

ANESTHESIOLOGY

Individualized *versus* Fixed Positive End-expiratory Pressure for Intraoperative Mechanical Ventilation in Obese Patients: A Secondary Analysis


Anesthesiology 2021

R1 เกียรติศักดิ์/อ.สิทธิพันธ์

Background

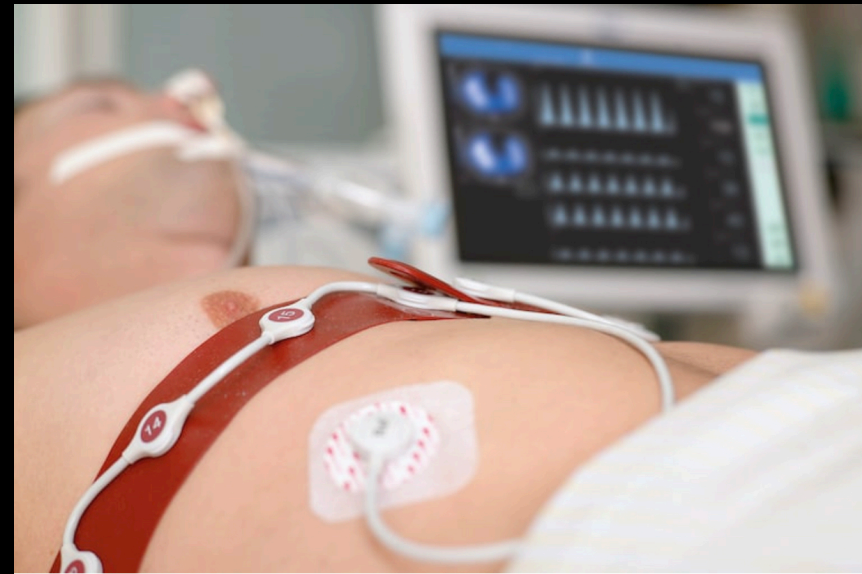
- General anesthesia may cause **atelectasis** and **deterioration in oxygenation** in obese patients >> exacerbated by pneumoperitoneum in laparoscopic
- Atelectasis and overinflation of the remaining ventilated lung >> ↑ postoperative pulmonary complication, prolong hospital stay, ↑ mortality

Background

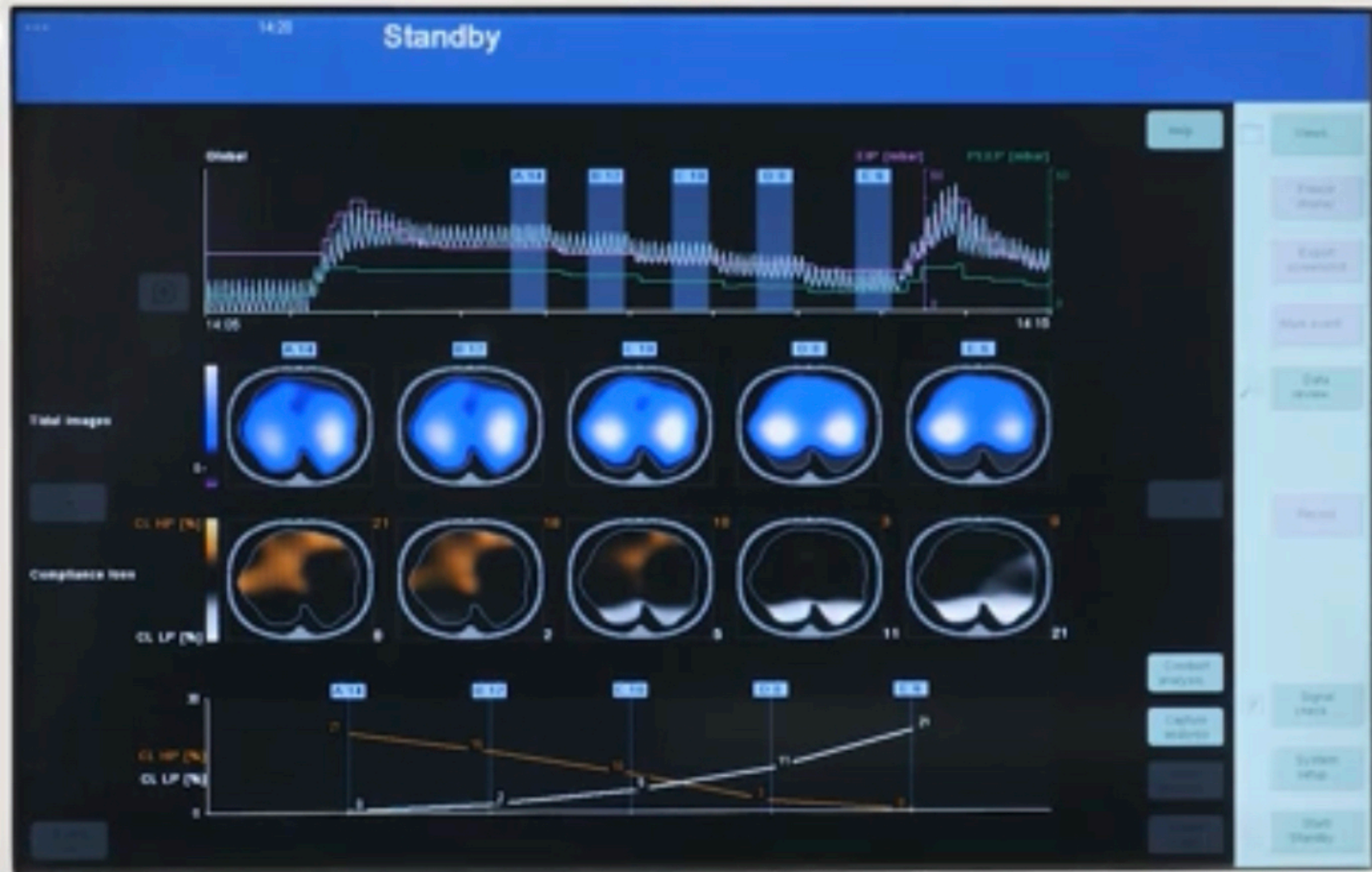
- **Atelectasis**
 - Reopened >> recruitment maneuvers
 - Keep open >> adequate positive end-expiratory pressure [PEEP]  **obese patient**
 - May require increase infusion volume and vasoactive drugs

Background

- Electrical impedance tomography
 - Individualize PEEP homogenize tidal ventilation and minimize atelectasis



Dräger



Infinity C500



Background

- Large multicenter, randomized trial
 - [protective intraoperative ventilation with High vs Low PEEP in Obese patient] >> **PROBESE study**
 - Compared **fix PEEP 12 cm H₂O & hourly repeated recruitment** with PEEP 4 cm H₂O in obese > 2000 patients
 - No difference postoperative pulmonary complication
 - **Fix high PEEP >> better intraoperative lung function parameter [dynamic compliance and driving pressure]**

Background

The hypothesis of this study

- Individualized PEEP titration improves oxygenation and better restore ventilation distribution to dependent lung than fixed PEEP

Methods

Design

- Secondary analysis
- Randomized, Double-blind, and controlled study
- Approved by the Leipzig University Ethics Committee, Germany
- Informed consent from all patient before inclusion

Methods

Participants : Patient were recruited from

- Single-center trial
[NOV 2012 – JUL 2013] **n = 54**
- PROBESE trial at Leipzig site
[OCT 2016 – JAN 2018] **n = 42**

Methods

Participants

- Inclusion criteria both trial
 - BMI ≥ 35 kg/m²
 - Age ≥ 18 yr
 - Medium or high risk of postoperative pulmonary complication [ARISCAT ≥ 26]
 - Elective abdominal surgery

TABLE 31.14 Scoring Scheme for the ARISCAT*
Perioperative Pulmonary Risk Index

Components of ARISCAT Score	Points Assigned
Age	
■ ≤50 years	0
■ 51–80 years	3
■ >80 years	16
Preoperative oxygen saturation	
■ ≥96%	0
■ 91%–95%	8
■ ≤91%	24
Respiratory infection in prior month	17
Preoperative anemia (<100 g/L)	11
Surgical incision location	
■ Peripheral	0
■ Upper abdominal	15
■ Intrathoracic	24
Duration of surgery	
■ ≤2 h	0
■ >2–3 h	16
■ >3 h	23
Emergency procedure	8

ARISCAT Score	Risk of Pulmonary Complications[†]
Low-risk: < 26 points	1.6%
Intermediate risk: 26–44 points	13.3%
High-risk: ≥ 45 points	42.1%

Methods

- Primary outcome
 - P_{ao_2}/F_{io_2} ratio before tracheal extubation
- Secondary outcome
 - Tidal ventilation of dependent lung [%]
 - Intraoperative lung function parameter [driving pressure, compliance]

Methods

- Single-center study
 - Patient were randomized into two group by computer
 - Individualized PEEP group
 - Fixed PEEP 5 cm H₂O group
- PROBESE study
 - Patient were randomized into two group by computer
 - Fixed PEEP 12 cm H₂O
 - Fixed PEEP 4 cm H₂O group

Methods

- Then divide to **three groups n = 90**
 - Individualized PEEP group n = 25
 - Fixed PEEP 12 cm H₂O n= 21
 - Fixed PEEP 4-5 cm H₂O group n= 44

Study protocol

- Anesthesia
 - Total intravenous anesthesia with propofol and remifentanil [single center trial]
 - Balance anesthesia with desflurane/sevoflurane and sufentanil/remifentanil [PROBESE trial]

Ventilator setting

single center trial

- Tidal volume 8 ml/kg
- Fio₂ 0.4 or higher
keep o₂ sat > 92%
- Respiratory rate 12 /min
- Maintain normocapnia
keep Paco₂ 35-45

PROBESE trial

- Tidal volume 7 ml/kg
- Fio₂ 0.4 or higher
keep o₂ sat > 92%
- Respiratory rate 12 /min
- Maintain normocapnia
keep Paco₂ 35-45

Study protocol

- Fixed low PEEP group
 - Fixed PEEP 4 – 5 cm H₂O without recruitment maneuver

Study protocol

Individual PEEP group

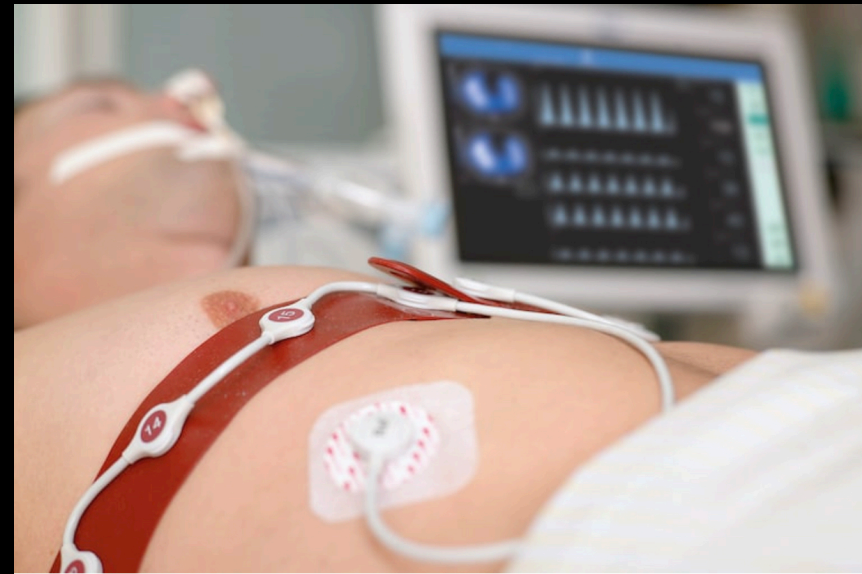
- Recruitment maneuvers
[I:E 1:1, peak pressure 50,
PEEP 30, RR 6] for 10 breath
- PEEP titration before
insufflation start with PEEP
26 cm H₂O decrease in steps
2-4 cm H₂O

Fixed PEEP 12 group

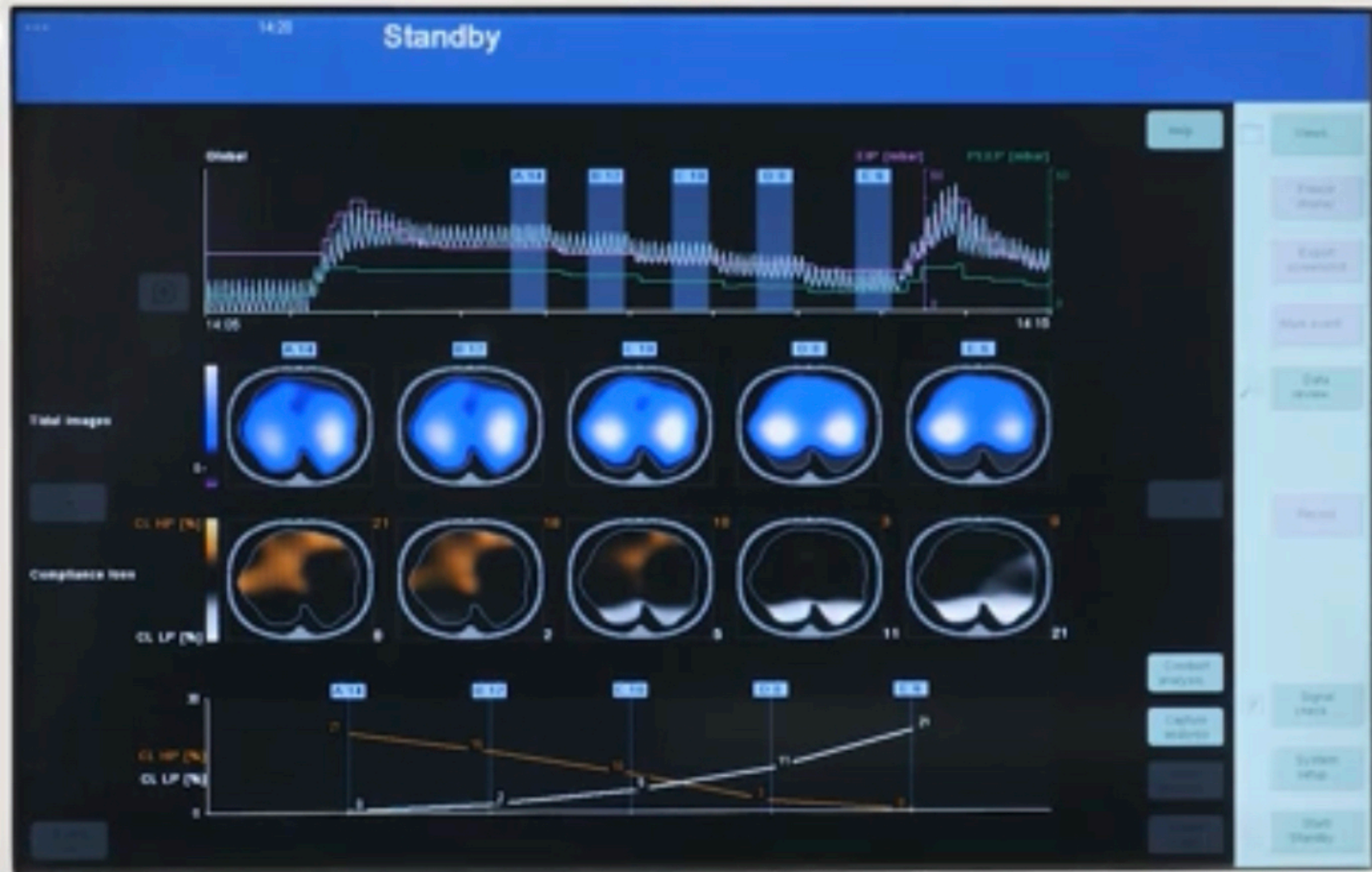
- Fixed PEEP 12 cm H₂O
- Recruitment maneuvers
[I:E 1:1, PEEP 12, RR 6,
increase VT in step 4 ml/kg
until plateau pressure 40 >>
follow 3 breath] after
intubation then q 1 hr

Study protocol

- Electrical Impedance Tomography
 - Electrode belt containing 16 or 32 electrodes placed around the chest at third to fourth ICS



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Study protocol

- Measurement
 - P_{aO_2}/F_{iO_2} ratio before tracheal extubation
 - Tidal ventilation of dependent lung [%]
 - Intraoperative lung function parameter [driving pressure, compliance]
 - Ventilation parameter were record by the display of mechanical ventilator

Statistical analysis

- Secondary analysis
- The data express as the mean \pm SD
- Chi-square test : category data between groups
- Linear correlation : association between continuous data
- Paired *t* test ; ventilation distribution at different PEEP level during titration process
- R Studio ; version 3.6.1

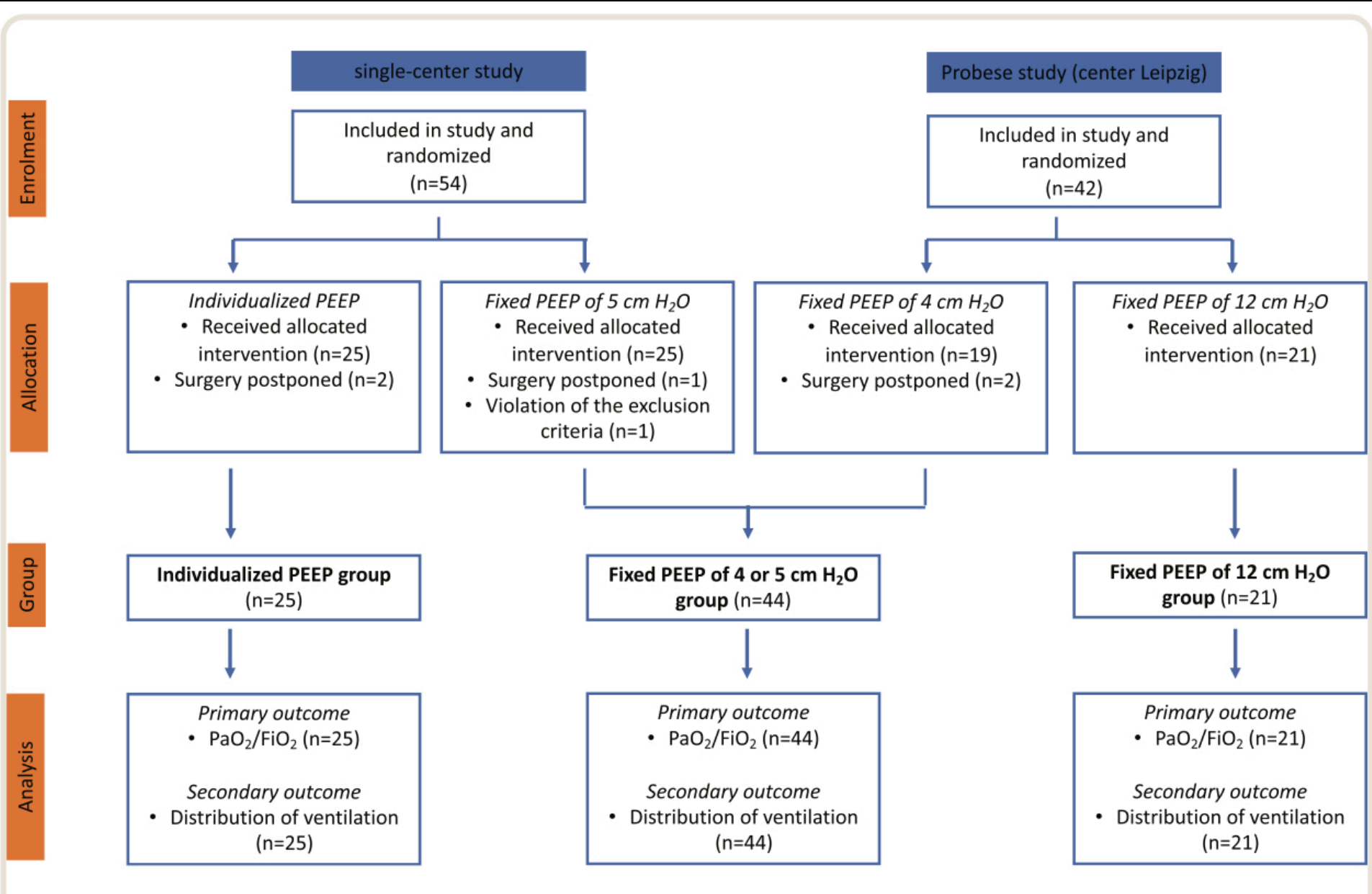


Fig. 1. Flowchart of enrollment and outcomes, end-expiratory lung volume. FiO_2 was adjusted to achieve a target oxygen saturation measured by pulse oximetry greater than or equal to 92% in both trials. FiO_2 , fraction of inspired oxygen; PaO_2 , partial pressure of oxygen in arterial blood; PEEP, positive end-expiratory pressure.

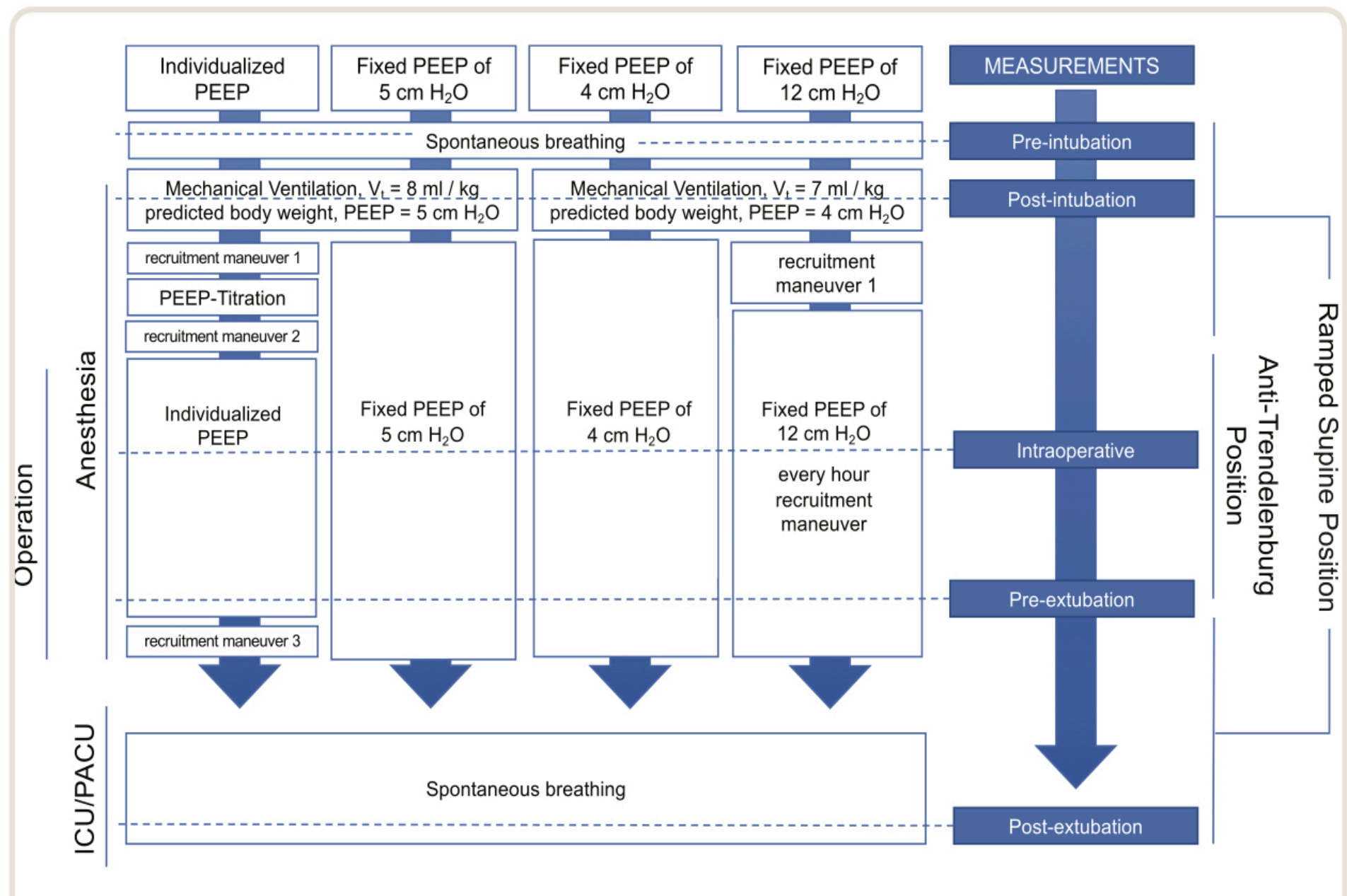


Fig. 2. Schematic diagram of study protocol and interventions for all groups. ICU, intensive care unit; PACU, postanesthesia care unit; PEEP, positive end-expiratory pressure.

Result

Table 1. Patient Characteristics

	Fixed PEEP of 4 to 5 cm H ₂ O (n = 44)	Fixed PEEP of 12 cm H ₂ O (n = 21)	Individualized PEEP (n = 25)
Female, No. (%)	29 (66)	15 (71)	17 (68)
Age, yr	46.5 ± 14.1	43.6 ± 11.3	44.9 ± 10.3
< 45, No. (%)	21 (48)	11 (52)	11 (44)
Height, cm	171 ± 11.9	169 ± 8.7	173 ± 10.7
Body mass index, kg/m ²	51.0 ± 9.5	51.4 ± 13.4	48.2 ± 7.0
Assess Respiratory Risk in Surgical Patients in Catalonia score*	35.0 ± 6.0	33.5 ± 5.5	33.4 ± 4.6
> 44, No. (%)	5 (12)	2 (10)	1 (4)
Smoking status, † No. (%)			
Never	24 (57)	11 (61)	12 (48)
Former	10 (24)	7 (39)	5 (20)
Current	8 (19)	0 (0)	8 (32)

Entries are mean ± SD or No. (%).

*One value missing (fixed PEEP of 4 to 5 cm H₂O). †Five values missing (two in fixed PEEP of 4 to 5 cm H₂O group, three in fixed PEEP of 12 cm H₂O group).

PEEP, positive end-expiratory pressure.

Result

Table 2. Intraoperative Respiratory Parameter during Mechanical Ventilation

	Fixed PEEP of 4 to 5 cm H ₂ O (n = 44)			Fixed PEEP of 12 cm H ₂ O (n = 21)			Individualized PEEP (n = 25)			P Value
	After Intubation	Intraoperative	Before Extubation	After Intubation	Intraoperative	Before Extubation	After Intubation	Intraoperative	Before Extubation	
Tidal volume, ml	476 ± 92	476 ± 92	481 ± 96	443 ± 77	435 ± 65	424 ± 61	525 ± 93	526 ± 91	532 ± 94	0.003
Tidal volume/predicted body weight, ml/kg	7.26 ± 0.47	7.26 ± 0.36	7.27 ± 0.35	7.16 ± 0.42	7.03 ± 0.17	6.91 ± 0.26	7.50 ± 0.29	7.51 ± 0.28	7.53 ± 0.29	—
PEEP, cm H ₂ O	4.6 ± 0.5	4.6 ± 0.5	4.6 ± 0.5	4.8 ± 2.4	12 ± 0	12 ± 0	5 ± 0	18.5 ± 4.6	18.5 ± 4.6	< 0.001
Peak pressure, cm H ₂ O	23.5 ± 4.8	28.0 ± 4.1	25.2 ± 4.1	23.7 ± 6.9	29.0 ± 4.8	27.6 ± 3.3	26.1 ± 5.4	33.8 ± 5.6	31.7 ± 6.5	< 0.001
Plateau pressure, cm H ₂ O	17.9 ± 3.9	23.4 ± 3.9	21.1 ± 5.2	21.8 ± 7.1	26.4 ± 5.1	25.5 ± 5.2	19.6 ± 4.7	28.3 ± 4.6	25.6 ± 5.1	< 0.001
Driving pressure, cm H ₂ O	13.3 ± 4.1	18.8 ± 4.1	16.5 ± 5.5	16.9 ± 7.6	14.4 ± 5.1	13.5 ± 5.2	14.6 ± 4.7	9.8 ± 1.4	7.1 ± 1.4	< 0.001
Dynamic compliance, ml/cm H ₂ O	39.4 ± 14.1	26.6 ± 7.9	32.6 ± 12.0	30.3 ± 13.1	32.8 ± 10.0	30.2 ± 7.2	40.2 ± 12.3	55.1 ± 12.5	79.9 ± 18.9	< 0.001
Pao ₂ /Fio ₂ , mmHg	305 ± 115	325 ± 110	327 ± 118	261 ± 101	397 ± 109	371 ± 106	260 ± 127	485 ± 80	515 ± 86	< 0.001
Paco ₂ , mmHg	41.0 ± 4.9	45.4 ± 5.2	46.0 ± 6.0	42.7 ± 6.7	44.9 ± 4.1	48.8 ± 6.4	40.5 ± 5.1	44.6 ± 2.0	43.3 ± 3.1	0.099*
Petco ₂ , mmHg	37.9 ± 6.3	39.1 ± 5.3	40.5 ± 6.2	37.7 ± 5.8	42.3 ± 2.3	44.2 ± 4.3	41.0 ± 10.1	42.0 ± 9.5	40.9 ± 4.7	0.169*
Respiratory rate, breaths/min	12.9 ± 1.5	16.3 ± 2.6	17.7 ± 2.8	12.2 ± 0.7	16.5 ± 2.7	18.5 ± 2.9	12.3 ± 1.2	15.7 ± 3.3	16.3 ± 2.9	0.204
Minute ventilation (l/min)	6.1 ± 1.2	7.6 ± 1.3	8.4 ± 1.3	5.4 ± 1.2	7.2 ± 1.4	7.8 ± 1.4	6.5 ± 1.1	8.1 ± 1.4	8.5 ± 1.4	0.028
Ventilatory ratio	1.02 ± 0.20	1.40 ± 0.32	1.57 ± 0.36	0.99 ± 0.16	1.39 ± 0.24	1.67 ± 0.41	1.00 ± 0.16	1.36 ± 0.29	1.39 ± 0.27	0.438*

Gas volumes are given in body temperature and pressure saturated conditions. Note that tidal volume/predicted body weight was prescribed and cannot be tested statistically. Entries are the mean ± SD, and P values compare the three arms from a repeated-measures ANOVA.

*Evidence for an interaction between group and time.

PEEP, positive end-expiratory pressure; Petco₂, end-tidal partial pressure of carbon dioxide.

Result

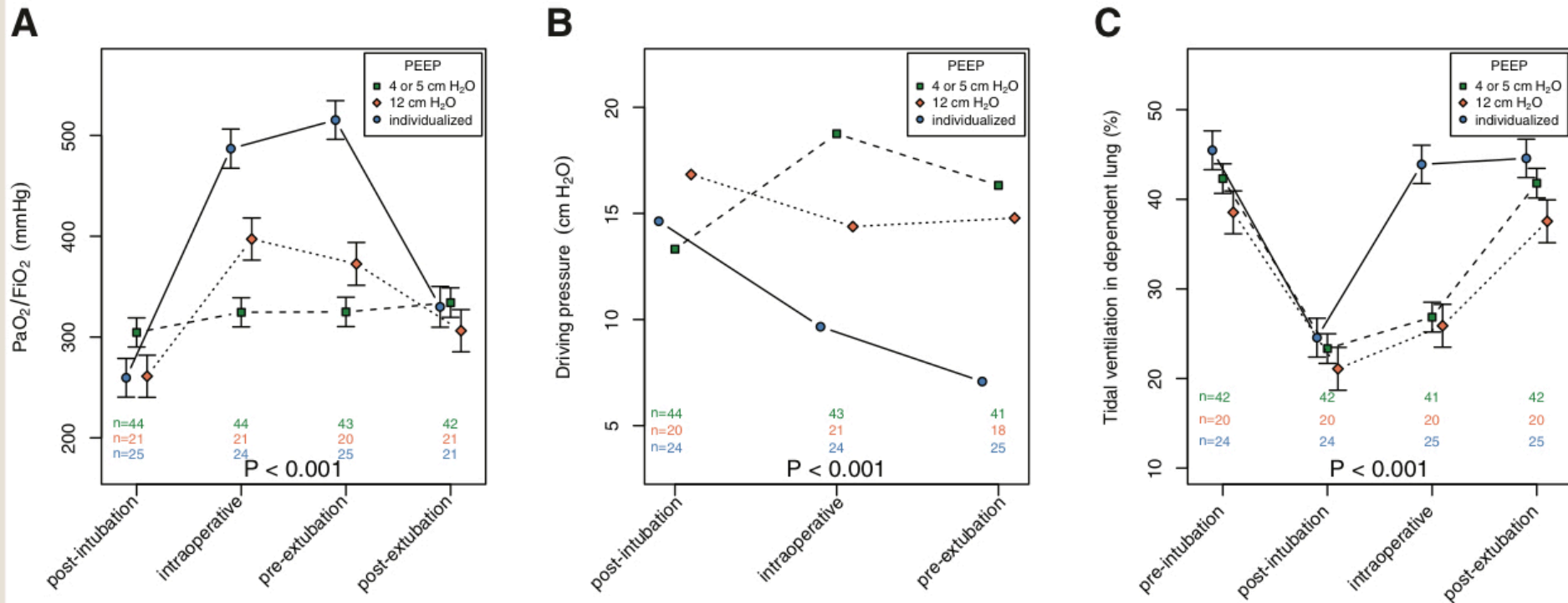


Fig. 3. Time course of PaO₂/FiO₂ (mmHg) (A), driving pressure during mechanical ventilation (cm H₂O) (B), and distribution of regional ventilation of tidal volume (V_T) distributed to the nondependent lung calculated from electrical impedance tomography (%) (C). Points represent estimated means, and whiskers indicate the standard errors from the linear mixed models. The intraoperative measurement point was made 30 min before the estimated end of the surgical procedure. The arterial blood gas analysis for measurement of PaO₂/FiO₂ was obtained after a 3-min period with an FiO₂ of 1.0. FiO₂, fraction of inspired oxygen; PaO₂, partial pressure of oxygen in arterial blood; PEEP, positive end-expiratory pressure.

Result

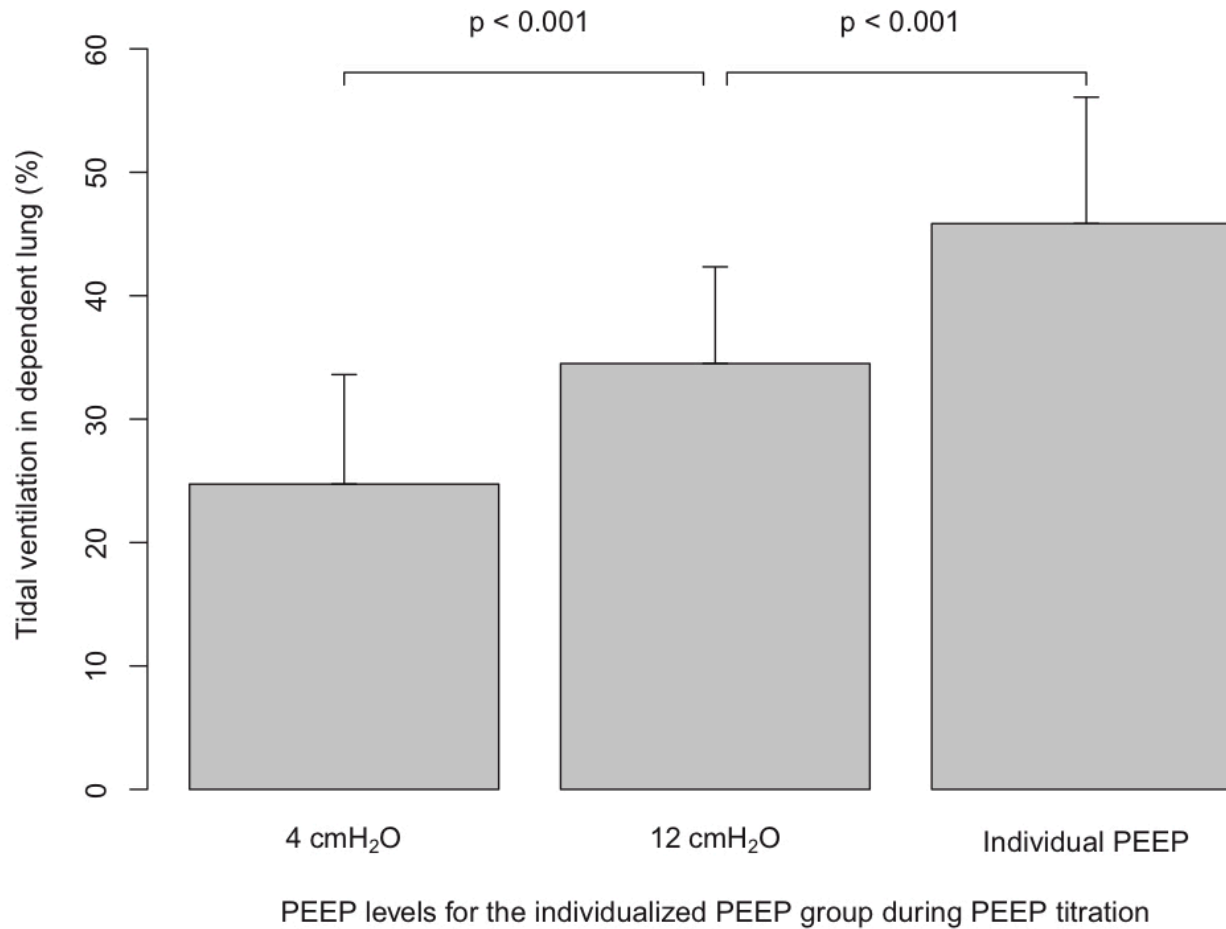


Fig. 4. Intraindividual comparison of the percentage tidal volume in the dependent lung at different PEEP titration stages in the individualized PEEP group calculated from electrical impedance tomography. *Whiskers* represent SDs. PEEP, positive end-expiratory pressure.

Table 3. Vital Parameters, Vasoactive Medication, and Complications during and after Surgery

	Fixed PEEP of 4 to 5 cm H ₂ O (n = 44)	Fixed PEEP of 12 cm H ₂ O (n = 21)	Individualized PEEP (n = 25)	<i>P</i> Value
During surgery				
Heart rate, beats/min	65 ± 12	67 ± 13	69 ± 12	0.060
Mean arterial blood pressure, mmHg	73 ± 13	79 ± 11	77 ± 14	0.078
Lactate, mmol/l	0.87 ± 0.30	0.91 ± 0.26	0.71 ± 0.22	0.007
Base excess, mmol/l	-1.5 ± 2.7	-2.2 ± 2.2	-2.1 ± 2.7	0.442
Total fluid infusion rate, ml · h ⁻¹ · kg ⁻¹	3.5 ± 1.1	3.7 ± 1.3	4.2 ± 1.0	0.028
Bradycardia (< 50 beats/min), during recruitment maneuvers	—	7 (33)	7 (28)	0.755
Bradycardia (< 50 beats/min), any time	11 (25)	10 (48)	7 (28)	0.170
Mean arterial pressure < 60 mmHg, any time	22 (50)	7 (33)	10 (40)	0.414
Vasoactive injections				
Received medication, during recruitment maneuvers	—	10 (48)	23 (92)	0.003
Received medication, any time	39 (89)	18 (86)	20 (80)	0.585
Amount, without recruitment maneuver, bolus equivalents	12.0 [15.5]	3.5 [5.3]	10 [13.8]	0.017
Norepinephrine infusion				
Received medication	14 (32)	8 (38)	7 (28)	0.764
Maximal rate, ng · kg ⁻¹ · min ⁻¹	48 ± 34	30 ± 27	40 ± 16	0.174
Cumulative dose, mg/kg	4.5 [8.2]	3.2 [6.0]	5.2 [4.4]	0.403
Duration of infusion, min	143 [64]	147 [42]	177 [37]	0.281
After operation (first postoperative day until hospital discharge)				
Pulmonary complications	2 (5)	1 (5)	2 (8)	0.842

Entries are the mean ± SD, median [interquartile range], or No. (%), where means for vasoactive medication refer only to those who received it. Bolus equivalents are measured in units of single ampoules of 1 + 20 mg for theodrenaline + cafedrine or 5 µg of norepinephrine. The pulmonary complications are explained in the main text. Fluid infusion was entirely crystalloid; no colloids were used. A recruitment maneuver was not performed in the fixed PEEP of 4 to 5 cm H₂O arm. Individualized PEEP indicates designation for the intervention arm, where an individualized PEEP was used; fixed PEEP of 4 to 5 cm H₂O indicates the arm for which a standard PEEP of 4 or 5 cm H₂O was used; fixed PEEP of 12 cm H₂O indicates the arm for which a standard PEEP of 12 cm H₂O was used.

PEEP, positive end-expiratory pressure.

Discussion

- This study show Obese patients undergoing laparoscopic >> recruitment follow individualized PEEP result in
 - Higher PEEP
 - Better arterial oxygenation
 - Lower driving pressure
 - Redistribution of ventilation to dependent lung areas

Discussion

- Strongly suggest that **individualize titrate PEEP**
 - **reduce atelectasis**
 - **significant higher ventilation of the dependent lung**
- Recruitment maneuver followed by high PEEP of 12 cm H₂O is not sufficient to recruit lung completely

Discussion

- Regional ventilation
 - Setting PEEP from regional ventilation delay index approach
 - Lowest PEEP that minimizes tidal alveolar collapse
 - Individualized PEEP values of 10-26 [median 18] cm H₂O >> significant higher than 12 cm H₂O

Discussion

- Regional ventilation
 - Other studies in bariatric surgery using optimization parameters found PEEP level > 15 cm H₂O
 - In laparoscopic nonobese patients mean PEEP was about 15 cm H₂O
- Practical issue some anesthesia machines may not allow PEEP > 20 cm H₂O

Discussion

- The large **PROBESE trial** could not confirm higher PEEP 12 cm H₂O and recruitment maneuvers reduce postoperative pulmonary complication, **despite reduction in driving pressure**
- Individualized PEEP have to be weigh against hemodynamic depression and increase use of vasoactive medication

Limitation

- Analyses combining data from different studies spanning several years >> **systematic bias that difficult to detect**
 - **Slight differences in tidal volume and recruitment maneuvers**
- Surgery was perform in reverse trendelenburg position >> result cannot use with different position

Limitation

- This study was not designed to investigate the impact of an individualized PEEP on the incidence of postoperative pulmonary complication

Conclusion

- In obese patients undergoing laparoscopic surgery
- Individualized PEEP was associated with
 - Higher intraoperative respiratory compliance
 - Better oxygenation and distribution of ventilation to dependent lung areas
 - These benefit vanished after extubation

Critical Appraisal

	Yes	Can't tell	No
1. Were the following clearly stated:			
• Patients	✓		
• Intervention	✓		
• Comparison Intervention	✓		
• Outcome(s)	✓		

Critical Appraisal

	Yes	Can't tell	No
2. Was the assignment of patients to treatments randomised?	✓		
3. Was the randomisation list concealed? Can you tell?	✓		
4. Were all subjects who entered the trial accounted for at it's conclusion?			✓
5. Were they analysed in the groups to which they were randomised, i.e. intention-to-treat analysis	✓		

Critical Appraisal

	Yes	Can't tell	No
6. Were subjects and clinicians 'blind' to which treatment was being received, i.e. could they tell?	✓		
7. Aside from the experimental treatment, were the groups treated equally?	✓		
8. Were the groups similar at the start of the trial?	✓		

Critical Appraisal

9. How large was the treatment effect?

Consider

- How were the results expressed (RRR, NNT, etc).

?

10. How precise were the results?

Were the results presented with confidence intervals?

yes

Critical Appraisal

	Yes	Can't tell	No
<p>11. Do these results apply to my patient?</p> <ul style="list-style-type: none">• Is my patient so different from those in the trial that the results don't apply?• How great would the benefit of therapy be for my particular patient?	✓		✓
<p>12. Are my patient's values and preferences satisfied by the intervention offered?</p> <ul style="list-style-type: none">• Do I have a clear assessment of my patient's values and preferences?• Are they met by this regimen and its potential consequences?	✓ ✓		