

Optimal PEEP

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DEFINITIONS

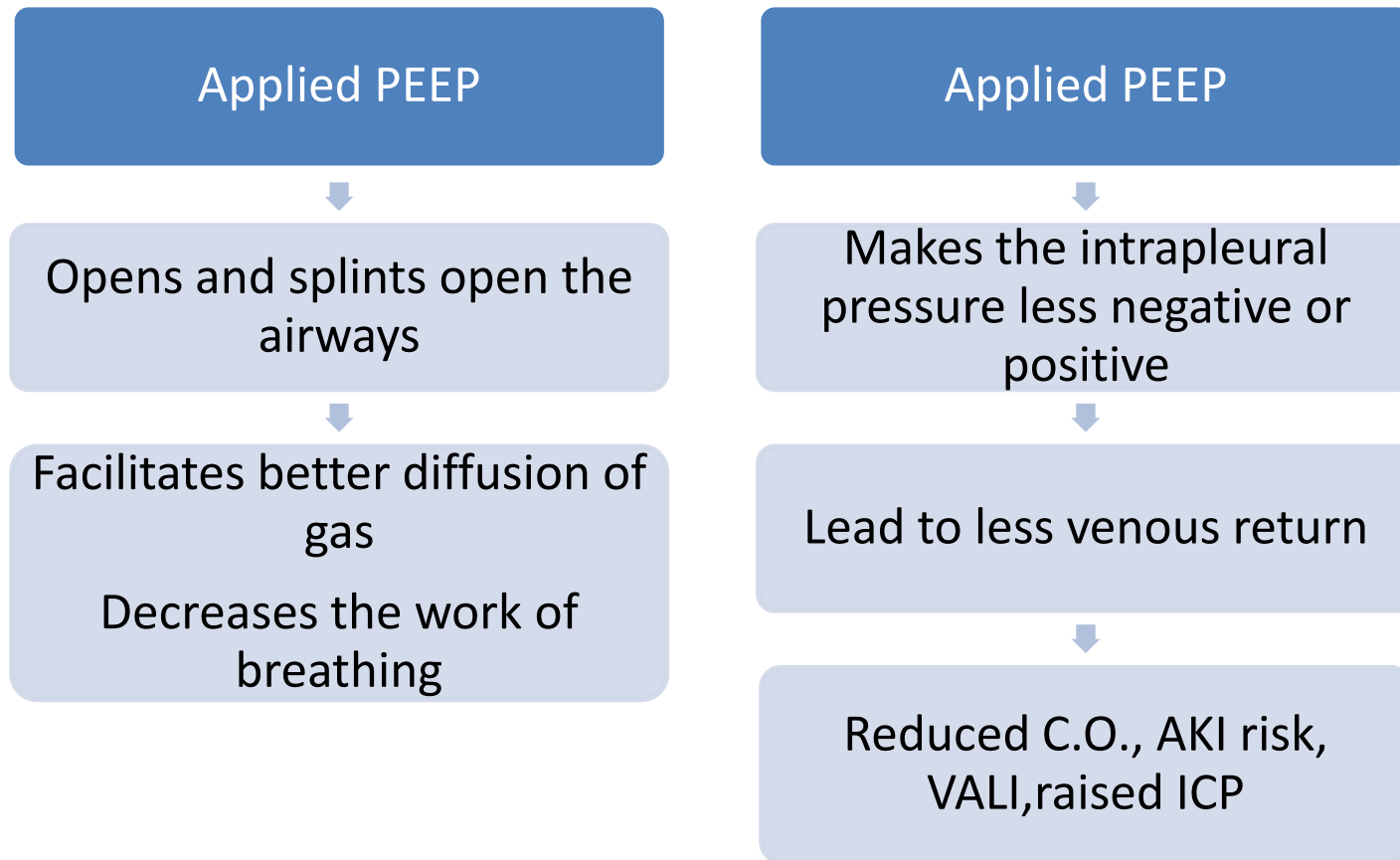
Positive end expiratory pressure is the alveolar pressure above the atmospheric pressure

EXTRINISTIC PEEP – PEEP provided by the mechanical ventilator termed as applied PEEP

INTRINISTIC PEEP- PEEP that is secondary to incomplete expiration termed as intrinsic or auto PEEP

CONCEPT OF PEEP

- Henry's law – solubility of gas depends on the pressure of gas above the solution.



CONCEPT OF PEEP TITRATION

- Improve oxygenation
- Minimize ventilator associated lung injury, hemodynamic imbalance

How PEEP is titrated?

- Oxygenation
- Pressure volume loop
- Oesophageal pressure guided
- Driving pressure
- Imaging studies – LUS, CT chest, EIT

PEEP titration based on oxygenation

- We currently use PEEP-FIO₂ combination used in ARMA trial[^].

Lower-PEEP group

FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

- Principle of HENRY'S Law
- PEEP-FIO₂ combination table has been correlated well with oesophageal pressure guided PEEP titration*.
- A secondary analysis data of 4 ARDS-NET group trial participants suggest to start PEEP of 5 cm H₂O if FIO₂ <0.5 and PEEP of 10 cm H₂O if FIO₂ ≥1.0[‡]
- Data from ALVEOLI trial suggest no mortality benefit with higher PEEP versus lower PEEP strategy (p-value >0.05), but higher PEEP would reduce duration of mechanical ventilation and increase oxygenation**.
- Higher requirement of FIO₂ in a given PaO₂/FiO₂ group predicted mortality in ARDS better than PEEP levels (p-value <0.05)[‡].

[^]Roy G Brower et. Al. N Engl J Med 2004; 351:327-336

**Roy G Brower et. Al. N Engl J Med 2000 May 4;342(18):1301-8

[‡]Martin Britos et. Al., Crit Care Med. 2011 September ; 39(9): 2025-2030

Mortality rates according to PaO₂/FiO₂ tertiles and PEEP levels.

	PEEP ≤ 5 (n = 731)	5 < PEEP ≤ 10 (n = 999)	11 ≥ PEEP (n = 582)	Total ^B
PaO ₂ /FiO ₂ > 175 (n = 771)	23.1 ± 5%	22.0 ± 6%	25.9 ± 18%	23.1 ± 2% (p > 0.70)
110 < PaO ₂ /FiO ₂ ≤ 175 (n = 763)	31.4 ± 9%	25.4 ± 5%	28.1 ± 13%	27.8 ± 3% (p > 0.37)
PaO ₂ /FiO ₂ ≤ 115 (n = 778)	35.7 ± 2%	35.2 ± 7%	38.2 ± 7%	36.5 ± 3% (p > 0.49)
Total ^A	27.8 ± 3% (p < 0.0001)	27.8 ± 2% (p < 0.0001)	33.3 ± 4% (p < 0.0001)	

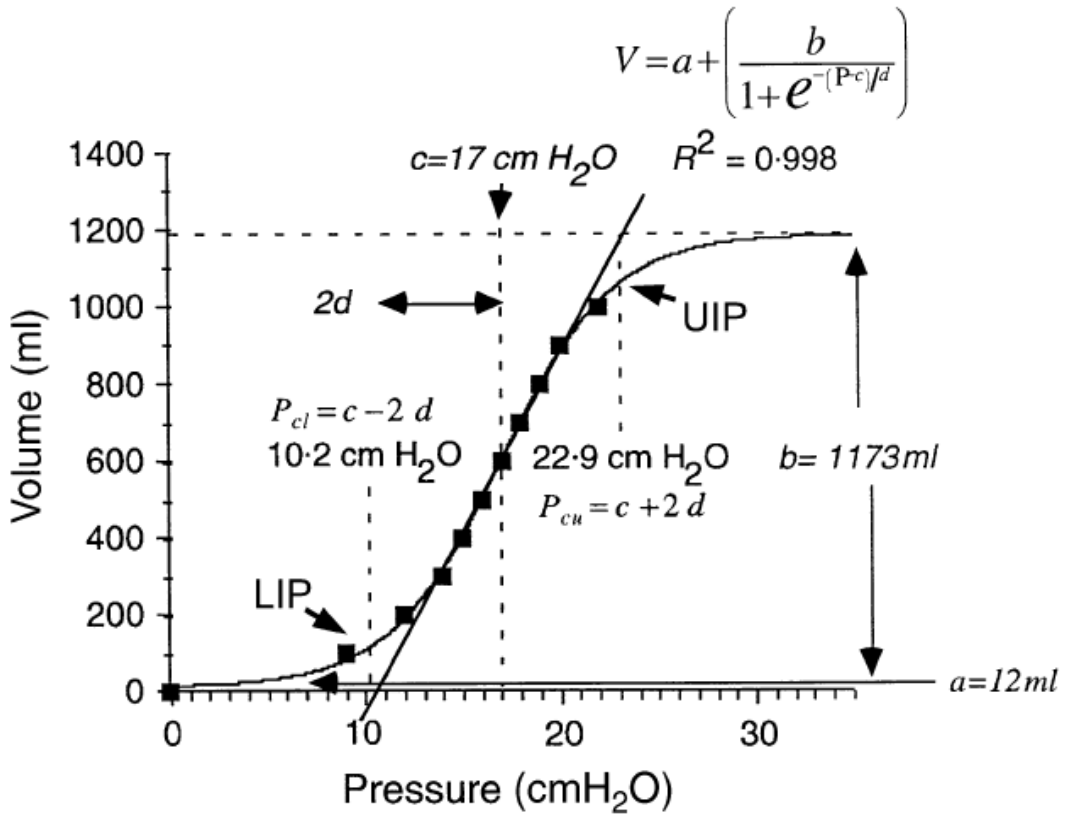
Mortality rates according to PaO₂/FiO₂ tertiles and FiO₂ levels.

	FiO ₂ ≤ 0.50 (n = 946)	0.50 < FiO ₂ < 0.70 (n = 553)	0.70 ≤ FiO ₂ (n = 819)	Total ^B
PaO ₂ /FiO ₂ > 175 (n = 771)	21 ± 2% (n = 593)	26 ± 4% (n = 98)	33 ± 5% (n = 84)	23 ± 2% (p = 0.015)
115 < PaO ₂ /FiO ₂ ≤ 175 (n = 763)	25 ± 2% (n = 330)	26 ± 3% (n = 287)	36 ± 4% (n = 148)	28 ± 3% (p = 0.016)
PaO ₂ /FiO ₂ ≤ 115 (n = 778)	30 ± 10% (n = 23)	28 ± 3% (168)	39 ± 2% (n = 587)	37 ± 3% (p = 0.017)
Total ^A	23 ± 2% (p = 0.014)	27 ± 2% (p = .019)	38 ± 2% (p = 0.017)	

- Higher requirement of FiO₂ in a given subset of PaO₂/FiO₂ suggest higher mortality than PEEP levels at individual subset.
- Overall higher PEEP and higher FiO₂ requirement predicts mortality in severe group.

PV loop concept

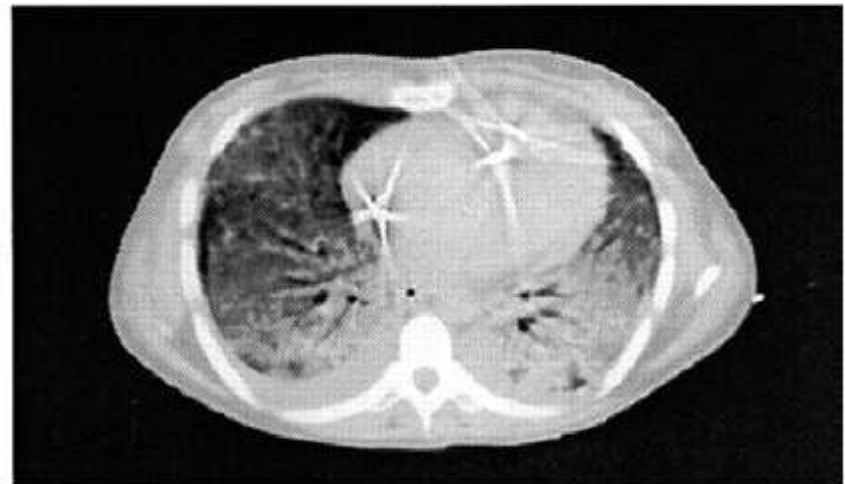
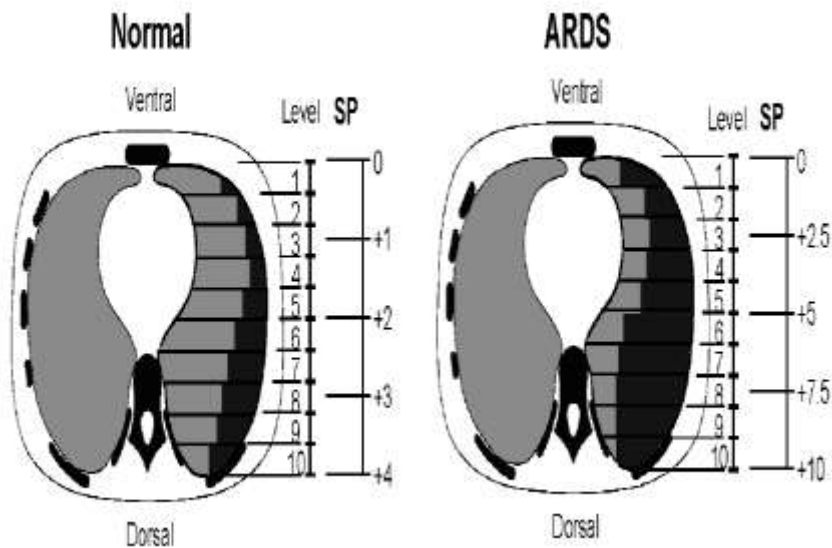
- Inflection points
- Compliance



PEEP titration concept based on PV tool

- Recruitment – baby lung, sponge lung concept

- three lung zones in ARDS-H,R,D zones



Lucciano Gattinoni et. Al., Intensive Care Med (2005) 31:776–784
Ryan La Follette et. Al., Nurs crit care 2007 Sep-Oct;12(5):231-41

- Opening atelectatic alveoli with recruitment manoeuvre is called “open lung approach”
- Theories of recruitment: Threshold opening pressure, Avalanche recruitment**
- Methods of lung recruitment:
 - a) Sigh
 - b) Sustained inflation
 - c) PV Loop

Indications:- Moderate to severe ARDS patients with persistent hypoxemia
-Following ventilator disconnections

Complications:

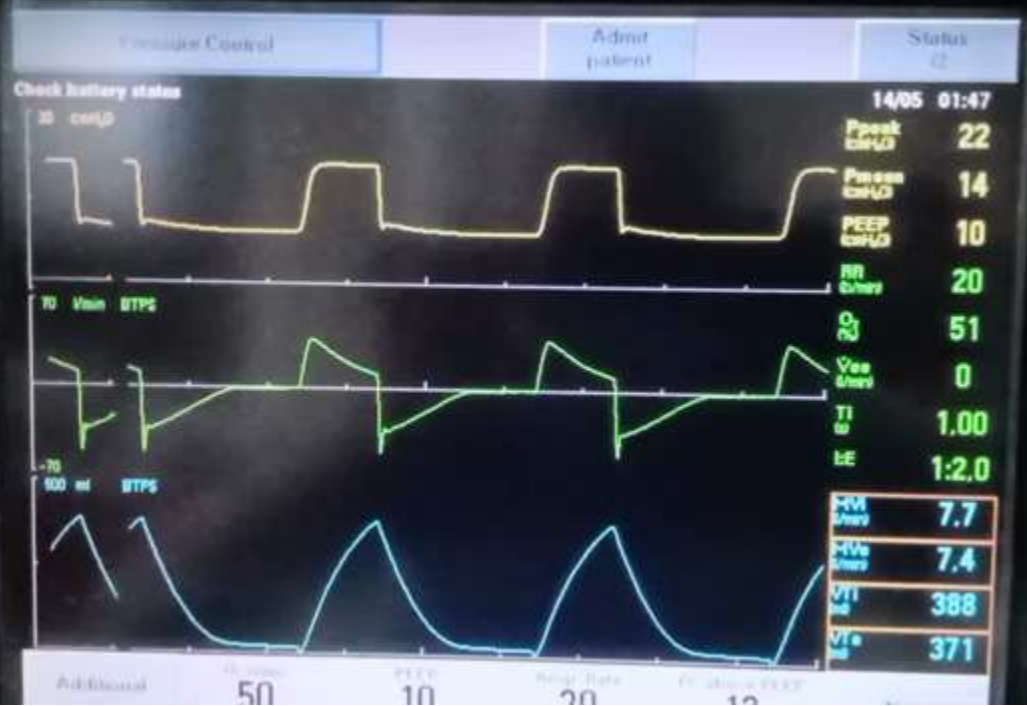
- Desaturation
- Hypotension
- Barotrauma
- Arrhythmias

Repetitive application of lung recruitment manoeuvres rises the incidence of complications.

Sustained inflation

- Sedated and paralysed
- ensure hemodynamic stability
- pressure support/cpap ventilation
- adjust alarm settings
- Cuff pressure – increase to 50 cm H₂O
- Increase the airway pressure to 40 cm H₂O in increments of 5 cm H₂O and maintain at 40 cm H₂O for 30 secs and decrease in decrements of 5 cm H₂O.
- terminate early if hemodynamic instability or desaturation (spo₂<90%)
- change to baseline parameters

Study	type	No. of patients	Interventions	outcomes
Amato et. Al 1998	RCT	53 patients(early ARDS)	Conventional ventilation strategy (12ml/kg VT, PEEP - 6.2±0.5 cm H2O) versus lung protective ventilation (6ml/kg VT, PEEP – 16.4±0.4)	38% versus 71% mortality at the end of 28 days in lung protective ventilation group (p-value -0.001)
Arnal et. Al 2011	Prospective observational study	50 patients	Sustained inflation maneuvers	<p>Volume increase measured by flow requirement to maintain 40 cm H2O pressure</p> <p>Volume increase was 210±198 ml</p> <p>Hemodynamic effects occurs after 10 sec and settle 30 s after cessation</p>



SIGH

- A cyclically delivered recruitment manoeuvre
- Uses – pressure support ventilation
- Mimic physiological breathing
- Consists of high VT in controlled mode or high PEEP up to a specific plateau pressure level, for a selected number of cycles
- 3 consecutive sighs/ minute at 45 cm H₂O plateau pressure*
- Improvement in oxygenation, lung elastance, and functional residual capacity compared to patients who did not receive sighs*

*Pelosi P, et al. Am J Respir Crit Care Med 1999; 159: 872-880

Moraes et al. Critical Care 2014, 18:474

PV LOOP



Limitations of PV tool

- Represents global lung recruitability, cannot measure regional alveoli recruitability.
- Hemodynamic derangement due to application of higher pressure.

Oesophageal pressure guided PEEP concept

Transpulmonary pressure = $P_{alv} - P_{pleural}$ pressure

Should be positive to keep alveoli open

Oesophageal pressure helps to measure the pleural pressure

- Sedated and paralysed
- Esophageal balloon catheter is advanced upto 60 cm into stomach(transient increase in pressure by abdominal compression) then withdrawn to 40 cm(cardiac artifact waves)
- Transpulmonary pressure should be calculated from the measured oesophageal pressure
- Transpulmonary pressure should be kept between 0 to 10 cm H₂O during expiration and less than 20 cm H₂O during end inspiration.
- PEEP should be titrated accordingly to keep the pressures at above mentioned targets.

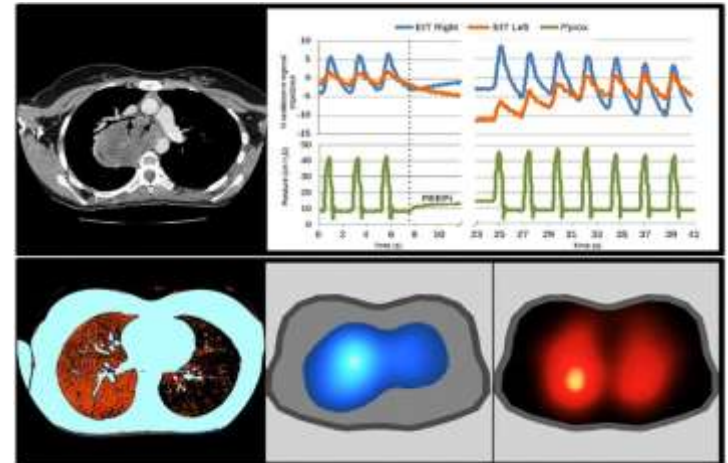
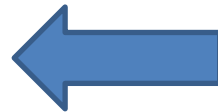
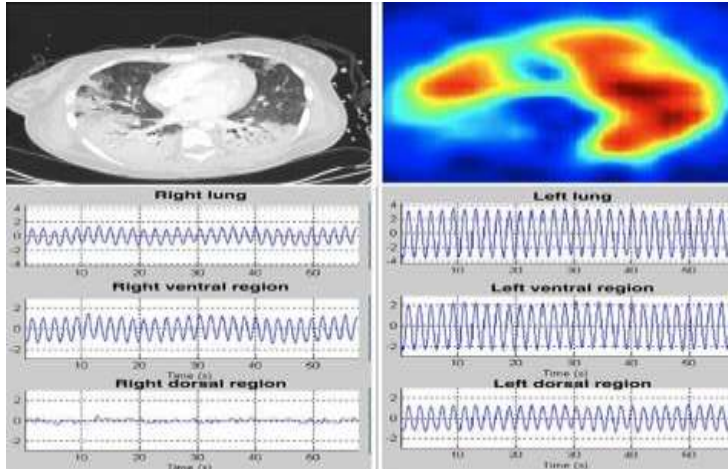
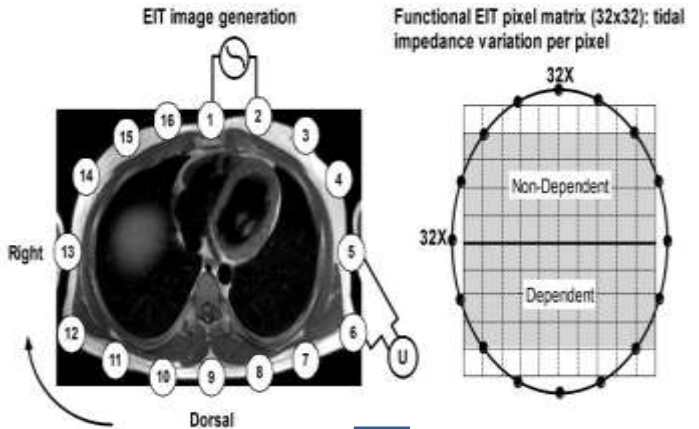


- Esophageal balloon guided PEEP value(18 ± 5) is higher than the conventionally used PEEP titration methods with PEEP-FiO₂ table(12 ± 5)*.
- Improves oxygenation (average increase PaO₂ – 88 mm hg at 72 hours) than conventional PEEP titration based on oxygenation.
- No mortality benefit, increase in ventilator free days when compared with conventional PEEP titration (EPVENT 2 trial).

Jeremy R. Beitler et. Al ., JAMA. 2019;321(9):846–857

Daniel Talmor et. Al.,N Engl J Med 2008; 359;20

EIT guided PEEP concept



- Image distribution of electrical resistivity of lung.
- Displays information on regional ventilation, regional alveolar behaviour (recruitability, collapse, hyperinflation), pulmonary blood flow
- Helps to optimize PEEP.

- Contraindications to EIT placement:
 - Pacemaker
 - spinal cord injury
 - inadequate EIT signal (e.g., thoracic bandages, pneumothorax)
 - hemodynamic instability

- Sedated and paralysed.
- PEEP titration started from 5-8 cm H₂O at steps of 2cm H₂O increments for 2 min until plateau pressure <35 cm H₂O or unstable blood pressure.
- Then decreased in decrements of 2 cm H₂O.
- The best point of intercept between collapse and overdistension percentage reflects the optimal PEEP.



- EIT is a bedside tool that can assess regional distribution of the ventilation in lungs, there by facilitates better optimization of PEEP.
- In patients receiving lung protective ventilation, comparing PV guided titration PEEP with EIT guided peep titration the oxygenation is better, driving pressures are lower(p-value <0.05) however does not have mortality benefit.
- compared with PEEP guided by Fio2, EIT patient requires increments or decrements to PEEP for optimal oxygenation*.

Imaging guided PEEP titration

TABLE 3 | Observed recruitment maneuver re-aeration effect and findings related to potential for lung re-aeration after recruitment maneuver according to the imaging module and the presence or not ARDS.

ARDS	Non-ARDS
Observed lung re-aeration with imaging analysis	
<p>LUS 8% of evaluated consolidations did not respond to RM (Rode et al., 2012) 27% of patients had a re-aeration score ≥ 8 and an increase in lung volume more than 600 ml after RM (Bouhemad et al., 2011)</p> <p>EIT Extremely high variability in changes of the ratio between overdistention and collapsed ration (He et al., 2020)</p> <p>CT High variability* of potential recruitment tissue (Caironi et al., 2015) Potential recruitable tissue: 45% (range 5–75%; de Matos et al., 2012) Potential recruitable tissue: 9% (range –10–60%; Gattinoni et al., 2006) Potential recruitable tissue: 24.9% (range –2–76; Camporota et al., 2019) High variability of opening lung pressures (Caironi et al., 2015)</p>	<p>No change of LUS score after RM (Généreux et al., 2020) 10% of patients do not respond to RM (Longo et al., 2017)</p> <p>Variable* compromise between the extension of lung collapse and overdistention after RM (Karsten et al., 2019)</p>
Findings that predicted more lung re-aeration	
<p>LUS Anterior located consolidations (Bouhemad et al., 2011; Tang et al., 2017) Crater-like sub-pleural consolidations (Rode et al., 2012)</p> <p>EIT Predominant ventilation in non-dependent areas (Zhao et al., 2019)</p> <p>CT Not aerated tissue (> -100 HU) >25–30% of total lung tissue (Gattinoni et al., 2006; Chiumello et al., 2016) Non-focal lung morphology (Nieszkowska et al., 2004; Constantin et al., 2010) Homogeneous cephalo-caudal distribution of 40–50% non-aeration area (Caironi et al., 2010) Opening and closing lung tissue (141 ± 81 g; Caironi et al., 2010)</p>	<p>Decreasing pattern of EELI (delta EELI $>10\%$ or EELI index <1; Eronia et al., 2017; Eichler et al., 2018)</p>

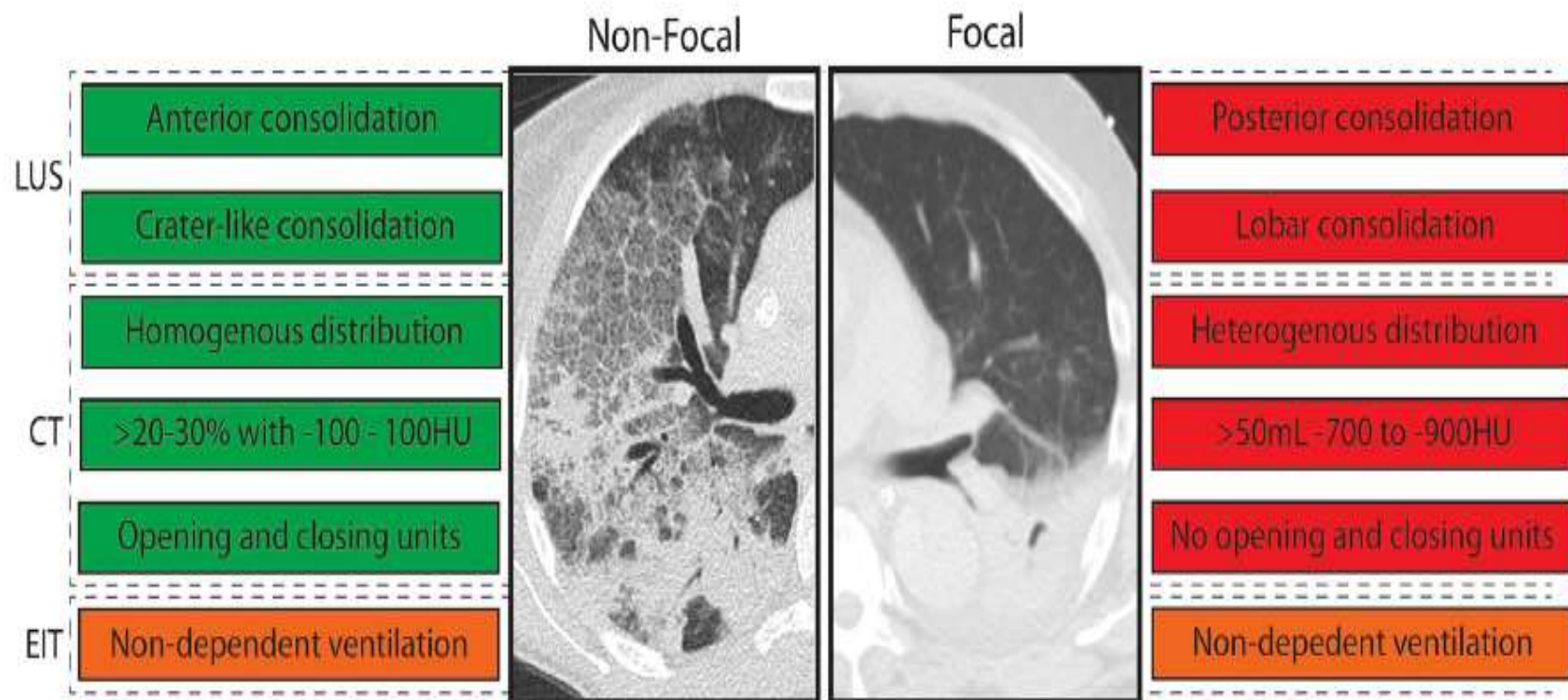


FIGURE 3 | Imaging abnormalities that predicted response to recruitment maneuvers (RM) stratified per morphology. LUS, lung ultrasound; EIT, electrical impedance tomography; CT, computed tomography; HU, Hounsfield units; green, imaging abnormality in line with responder to RM; red, imaging abnormality in line with non-responder to RM; orange, imaging abnormality in line with responder with high uncertainty. Text boxes on the left: consistent with non-focal morphology. Text boxes on the right: consistent with focal morphology.

Current evidence

Quantification data of the potential for lung recruitment by imaging is lacking.

Definition of positive response to recruitment by imaging is variable among studies.

Imaging modalities like LUS only can assess the sub-pleural areas more accurately, also over distension could not be identified by lung ultrasound

Diffuse involvement of lung parenchyma with ARDS predicts good recruitability.

CT imaging sometimes are impractical in critically ill patients.

Driving pressure concept

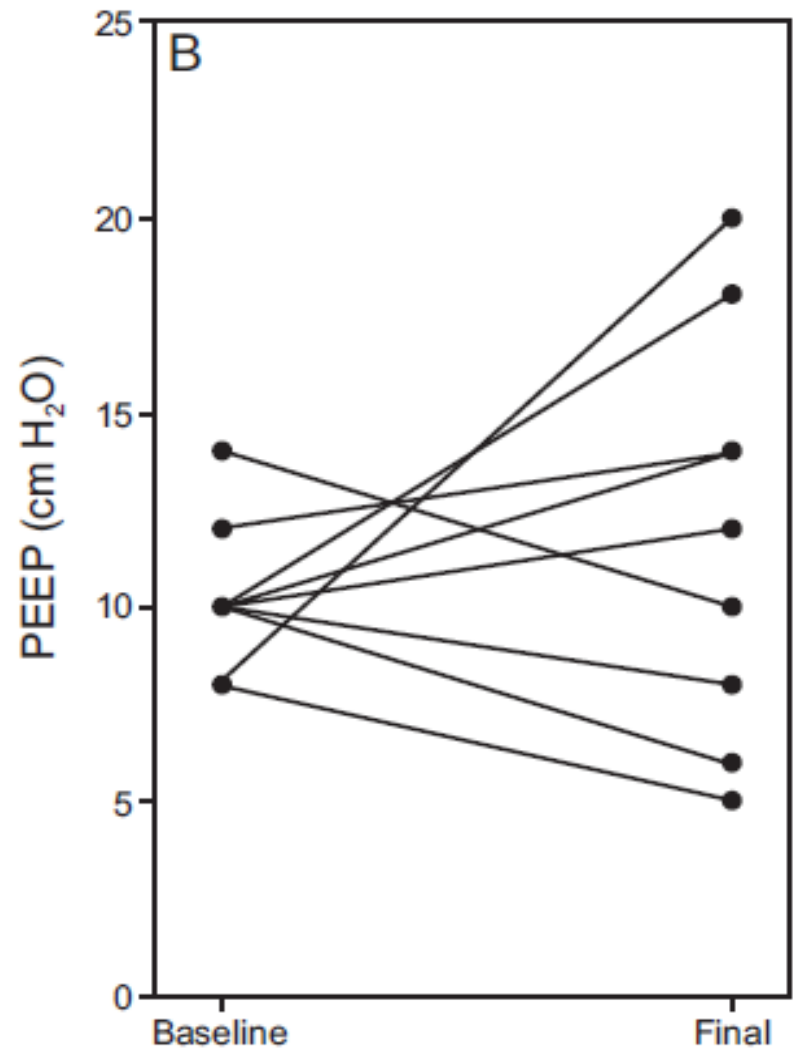
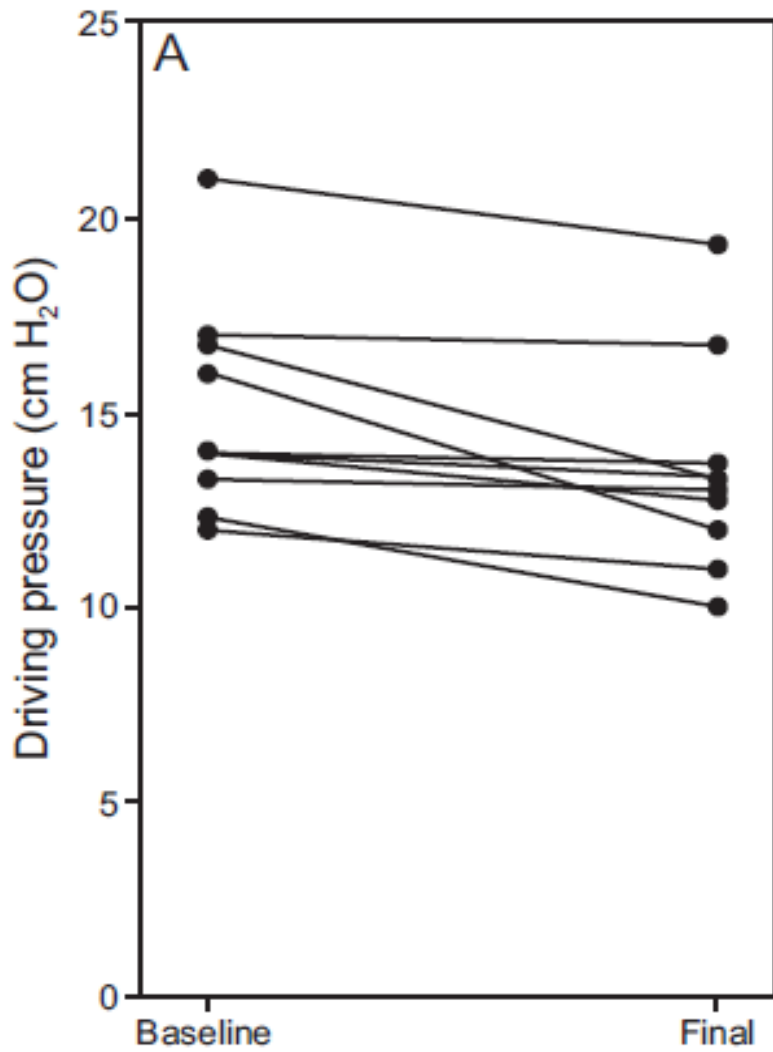
- P_{plateau} minus PEEP
- Correlates with tidal volume and respiratory compliance
- Minimal driving pressure to achieve adequate ventilation should be targetted.
- Most studies quote driving pressure of <13 H₂O has benefit.

Current evidence

- A pilot observational study of 10 patients with PEEP titration based on driving pressure suggest minimal change from baseline driving pressure when patients were enrolled.
- Since low tidal volume ventilation strategy being followed universally and driving pressure being dependent on other variable, solely titrating PEEP with driving pressure requires further studies.

Angela Meier et. Al., Anesthesiology. 2020 June ; 132(6):
1569–1576

[Sarina Sahetya et. Al., Respir care.2020 May;65\(5\):583-589](#)



Summary

- PEEP to be individualized in each patient.
- Optimal PEEP should be a range rather than a single value.
- Methods of optimal PEEP determination and titration are evolving