonary complications in obese patients u[ndergoing] surgery compared with a lower level of PEEP.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial of 2013 adults with b[ody mass] indices of 35 or greater and substantial risk for postoperative pulmonary complicati[ons who] were undergoing noncardiac, nonneurological surgery under general anesthesia. Th[e trial was] conducted at 77 sites in 23 countries from July 2014-February 2018; final follow-up[...]

INTERVENTIONS Patients were randomized to the high level of PEEP group (n = 9[...]) consisting of a PEEP level of 12 cm $H_2O$ with alveolar recruitment maneuvers (a st[epwise] increase of tidal volume and eventually PEEP) or to the low level of PEEP group (n[...]) consisting of a PEEP level of 4 cm $H_2O$. All patients received volume-controlled ve[ntilation] with a tidal volume of 7 mL/kg of predicted body weight.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of pulm[onary] complications within the first 5 postoperative days, including respiratory failure, a[cute] respiratory distress syndrome, bronchospasm, new pulmonary infiltrates, pulmon[ary] infection, aspiration pneumonitis, pleural effusion, atelectasis, cardiopulmonary e[dema, and] pneumothorax. Among the 9 prespecified secondary outcomes, 3 were intraoper[ative] complications, including hypoxemia (oxygen desaturation with $Sp_{O_2}$ ≤92% for >1[...]

RESULTS Among 2013 adults who were randomized, 1976 (98.2%) completed the [trial (mean] age, 48.8 years; 1381 [69.9%] women; 1778 [90.1%] underwent abdominal opera[tions).] In the intention-to-treat analysis, the primary outcome occurred in 211 of 989 patien[ts (21.3%)] in the high level of PEEP group compared with 233 of 987 patients (23.6%) in the [low level of] PEEP group (difference, −2.3% [95% CI, −5.9% to 1.4%]; risk ratio, 0.93 [95% CI, [...] 1.04]; $P = .23$). Among the 9 prespecified secondary outcomes, 6 were not signifi[cantly] different between the high and low level of PEEP groups, and 3 were significantly [different,] including fewer patients with hypoxemia (5.0% in the high level of PEEP group vs [...] the low level of PEEP group; difference, −8.6% [95% CI, −11.1% to 6.1%]; $P < .001$)[...]

CONCLUSIONS AND RELEVANCE Among obese patients undergoing surgery under [general] anesthesia, an intraoperative mechanical ventilation strategy with a higher level o[f PEEP and] alveolar recruitment maneuvers, compared with a strategy with a lower level of P[EEP, did not] reduce postoperative pulmonary complications.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT02148692

JAMA. 2019;321(23):2292-2305. doi:10.1001/jama.2019.7505
Published online June 3, 2019.

Research

JAMA | Original Investigation

Effect of Intraoperative Low Tidal Volume vs Conventional Tidal Volume on Postoperative Pulmonary Complications in Patients Undergoing Major Surgery
A Randomized Clinical Trial

Dharshi Karalapillai, MD; Laurence Weinberg, MD; Philip Peyton, MD; Louise Ellard, MD; Raymond Hu, MD; Brett Pearce, MD; Chong O. Tan, MD; David Story, MD; Mark O'Donnell, MD; Patrick Hamilton, MD; Chad Oughton, MD; Jonathan Galtieri, MD; Anthony Wilson, MD; Ary Serpa Neto, MD, MSc, PhD; Glenn Eastwood, PhD; Rinaldo Bellomo, MD, PhD; Daryl A. Jones, MD, PhD

IMPORTANCE In patients who undergo mechanical ventilation during surgery, the ideal tidal volume is unclear.

OBJECTIVE To determine whether low-tidal-volume ventilation compared with conventional ventilation during major surgery decreases postoperative pulmonary complications.

DESIGN, SETTING, AND PARTICIPANTS Single-center, assessor-blinded, randomized clinical trial of 1236 patients older than 40 years undergoing major noncardiothoracic, nonintracranial surgery under general anesthesia lasting more than 2 hours in a tertiary hospital in Melbourne, Australia, from February 2015 to February 2019. The last date of follow-up was February 17, 2019.

INTERVENTIONS Patients were randomized to receive a tidal volume of 6 mL/kg predicted body weight (n = 614; low tidal volume group) or a tidal volume of 10 mL/kg predicted body weight (n = 592; conventional tidal volume group). All patients received positive end-expiratory pressure (PEEP) at 5 cm $H_2O$.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of postoperative pulmonary complications within the first 7 postoperative days, including pneumonia, bronchospasm, atelectasis, pulmonary congestion, respiratory failure, pleural effusion, pneumothorax, or unplanned requirement for postoperative invasive or noninvasive ventilation. Secondary outcomes were postoperative pulmonary complications including development of pulmonary embolism, acute respiratory distress syndrome, systemic inflammatory response syndrome, sepsis, acute kidney injury, wound infection (superficial and deep), rate of intraoperative need for vasopressor, incidence of unplanned intensive care unit admission, rate of need for rapid response team call, intensive care unit length of stay, hospital length of stay, and in-hospital mortality.

RESULTS Among 1236 patients who were randomized, 1206 (98.9%) completed the trial (mean age, 63.5 years; 494 [40.9%] women; 681 [56.4%] undergoing abdominal surgery). The primary outcome occurred in 231 of 608 patients (38%) in the low tidal volume group compared with 232 of 590 patients (39%) in the conventional tidal volume group (difference, −1.3% [95% CI, −6.8% to 4.2%]; risk ratio, 0.97 [95% CI, 0.84-1.11]; $P = .64$). There were no significant differences in any of the secondary outcomes.

CONCLUSIONS AND RELEVANCE Among adult patients undergoing major surgery, intraoperative ventilation with low tidal volume compared with conventional tidal volume, with PEEP applied equally between groups, did not significantly reduce pulmonary complications within the first 7 postoperative days.

TRIAL REGISTRATION ANZCTR Identifier: ACTRN12614000790640

JAMA. 2020;324(9):848-858. doi:10.1001/jama.2020.12866

Visual Abstract
Supplemental content
CME Quiz at jamacmelookup.com and CME Questions page 892

Author Affiliations: Author affiliations are listed at the end of this article.

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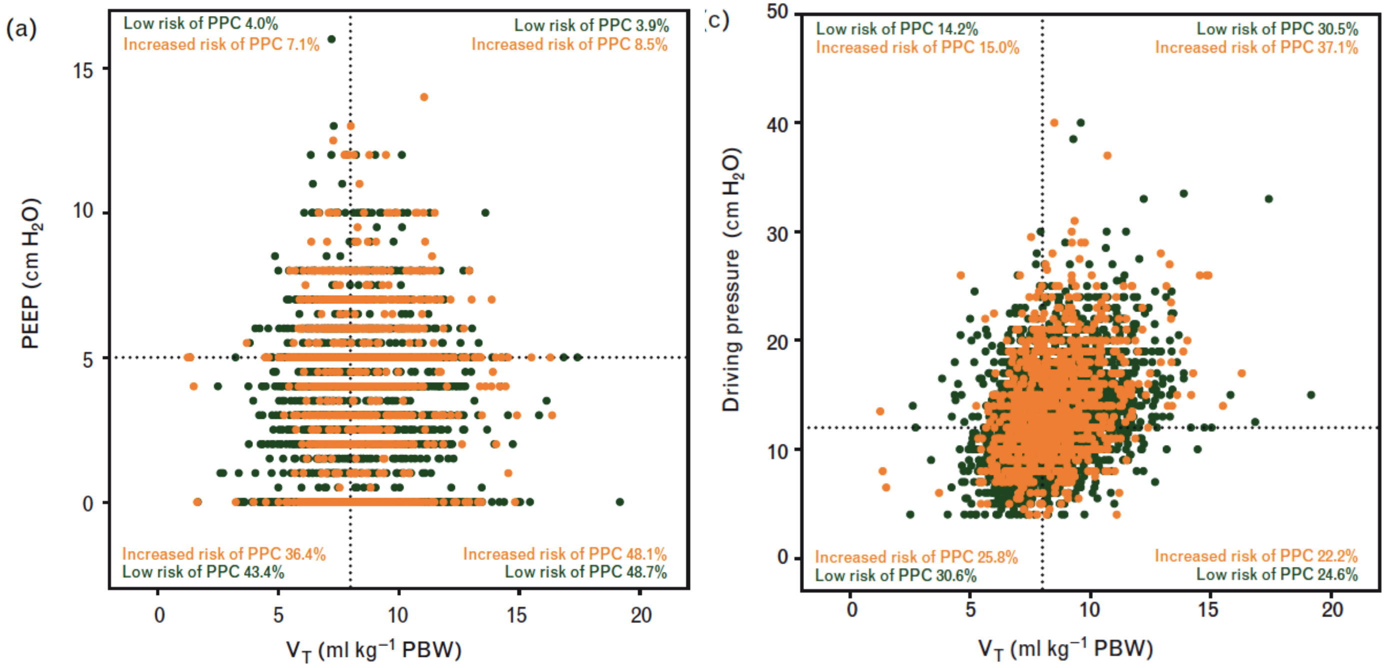
# Epidemiology, practice of ventilation and outcome for patients at increased risk of postoperative pulmonary complications

*LAS VEGAS - an observational study in 29 countries*

**Fig. 3** Distributions of (a) VT with PEEP, (b) VT with DP

**L**ocal **AS**sessment of **VE**ntilatory management during **G**eneral **A**naesthesia for **S**urgery (**LAS VEGAS** study)

- Multicenter prospective study (146 centers)
- 9864 patients over a period of 7 consecutive days
- Primary outcome: Incidence of patients at increased risk of PPC (ARISCAT score ≥ 26 pts): **28.3%**




**Patients at <u>increased risk of PPCs</u> received <u>higher VT</u> (ml/kg PBW)**
**A combination of low VT ventilation and PEEP (>5 cm$H_2O$) used in a minority of patients**

*Eur J Anaesthesiol* 2017; **34:**492−507

BJA

*British Journal of Anaesthesia*, 123 (6): 898–913 (2019)

RESPIRATION AND THE AIRWAY

# Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommendations

Christopher C. Young[1,2,*], Erica M. Harris[2], Charles Vacchiano[1,3], Stephan Bodnar[3], Brooks Bukowy[3], R. Ryland D. Elliott[2], Jaclyn Migliarese[3], Chad Ragains[2], Brittany Trethewey[3], Amanda Woodward[4], Marcelo Gama de Abreu[5], Martin Girard[6], Emmanuel Futier[7], Jan P. Mulier[8], Paolo Pelosi[9,10] and Juraj Sprung[11]

BJA

British Journal of Anaesthesia, 123 (6): 898–913 (2019)

RESPIRATION AND THE AIRWAY

# Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommendations

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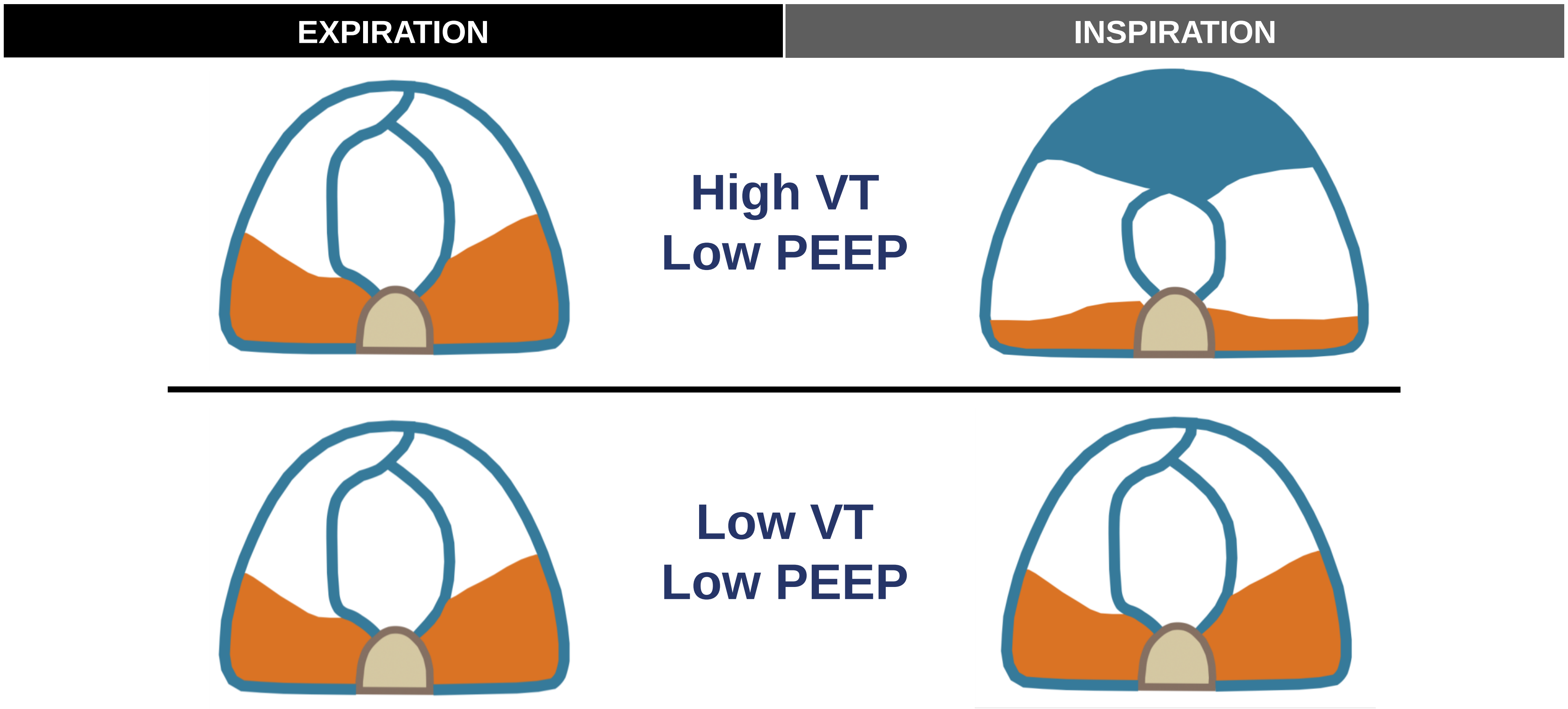
**Table 1** Recommendations and statements

| Question | Statement/recommendation |
|---|---|
| 1.2 | Use of **low-tidal-volume protective-ventilation** strategy (6-8 ml $kg^{-1}$ PBW). |
| 2.2 | We recommend that the ventilator should initially be set to deliver **VT ≤6-8 ml/kg PBW** and **PEEP of 5 $cmH_2O$**. |
| | **ZEEP is not recommended**. |

Consensus: 86%    Quality of evidence: Moderate    Strength of recommendation: Strong

# VILI: Dynamic and Static Strain

Lung volume can be dynamically increased by VT (**dynamic strain**)



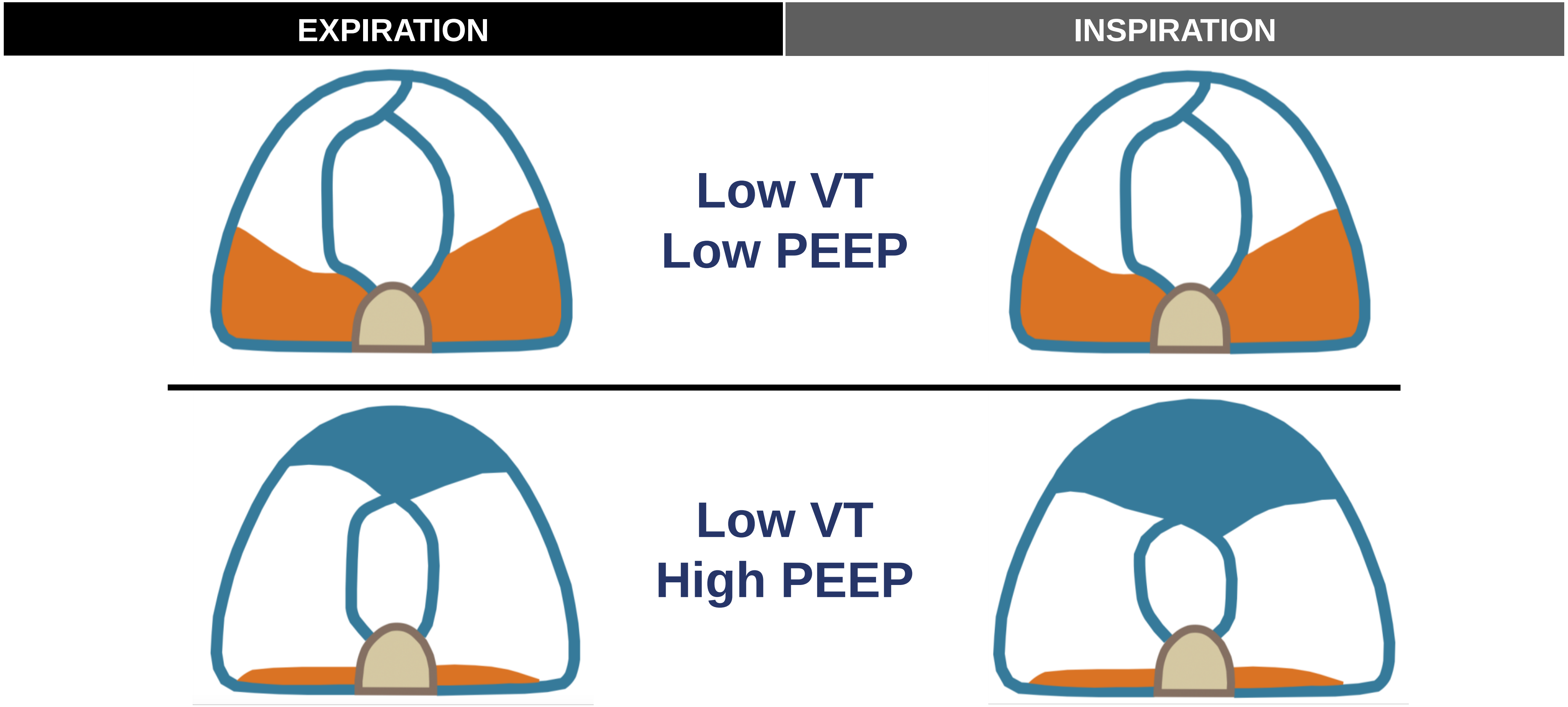

Dynamic strain = **VT** / (EELV $PEEP_{low}$ + VRec $_{PEEPhigh-PEEPlow}$)

Normally aerated | Atelectasis | Overinflation

Anesthesiology 2015; 123:692–713

# VILI: Dynamic and Static Strain

High PEEP does not benefit all patients and may generate overinflation with lung injury in already open alveoli (**static strain**)




Static strain = Vol $\mathbf{PEEP}_{high}$ / (EELV $\mathbf{PEEP}_{low}$ + $V_{Rec}$ [$\mathbf{PEEP}_{high}$-$\mathbf{PEEP}_{low}$])

**Normally aerated** **Atelectasis** **Overinflation**

Anesthesiology 2015; 123:692–713

EDITORIAL

March 21, 2017

# Optimizing the Settings on the Ventilator Settings

## High PEEP for All?

Ary Serpa Neto,MD, MSc, PhD; Marcus J. Schultz, MD, PhD

*JAMA.* Published online March 21, 2017. doi:10.1001/jama.2017.2570

# Higher *vs* Lower PEEP levels

## PROVHILO study (2014)

Articles

### High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial

*The PROVE Network Investigators* for the Clinical Trial Network of the European Society of Anaesthesiology*


**Summary**

**Background** The role of positive end-expiratory pressure in mechanical ventilation during general anaesthesia for surgery remains uncertain. Levels of pressure higher than 0 cm $H_2O$ might protect against postoperative pulmonary complications but could also cause intraoperative circulatory depression and lung injury from overdistension. We tested the hypothesis that a high level of positive end-expiratory pressure with recruitment manoeuvres protects against postoperative pulmonary complications in patients at risk of complications who are receiving mechanical ventilation with low tidal volumes during general anaesthesia for open abdominal surgery.

**Methods** In this randomised controlled trial at 30 centres in Europe and North and South America, we recruited 900 patients at risk for postoperative pulmonary complications who were planned for open abdominal surgery under general anaesthesia and ventilation at tidal volumes of 8 mL/kg. We randomly allocated patients to either a high level of positive end-expiratory pressure (12 cm $H_2O$) with recruitment manoeuvres (higher PEEP group) or a low level of pressure (≤2 cm $H_2O$) without recruitment manoeuvres (lower PEEP group). We used a centralised computer-generated randomisation system. Patients and outcome assessors were masked to the intervention. Primary endpoint was a composite of postoperative pulmonary complications by postoperative day 5. Analysis was by intention-to-treat. The study is registered at Controlled-Trials.com, number ISRCTN70332574.

**Findings** From February, 2011, to January, 2013, 447 patients were randomly allocated to the higher PEEP group and 453 to the lower PEEP group. Six patients were excluded from the analysis, four because they withdrew consent and two for violation of inclusion criteria. Median levels of positive end-expiratory pressure were 12 cm $H_2O$ (IQR 12–12) in the higher PEEP group and 2 cm $H_2O$ (0–2) in the lower PEEP group. Postoperative pulmonary complications were reported in 174 (40%) of 445 patients in the higher PEEP group versus 172 (39%) of 449 patients in the lower PEEP group (relative risk 1·01; 95% CI 0·86–1·20; p=0·86). Compared with patients in the lower PEEP group, those in the higher PEEP group developed intraoperative hypotension and needed more vasoactive drugs.

**Interpretation** A strategy with a high level of positive end-expiratory pressure and recruitment manoeuvres during open abdominal surgery does not protect against postoperative pulmonary complications. An intraoperative protective ventilation strategy should include a low tidal volume and low positive end-expiratory pressure, without recruitment manoeuvres.


**Funding** Academic Medical Center (Amsterdam, Netherlands), European Society of Anaesthesiology.


*Lancet* 2014; 384: 495–503

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See Comment page 472

*PROVE (PROtective VEntilation) Network Investigators are listed in the appendix pp 1–3, and the Steering and Writing committees are listed at the end of the report

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See Online for appendix

**Introduction**

About 234 million major surgical procedures are undertaken worldwide every year. Of these interventions, around 2·6 million represent high-risk procedures, with 1·3 million patients developing complications that result in 315 000 in-hospital deaths.[1] Postoperative pulmonary complications are at least as frequent as cardiac complications during non-cardiac surgery[2] and are associated with increased risk of in-hospital death, particularly after open abdominal surgery.[3,4] Mechanical ventilation might affect the incidence of postoperative pulmonary complications[5] and, possibly, distal organ dysfunction.[6] Different mechanisms have been proposed to account for the injurious effects of ventilation. Both hyperinflation and repetitive tidal recruitment of lung units can induce the release of proinflammatory mediators, leading to lung and distal organ injury.[7]

Prevention of hyperinflation by use of low tidal volumes reduces mortality in patients with acute respiratory distress syndrome.[8] Mortality can also be decreased in individuals with severe acute respiratory distress syndrome by avoiding repetitive tidal recruitment with high levels of positive end-expiratory pressure.[9] Furthermore, use of low tidal volumes in patients without lung injury under general anaesthesia might also reduce the incidence of postoperative pulmonary complications.[5] This hypothesis was proven in a single-centre[10] and a national multicentre trial.[11] However, in both studies, use of lower tidal volumes was combined with higher levels of positive end-expiratory pressure; thus, did beneficial effects come from prevention of hyperinflation or avoidance of repetitive tidal recruitment? Use of very low levels of positive end-expiratory pressure could lead to atelectasis with ventilation strategies that incorporate

## PROBESE study (2019)

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

### Effect of Intraoperative High Positive End-Expiratory Pressure (PEEP) With Recruitment Maneuvers vs Low PEEP on Postoperative Pulmonary Complications in Obese Patients
A Randomized Clinical Trial

Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network (PROVEnet) for the Clinical Trial Network of the European Society of Anaesthesiology


**IMPORTANCE** An intraoperative higher level of positive end-expiratory positive pressure (PEEP) with alveolar recruitment maneuvers improves respiratory function in obese patients undergoing surgery, but the effect on clinical outcomes is uncertain.

**OBJECTIVE** To determine whether a higher level of PEEP with alveolar recruitment maneuvers decreases postoperative pulmonary complications in obese patients undergoing surgery compared with a lower level of PEEP.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized clinical trial of 2013 adults with body mass indices of 35 or greater and substantial risk for postoperative pulmonary complications who were undergoing noncardiac, nonneurological surgery under general anesthesia. The trial was conducted at 77 sites in 23 countries from July 2014-February 2018; final follow-up: May 2018.

**INTERVENTIONS** Patients were randomized to the high level of PEEP group (n = 989), consisting of a PEEP level of 12 cm $H_2O$ with alveolar recruitment maneuvers (a stepwise increase of tidal volume and eventually PEEP) or to the low level of PEEP group (n = 987), consisting of a PEEP level of 4 cm $H_2O$. All patients received volume-controlled ventilation with a tidal volume of 7 mL/kg of predicted body weight.

**MAIN OUTCOMES AND MEASURES** The primary outcome was a composite of pulmonary complications within the first 5 postoperative days, including respiratory failure, acute respiratory distress syndrome, bronchospasm, new pulmonary infiltrates, pulmonary infection, aspiration pneumonitis, pleural effusion, atelectasis, cardiopulmonary edema, and pneumothorax. Among the 9 prespecified secondary outcomes, 3 were intraoperative complications, including hypoxemia (oxygen desaturation with $Spo_2$ ≤92% for >1 minute).

**RESULTS** Among 2013 adults who were randomized, 1976 (98.2%) completed the trial (mean age, 48.8 years; 1381 [69.9%] women; 1778 [90.1%] underwent abdominal operations). In the intention-to-treat analysis, the primary outcome occurred in 211 of 989 patients (21.3%) in the high level of PEEP group compared with 233 of 987 patients (23.6%) in the low level of PEEP group (difference, −2.3% [95% CI, −5.9% to 1.4%]; risk ratio, 0.93 [95% CI, 0.83 to 1.04]; $P = .23$). Among the 9 prespecified secondary outcomes, 6 were not significantly different between the high and low level of PEEP groups, and 3 were significantly different, including fewer patients with hypoxemia (5.0% in the high level of PEEP group vs 13.6% in the low level of PEEP group; difference, −8.6% [95% CI, −11.1% to 6.1%]; $P < .001$).

**CONCLUSIONS AND RELEVANCE** Among obese patients undergoing surgery under general anesthesia, an intraoperative mechanical ventilation strategy with a higher level of PEEP and alveolar recruitment maneuvers, compared with a strategy with a lower level of PEEP, did not reduce postoperative pulmonary complications.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: NCT02148692


*JAMA*. 2019;321(23):2292-2305. doi:10.1001/jama.2019.7505
Published online June 3, 2019.

Visual Abstract

Editorial page 2285

Supplemental content


**Author and Group Information:** The PROBESE Collaborative Group authors and collaborators appear at the end of this article.

**Corresponding Author:** Marcelo Gama de Abreu, MD, MSc, PhD, DESA, Department of Anesthesiology and Critical Care Medicine, Pulmonary Engineering Group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany (mgabreu@uniklinikum-dresden.de).

**Section Editor:** Derek C. Angus, MD, MPH, Associate Editor, *JAMA* (angusdc@upmc.edu).

Lancet 2014; 384: 495–503

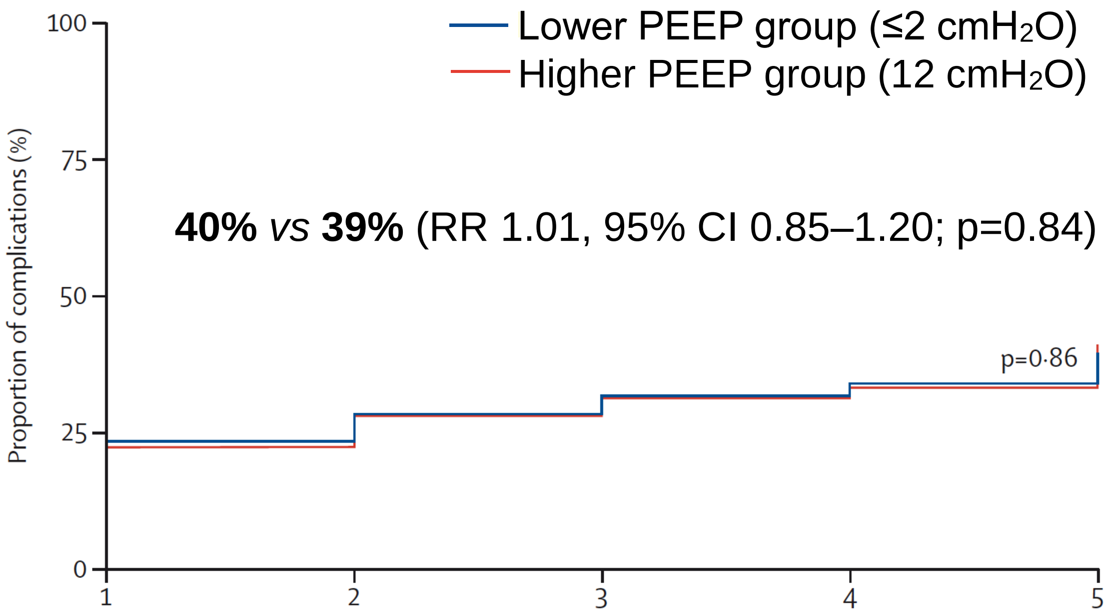


# High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial)

The PROVE Network Investigators* for the Clinical Trial Network of the European Society of Anaesthesiology

## PROVHILO study

- Multicenter, double-blind, parallel-group RCT
- N=894 patients with intermediate or high risk of PPCs
- Intervention: Fixed PEEP levels of 12 $cmH_2O$ *vs* ≤2 $cmH_2O$
- Primary endpoint: composite of PPCs within 5 days after surgery




| Number at risk | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Higher PEEP group | 445 | 345 | 319 | 304 | 297 |
| Lower PEEP group | 449 | 343 | 321 | 305 | 296 |

Lancet 2014; 384: 495–503



# High versus low positive end-expiratory pressure during general general anaesthesia for open abdominal surgery (PROVHILO trial)

*The PROVE Network Investigators* for the Clinical Trial Network of the European Society of Anaesthesiology*

| | Higher PEEP group (n=445) | Lower PEEP group (n=449) | Relative risk (95% CI) | p |
|---|---|---|---|---|
| **Intraoperative complications** | | | | |
| Rescue strategy for desaturation | 11/442 (2%) | 34/445 (8%) | 0·34 (0·18–0·67) | 0·0008 |
| Hypotension†† | 205/441 (46%) | 162/449 (36%) | 1·29 (1·10–1·51) | 0·0016 |
| Vasoactive drugs needed | 274/444 (62%) | 228/445 (51%) | 1·20 (1·07–1·35) | 0·0016 |
| New arrhythmias needing intervention | 12/442 (3%) | 5/445 (1%) | 2·38 (0·84–6·70) | 0·09 |

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

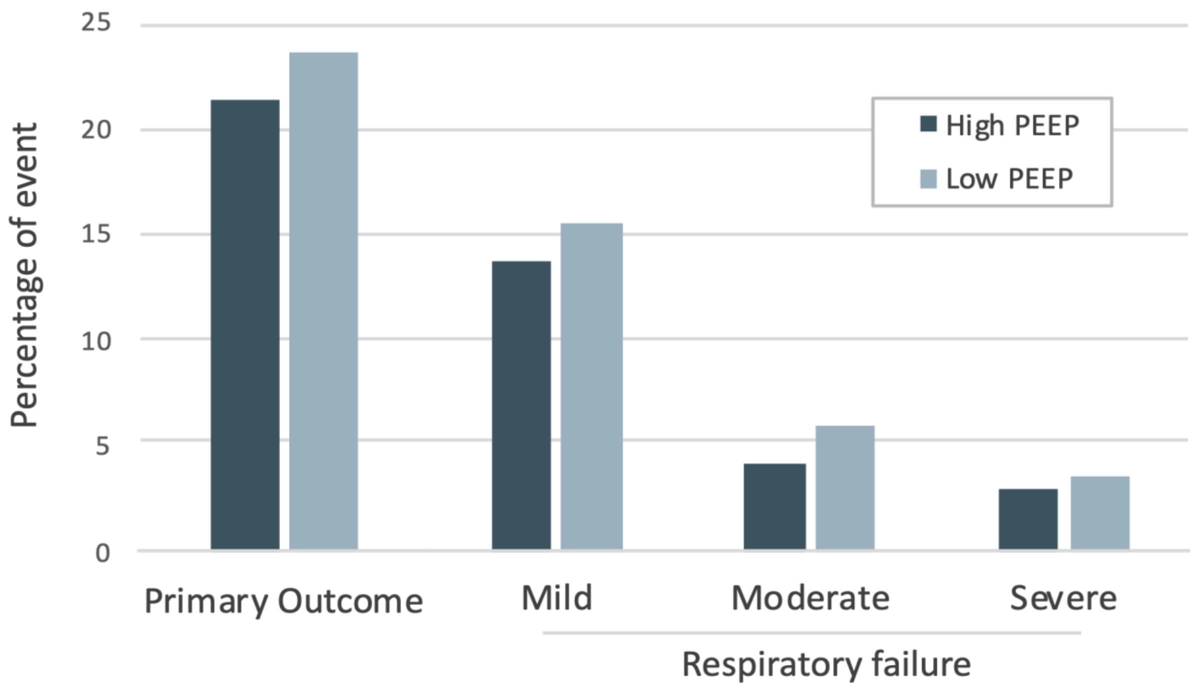
# Effect of Intraoperative High Positive End-Expiratory Pressure (PEEP) With Recruitment Maneuvers vs Low PEEP on Postoperative Pulmonary Complications in Obese Patients

## A Randomized Clinical Trial

Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network (PROVEnet) for the Clinical Trial Network of the European Society of Anaesthesiology

## PROBESE trial

- RCT (N=2013 adults with BMI ≥ 35 $kg/m^2$, abdominal surgery)
- Intervention:
  - **High** PEEP group: **12** $cmH_2O$ of PEEP + RM
  - **Low** PEEP group: **4** $cmH_2O$ of PEEP
- Primary outcome: A composite of PPCs within the first 5 postoperative days
  21.3% vs 23.6%; risk ratio 0.93 (95%CI, 0.83-1.04)




JAMA. 2019;321(23):2292-2305

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

# Effect of Intraoperative High Positive End-Expiratory Pressure (PEEP) With Recruitment Maneuvers vs Low PEEP on Postoperative Pulmonary Complications in Obese Patients

## A Randomized Clinical Trial

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**Table 3. Primary, Secondary, and Post Hoc Outcomes**

| | No. of Events (%) | | | |
|---|---|---|---|---|
| | High Level of PEEP (n = 989)[a] | Low Level of PEEP (n = 987)[a] | Risk Ratio (95% CI)[b] | *P* Value[c] |
| Intraoperative adverse events | | | | |
| Hypoxemia[i] | 49 (5.0) | 134 (13.6) | 0.51 (0.40 to 0.65) | <.001 |
| Hypotension[j] | 313 (31.6) | 170 (17.2) | 1.43 (1.31 to 1.56) | <.001 |
| Bradycardia[k] | 98 (9.9) | 59 (6.0) | 1.27 (1.11 to 1.45) | .001 |
| Mortality during hospital stay | 12 (1.2) | 5 (0.5) | 1.41 (0.95 to 1.81) | .09 |

Editorial

June 3, 2019

# Setting Positive End-Expiratory Pressure in Mechanically Ventilated Patients Undergoing Surgery

Thomas Godet, MD, PhD[1]; Emmanuel Futier, MD, PhD[1]

Do these predominantly neutral results mean higher levels of PEEP and recruitment maneuvers should not be applied in mechanically ventilated patients? Perhaps. Alternatively, it may be possible that the optimal level of PEEP may lie between these extreme PEEP values.

There is wide variability among patients in response to PEEP and recruitment maneuvers,[10] and a single, uniformly applied level of PEEP cannot reflect individual patient differences. Some may intuitively suggest that an individualized strategy to titrate PEEP tailored to individual patient physiology would have been more informative.[11]

*JAMA*. 2019;321(23):2285-2287. doi:10.1001/jama.2019.7540

BJA

British Journal of Anaesthesia, 123 (6): 898–913 (2019)

RESPIRATION AND THE AIRWAY

# Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommendations

Christopher C. Young[1,2,*], Erica M. Harris[2], Charles Vacchiano[1,3], Stephan Bodnar[3], Brooks Bukowy[3], R. Ryland D. Elliott[2], Jaclyn Migliarese[3], Chad Ragains[2], Brittany Trethewey[3], Amanda Woodward[4], Marcelo Gama de Abreu[5], Martin Girard[6], Emmanuel Futier[7], Jan P. Mulier[8], Paolo Pelosi[9,10] and Juraj Sprung[11]

**Table 1 Recommendations and statements**

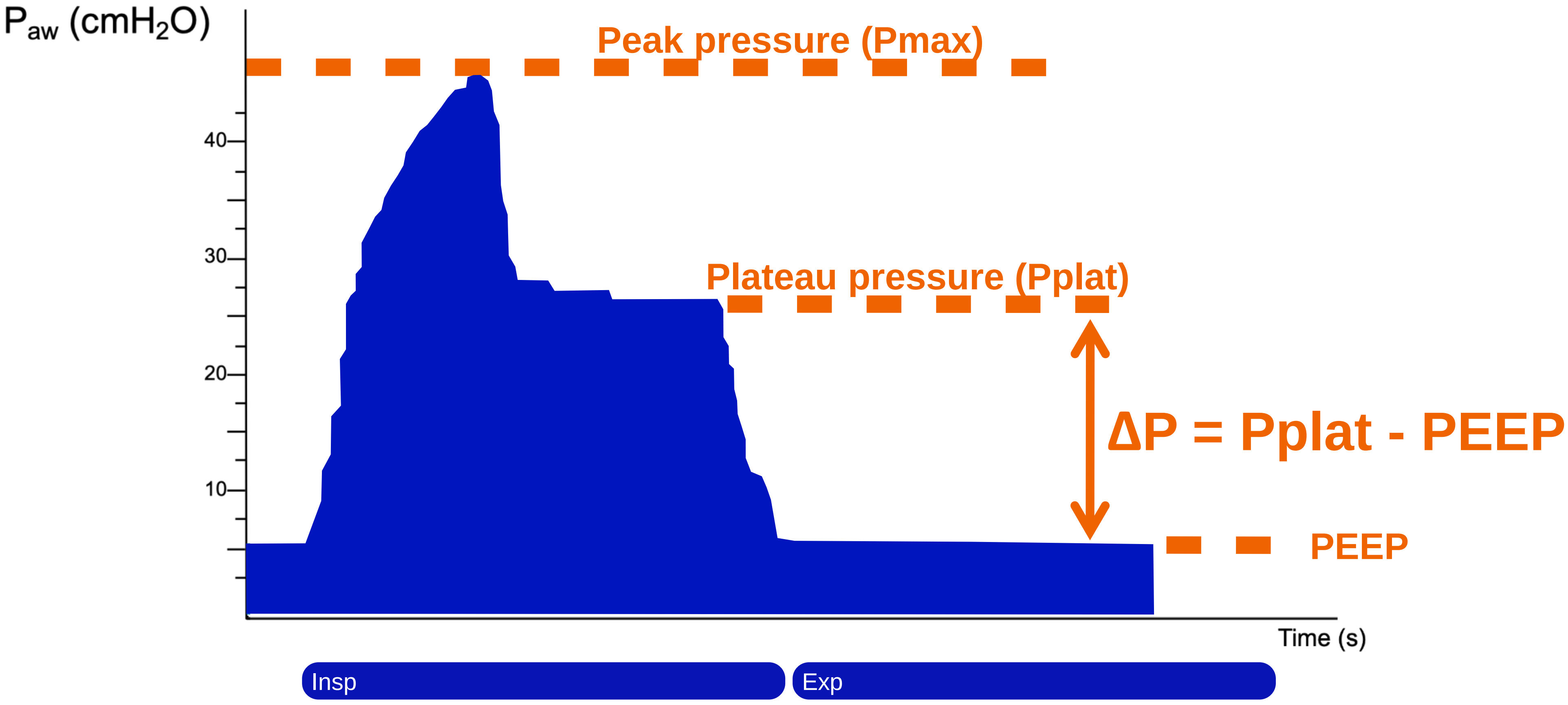
| Question | Statement/recommendation |
|---|---|
| 2.3 | **PEEP should be individualized** to the patient in order **to avoid increases in driving pressure (Pplat - PEEP)** whilst maintaining a low VT. |

Consensus: 100%    Quality of evidence: Low    Strength of recommendation: Strong

# Driving pressure (ΔP): Pplat – PEEP

(an index indicating the "functional" size of the lung)

$C_{rs}$ = $V_T$ / (Pplat - PEEP), thus **ΔP = $V_T$ / $C_{rs}$**



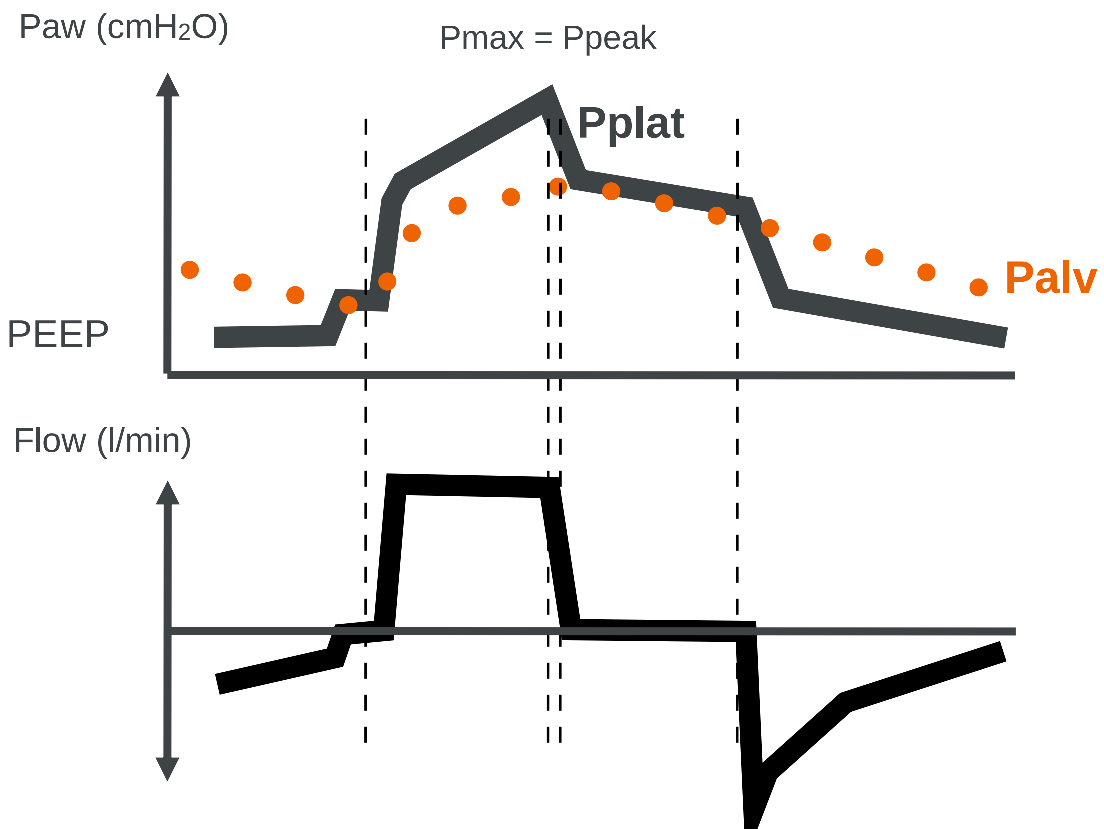

**(objective : ΔP ≤ 13-15 $cmH_2O$)**

# Mesures statiques pour le système respiratoire

$$P_{aw} = (E_{rs} \times V_{insp}) + (R_{rs} \times \dot{V}) + PEEPtot$$

## Pression de plateau : Pplat

Lors d'une EIO, $P_{aw,\ EIO}$ (donc Pplat) = PEEP + ($E_{rs} \times V_T$)

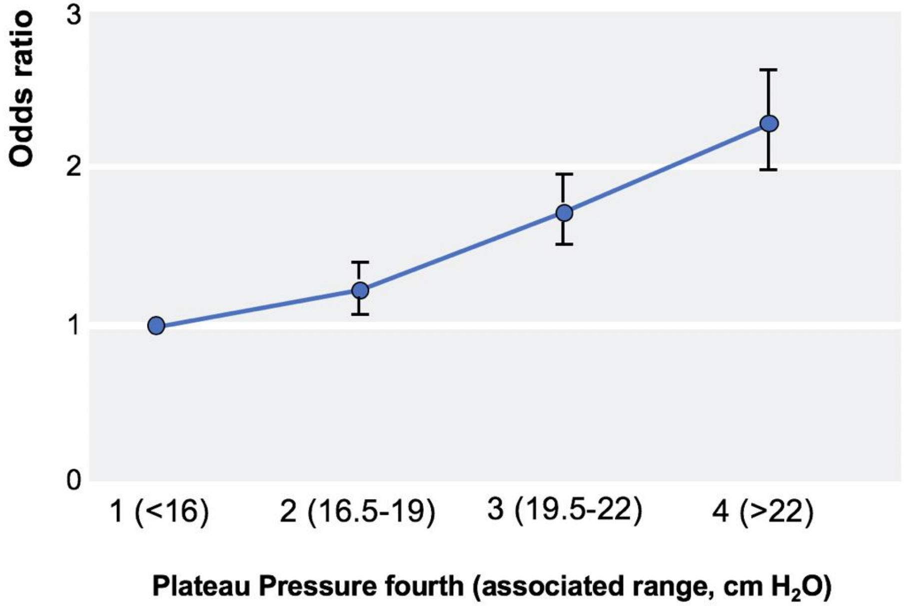


# Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study

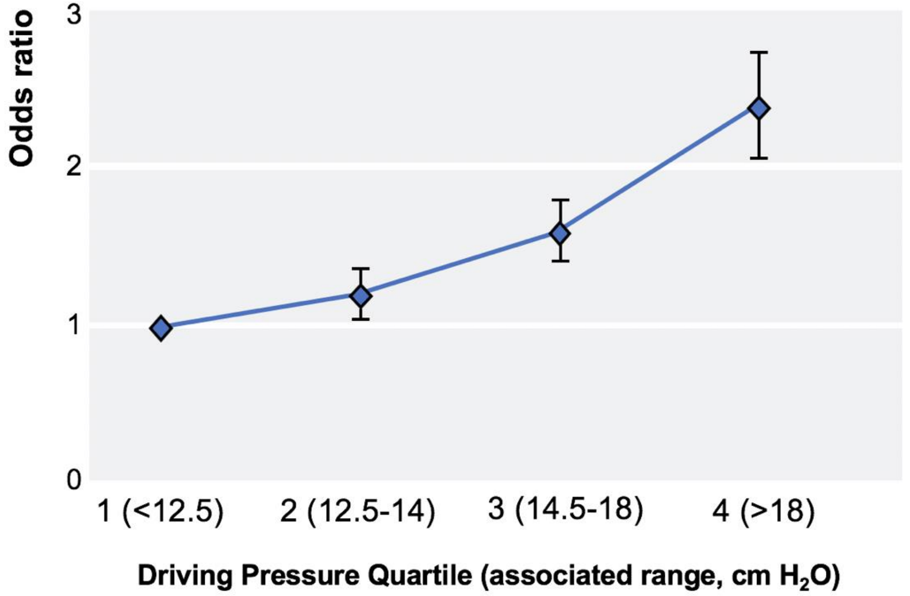
Karim Ladha,[1] Marcos F Vidal Melo,[1] Duncan J McLean,[1] Jonathan P Wanderer,[2] Stephanie D Grabitz,[1] Tobias Kurth,[3,4,5] Matthias Eikermann[1,6]

Hospital based registry study
69265 consecutive surgical patients who underwent general anesthesia between January 2007 and August 2014 at 3 hospitals (USA)

**Plateau pressure ($cmH_2O$)**



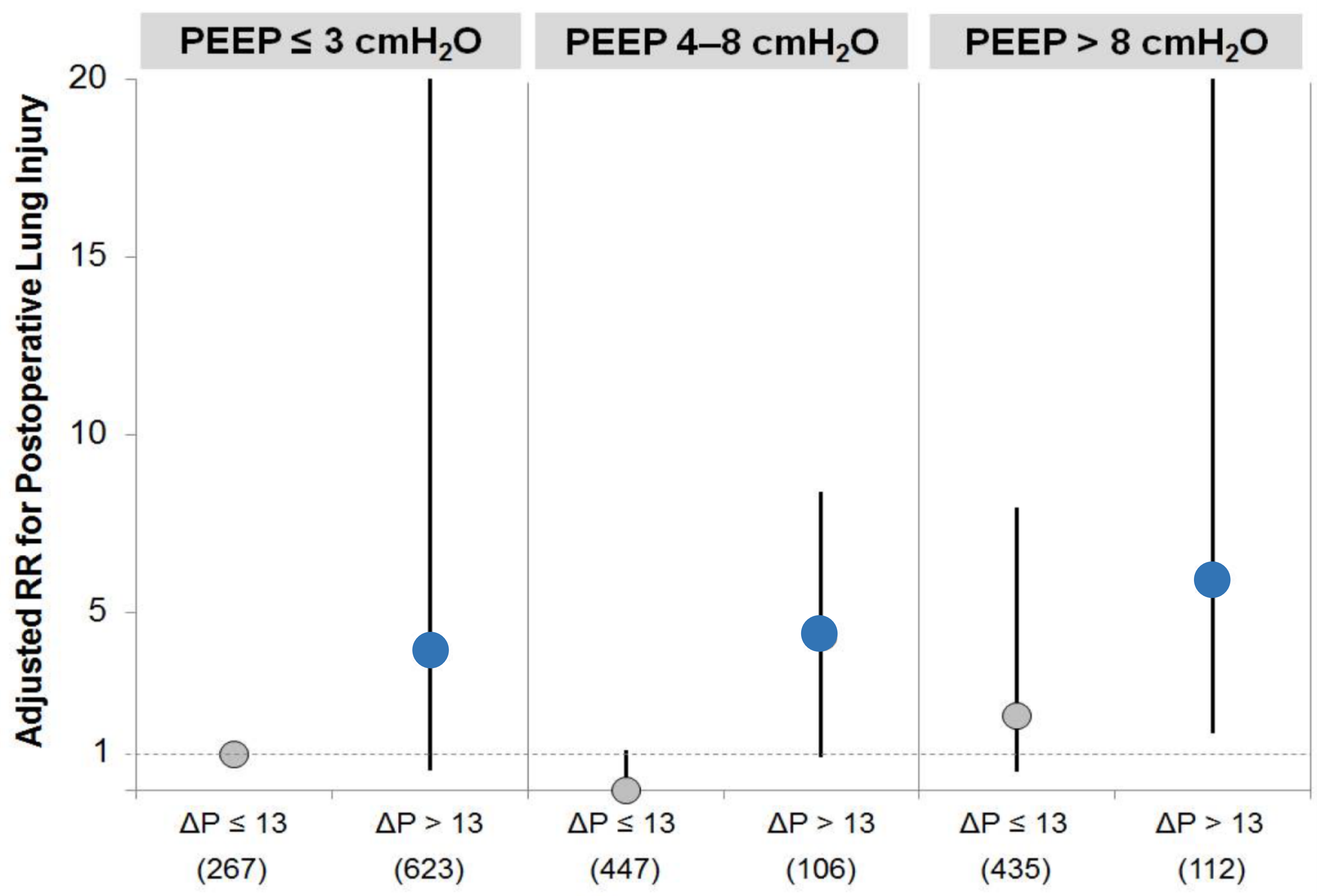

**Driving pressure ($cmH_2O$)**




BMJ 2015;351:h3646

# Dose-Response Relationship between Driving Pressure and PPC

Metanalysis of individual patient data from 17 RCTs (2250 patients)



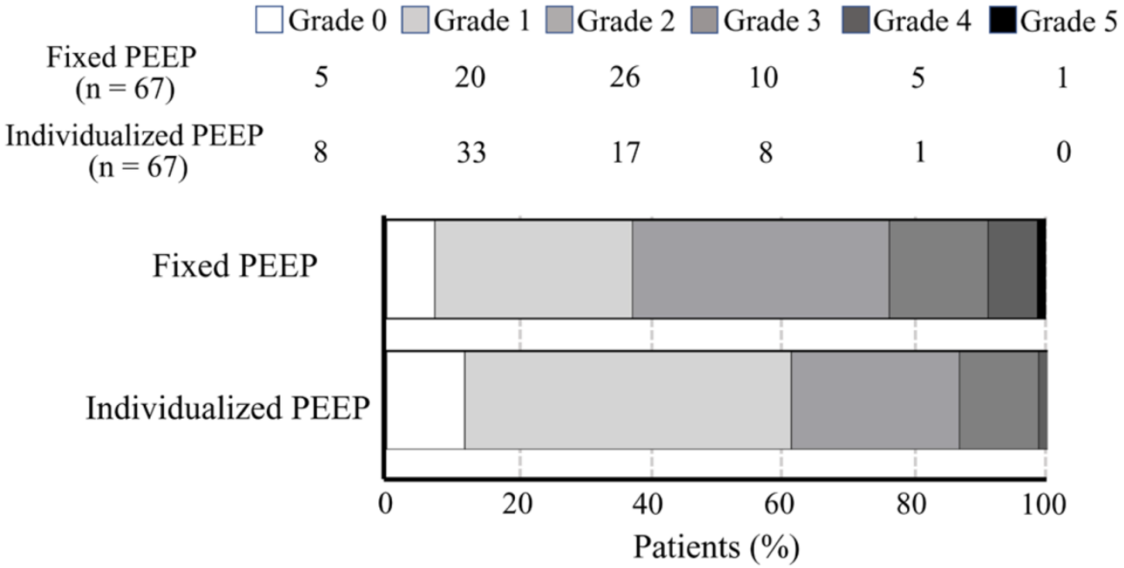

PROVE Network. Lancet Respir Med 2016,4:272-80

# Driving Pressure–Guided Individualized Positive End-Expiratory Pressure in Abdominal Surgery: A Randomized Controlled Trial

Chengmi Zhang, MD, PhD,* Fengying Xu, MD, PhD,† Weiwei Li, MD, PhD,* Xingyu Tong, MD,* Ran Xia, MD,* Wei Wang, MD,* Jianer Du, MD,* and Xueyin Shi, MD*

- Single center RCT
- N=148 patients - Open upper abdominal surgery
- Randomization 1:1 to
  - Fixed PEEP 6 $cmH_2O$
  - Individualized PEEP titration (an increment of 2 $cmH_2O$ for every 8 minutes from 0 to 14 $cmH_2O$) to identify the optimal individualized PEEP that resulted in minimum driving pressure
- **Primary outcome**: incidence of clinically significant PPCs (grade 2+) within the first 7 postoperative days

  32.8% vs 62.7%; RR 0.619 (95%CI 0.435–0.881), p=0.006



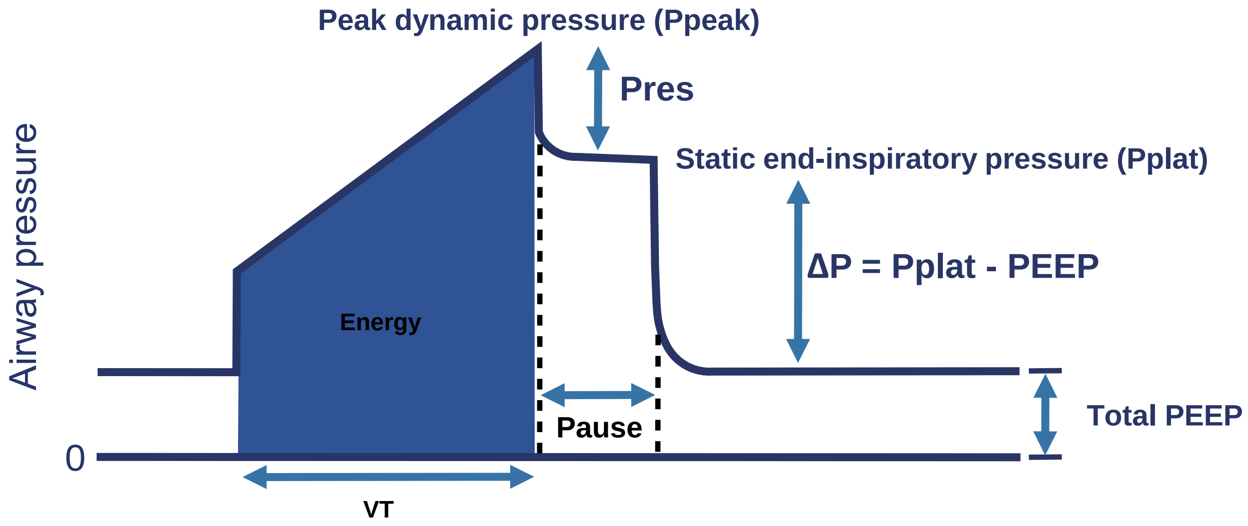

Anesth Analg 2021;133:1197–205

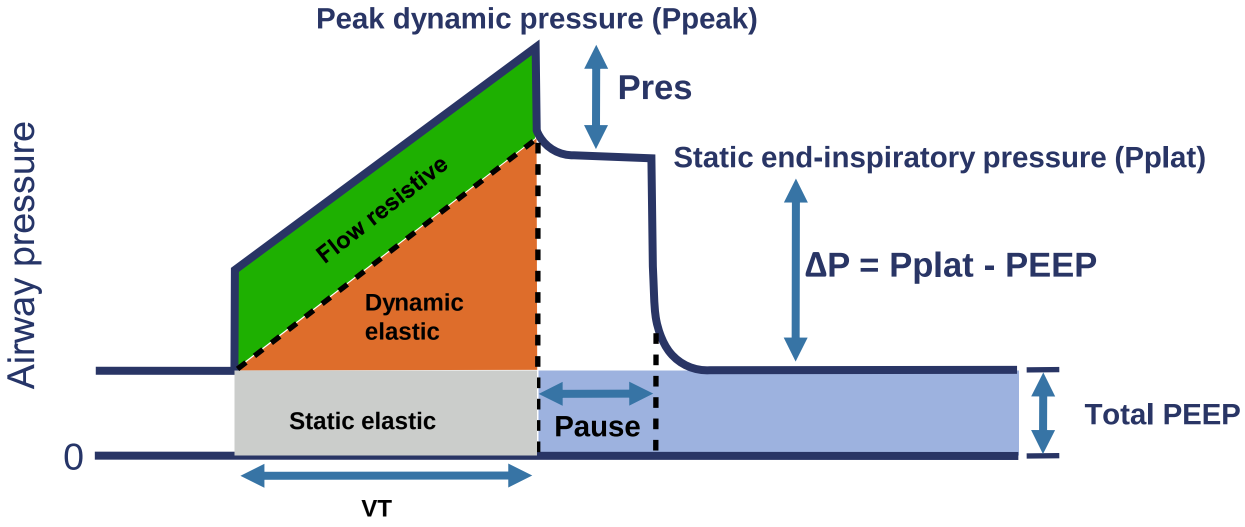
# Ventilator-causes of lung injury: Mechanical Power (MP)

## Energy per breath

## Mechanical power components

**Passive condition and constant flow**




$$MP\ (Joules/min) = 0.098 \times RR \times VT \times [PEEP \times (0.5\ \Delta P) \times (Ppeak - Pplat)]$$

- Static elastic MP (related to PEEP) = $0.098 \times RR \times VT \times PEEP$
- Dynamic elastic MP (related to ΔP) = $0.098 \times RR \times VT \times (0.5\ \Delta P)$
- Resistive MP (related to Pres) = $0.098 \times RR \times VT \times (Ppeak - Pplat)$

ANESTHESIOLOGY

ANESTHESIOLOGY 2022; 137:41–54

# Mechanical Power during General Anesthesia and Postoperative Respiratory Failure: A Multicenter Retrospective Cohort Study

Peter Santer, M.D., D.Phil., Luca J. Wachtendorf, cand.med., Aiman Suleiman, M.D., M.Sc., Timothy T. Houle, Ph.D., Philipp Fassbender, M.D., Eduardo L. Costa, M.D., Daniel Talmor, M.D., M.P.H., Matthias Eikermann, M.D., Ph.D., Elias Baedorf-Kassis, M.D., Maximilian S. Schaefer, M.D.

Fig. 4 Association of mechanical power and postoperative reintubation.

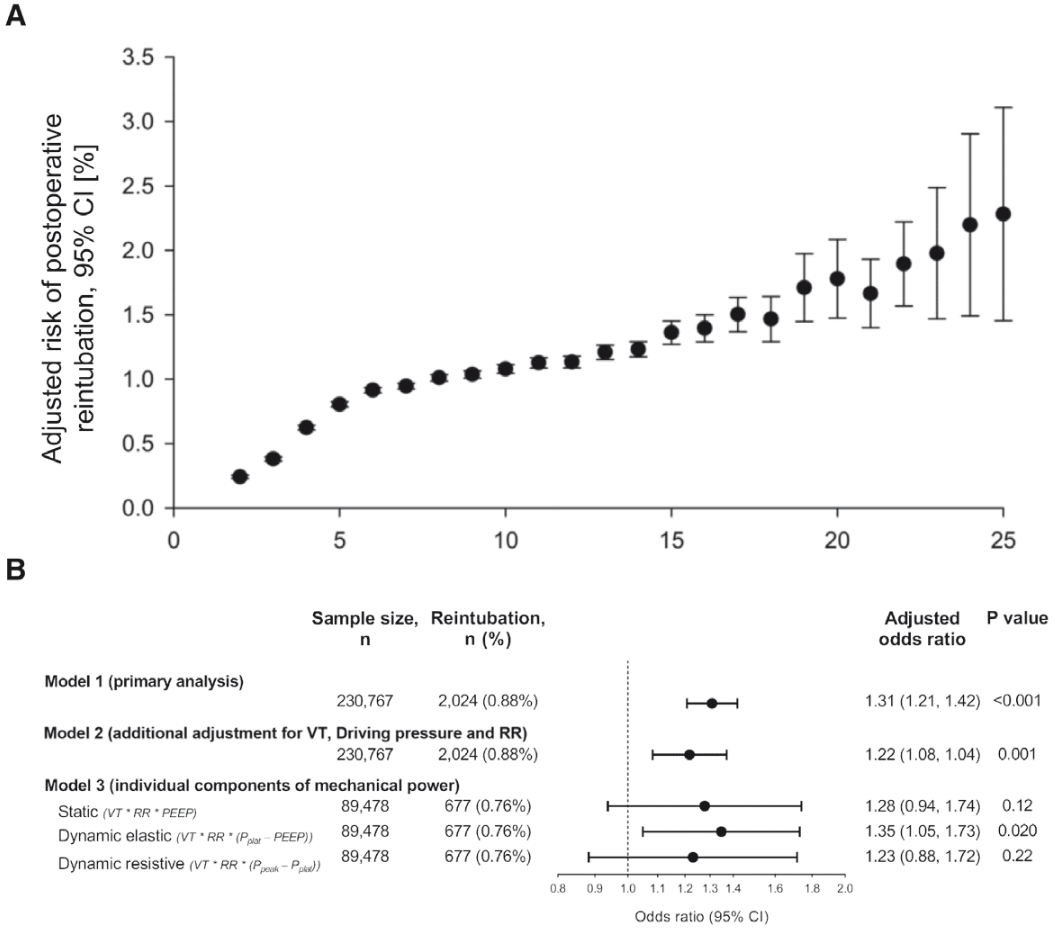
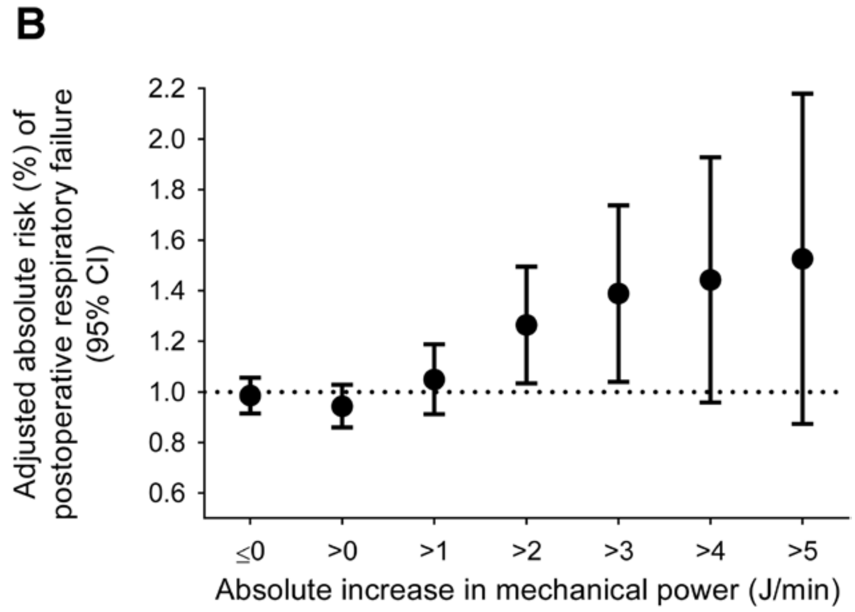



Fig. 5 Adjusted absolute risk of postoperative respiratory failure requiring reintubation within 7 days for different thresholds of increases in MP over time during surgery



ORIGINAL ARTICLE

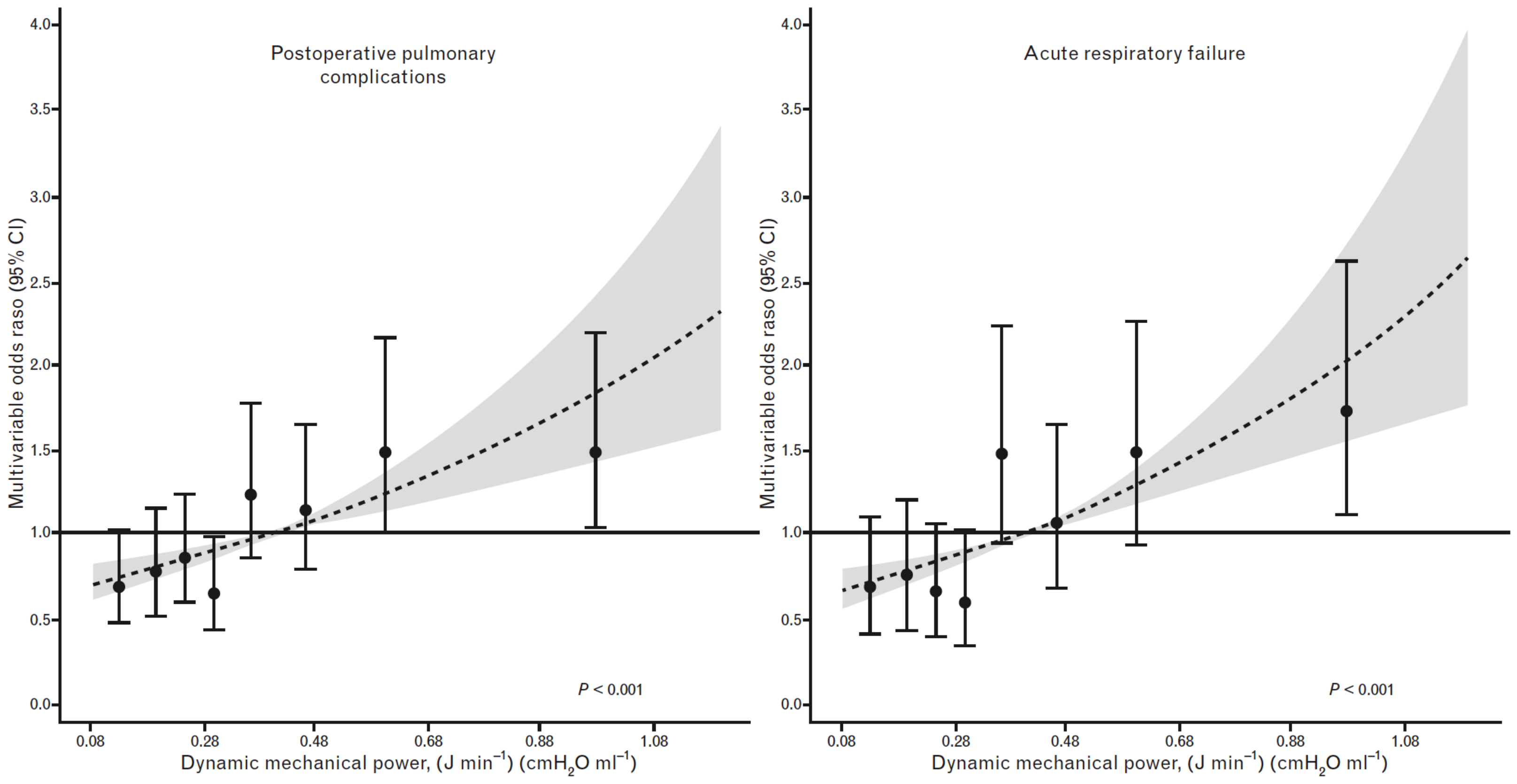
*Eur J Anaesthesiol* 2022; **39**:67–74

# Intra-operative ventilator mechanical power as a predictor of postoperative pulmonary complications in surgical patients

## *A secondary analysis of a randomised clinical trial*

Dharshi Karalapillai, Laurence Weinberg, Serpa Neto A, Philip Peyton, Louise Ellard, Raymond Hu, Brett Pearce, Chong O. Tan, David Story, Mark O'Donnell, Patrick Hamilton, Chad Oughton, Jonathan Galtieri, Anthony Wilson, Glenn Eastwood, Rinaldo Bellomo and Daryl A. Jones

**Fig. 2** Odds ratio for postoperative pulmonary complications and acute respiratory failure.



# **Stress** and **Strain**

**(Stress** = k × **Strain)**
(k: specific elastance)

- ↓ EELV: ↑ **Strain**
- ↓ VT: ↓ **Strain**

$$\textbf{Strain} = \frac{VT}{\textbf{EELV}}$$

- **VT alone does not determine risk of lung injury**
  (because it does not take into account the starting volume of the lung to which it is applied)
- **Low VT ventilation may lead to derecruitment and atelectasis**
- **Restoring EELV is critical to prevent lung injury**

*Editorial*

# Open up the lung and keep the lung open

B Lachmann

Department of Anesthesiology, Erasmus University Rotterdam, The Netherlands

"there is only one rational concept to preserve lung integrity: open up the whole lung and keep it totally open, with the least influence on the cardiocirculatory system."

Intensive Care Med **1992**; 18: 319-21

BJA

British Journal of Anaesthesia, 123 (6): 898–913 (2019)

RESPIRATION AND THE AIRWAY

# Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommendations

Christopher C. Young[1,2,*], Erica M. Harris[2], Charles Vacchiano[1,3], Stephan Bodnar[3], Brooks Bukowy[3], R. Ryland D. Elliott[2], Jaclyn Migliarese[3], Chad Ragains[2], Brittany Trethewey[3], Amanda Woodward[4], Marcelo Gama de Abreu[5], Martin Girard[6], Emmanuel Futier[7], Jan P. Mulier[8], Paolo Pelosi[9,10] and Juraj Sprung[11]

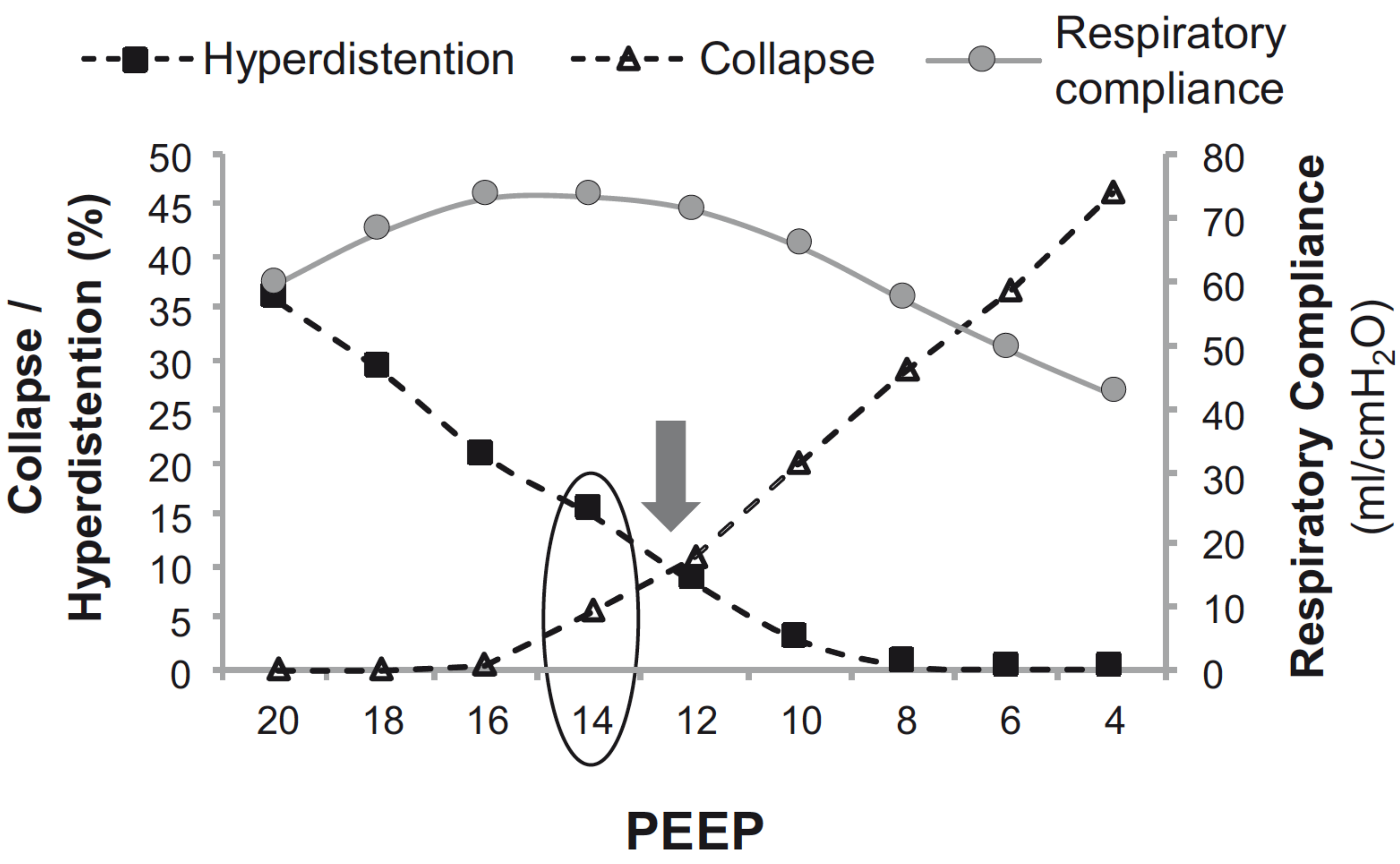
**Table 1** **Recommendations and statements**

| Question | Statement/recommendation |
|---|---|
| 5.5 | **PEEP should be individualised after an ARM** to avoid both alveolar overdistention and collapse. |

Consensus: 71% Quality of evidence: Low Strength of recommendation: Weak

# Individual Positive End-expiratory Pressure Settings Optimize Intraoperative Mechanical Ventilation and Reduce Postoperative Atelectasis

Sérgio M. Pereira, M.D., Mauro R. Tucci, M.D., Ph.D., Caio C. A. Morais, P.T., M.Sc., Claudia M. Simões, M.D., Ph.D., Bruno F. F. Tonelotto, M.D., Michel S. Pompeo, M.D., Fernando U. Kay, M.D., Ph.D., Paolo Pelosi, M.D., F.E.R.S., Joaquim E. Vieira, M.D., Ph.D., Marcelo B. P. Amato, M.D., Ph.D.




- **A compromise between overdistension and collapse**
- **High PEEP might result in more hyperdistension than collapse whereas low PEEP might result in more collapse than hyperdistension**

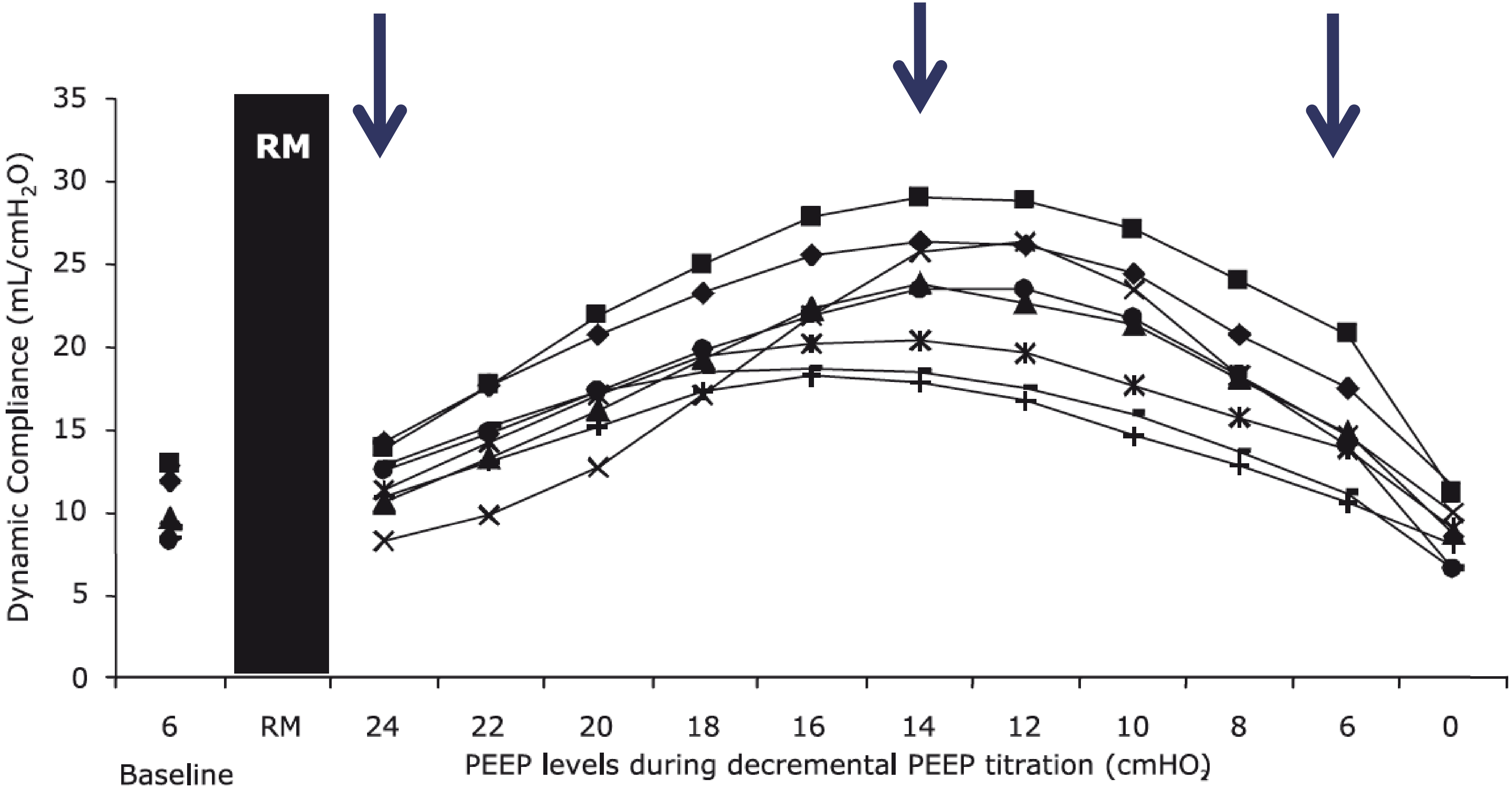
ANESTHESIOLOGY 2018; 129:1070-81

# Changes in compliance (C,rs) during a decremental PEEP titration trial

**Low compliance**
**= Overdistension**

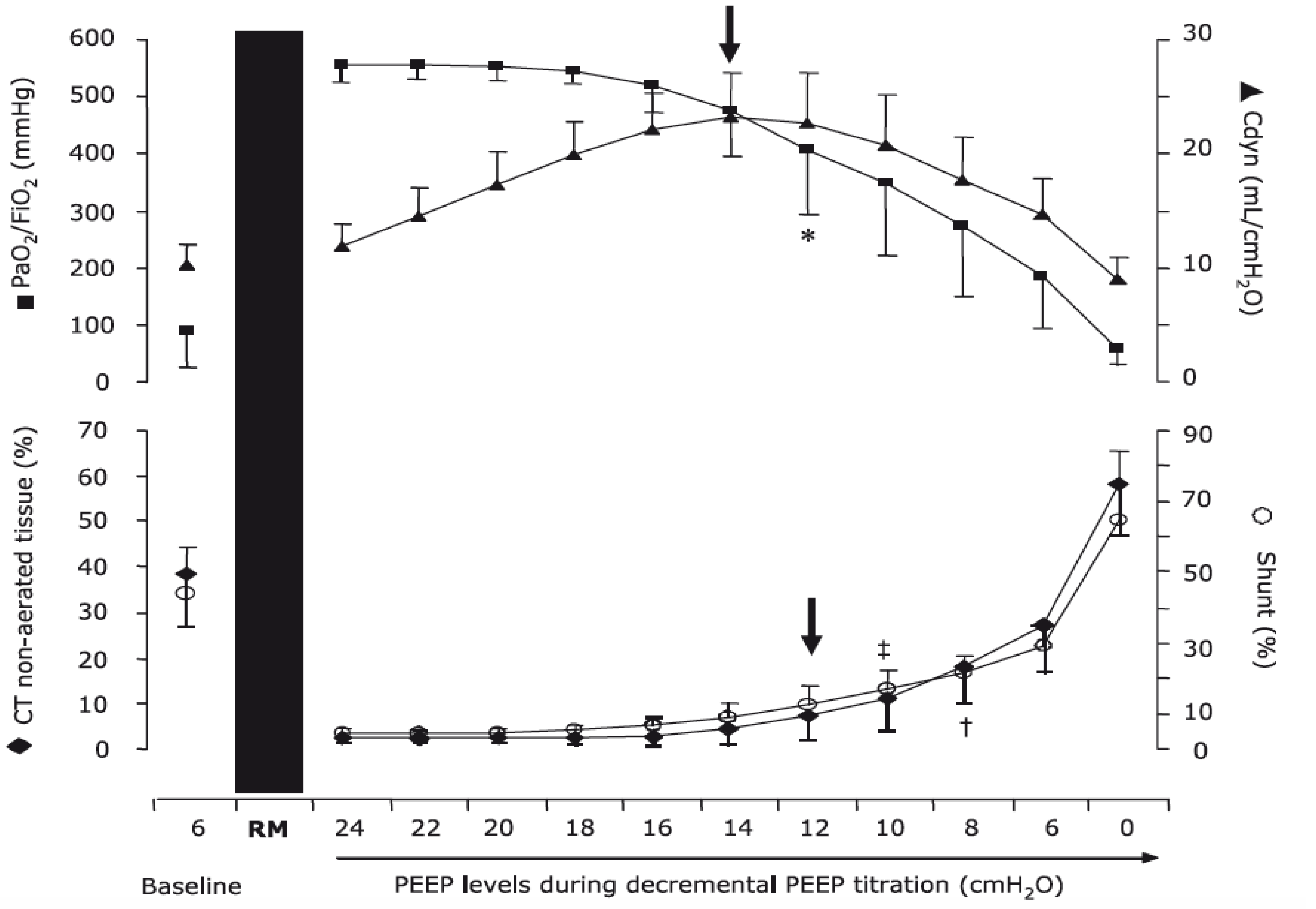
**Highest compliance**
**= Optimal PEEP**

**Low compliance**
**= Alveolar re-collapse**




Suarez-Sipmann F et al. Crit Care Med 2007; 35:214–221

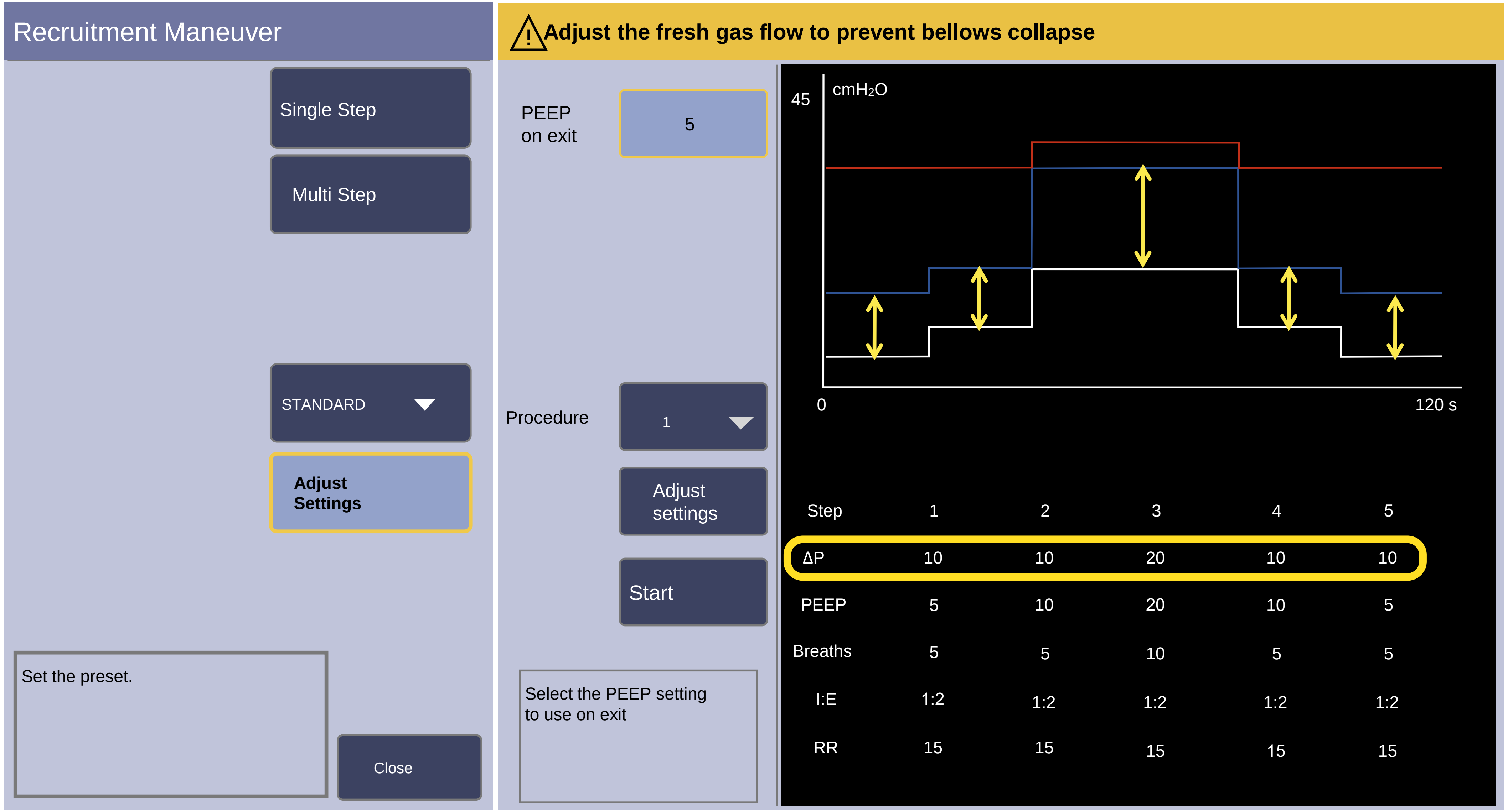
# Changes in compliance (C,rs) during a decremental PEEP titration trial




Suarez-Sipmann F et al. Crit Care Med 2007; 35:214–221

# Individualized PEEP titration

## (multistep procedure)




| Step | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| ΔP | 10 | 10 | 20 | 10 | 10 |
| PEEP | 5 | 10 | 20 | 10 | 5 |
| Breaths | 5 | 5 | 10 | 5 | 5 |
| I:E | 1:2 | 1:2 | 1:2 | 1:2 | 1:2 |
| RR | 15 | 15 | 15 | 15 | 15 |

**(Ventilator GE Healthcare Carestation 750)**

BJA

British Journal of Anaesthesia, 123 (6): 898–913 (2019)

RESPIRATION AND THE AIRWAY

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Christopher C. Young[1,2,*], Erica M. Harris[2], Charles Vacchiano[1,3], Stephan Bodnar[3], Brooks Bukowy[3], R. Ryland D. Elliott[2], Jaclyn Migliarese[3], Chad Ragains[2], Brittany Trethewey[3], Amanda Woodward[4], Marcelo Gama de Abreu[5], Martin Girard[6], Emmanuel Futier[7], Jan P. Mulier[8], Paolo Pelosi[9,10] and Juraj Sprung[11]

**Table 1** **Recommendations and statements**

| Question | Statement/recommendation |
|---|---|
| 3.3 | After intubation, $FiO_2$ should be set to ≤0.4. Thereafter, use **the lowest possible $FiO_2$ to achieve $SpO_2$ ≥94%**. |

**Consensus: 100%** **Quality of evidence: Very low** **Strength of recommendation: Weak**

# Take Home Messages

- CPPs restent une problématique commune en pratique clinique quotienne

- Des réglages inappropriés du ventilateur contribuent au risque de CPPs

- **Les recommandations suggèrent l'utilisation d'une stratégie de ventilation protectrice au bloc opératoire**

- **Les réglages initiaux du ventilateur devraient inclure un VT de 6-8 ml/kg PIT et une PEEP de 5 cm$H_2O$**

- **Réglage de la PEEP idéalement individualisé après un recrutement alvéolaire**