Original Article

Positive End-expiratory Pressure Titration after Alveolar Recruitment Directed by Electrical Impedance Tomography

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Abstract

Background: Electrical impedance tomography (EIT) is a real-time bedside monitoring tool, which can reflect dynamic regional lung ventilation. The aim of the present study was to monitor regional gas distribution in patients with acute respiratory distress syndrome (ARDS) during positive-end-expiratory pressure (PEEP) titration using EIT.

Methods: Eighteen ARDS patients under mechanical ventilation in Department of Critical Care Medicine of Peking Union Medical College Hospital from January to April in 2014 were included in this prospective observational study. After recruitment maneuvers (RMs), decremental PEEP titration was performed from 20 cmH_2O to 5 cmH_2O in steps of 3 cmH_2O every 5–10 min. Regional over-distension and recruitment were monitored with EIT.

Results: After RMs, patient with arterial blood oxygen partial pressure (PaO_2) + carbon dioxide partial pressure ($PaCO_2$) >400 mmHg with 100% of fractional inspired oxygen concentration were defined as RM responders. Thirteen ARDS patients was diagnosed as responders whose PaO_2 + $PaCO_2$ were higher than nonresponders (419 ± 44 mmHg vs. 170 ± 73 mmHg, $P < 0.0001$). In responders, PEEP mainly increased recruited pixels in dependent regions and over-distended pixels in nondependent regions. PEEP alleviated global inhomogeneity of tidal volume and end-expiratory lung volume. PEEP levels without significant alveolar derecruitment and over-distension were identified individually.

Conclusions: After RMs, PEEP titration significantly affected regional gas distribution in lung, which could be monitored with EIT. EIT has the potential to optimize PEEP titration.

Key words: Acute Respiratory Distress Syndrome; Electrical Impedance Tomography; Positive End-expiratory Pressure; Recruitment Maneuvers

Introduction

Protective lung ventilation limited the plateau pressure (P_{plat}) to 30 cmH_2O in order to avoid alveolar over-distension.[1,2] However, because of atelectasis, tidal ventilation might be restricted in relative normal lung regions instead of diseased lung regions given that positive-end-expiratory pressure (PEEP) was insufficient. Meanwhile, those aerated regions would become over-distended when a large amount of atelectatic regions were not involved in tidal ventilation.[3,4] Recruitment maneuvers (RMs), especially achieving full alveolar recruitment, is the possible way to alleviate the inhomogeneity of tidal ventilation when more lung regions participate in tidal ventilation.[5-7]

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Ideal alveolar recruitment is difficult to achieve. Some patients were difficult to be fully recruited because the requested P_{plat} was too high.[8] Borges *et al*.[9] suggested to use maximal alveolar recruitment (MAR) instead of full alveolar recruitment. Patients whose arterial blood oxygen partial pressure (PaO_2) plus carbon dioxide partial pressure ($PaCO_2$) were higher than 400 mmHg with 100% of fractional inspired oxygen concentration (FiO_2) achieved MAR. The optimal PEEP level is hard to decide for an individual because recruitment and over-distension sometimes happen simultaneously during PEEP titration.[5,10]

Electrical impedance tomography (EIT) is a real-time bedside monitoring tool, which can reflect dynamic regional lung ventilation instead of the static image like computed tomography (CT) scan.[11-13] In this study, we monitored the regional gas distribution during RMs and

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consequent PEEP titration with EIT. The aim was to explore if the choice of optimal PEEP could be directed by the optimal gas distribution monitored with EIT for patients with acute respiratory distress syndrome (ARDS) on the bedside.

Methods

Patients and experimental protocol

Consecutive ARDS patients under mechanical ventilation in Department of Critical Care Medicine of Peking Union Medical College Hospital were included in this prospective study from January to April in 2014. Exclusion criteria were: Age <18 years, pregnancy and lactation period, and any contraindication to the use of EIT (pacemaker, automatic implantable cardioverter defibrillator, and implantable pumps). The study was approved by the Ethics Committee of Peking Union Medical College Hospital. Written informed consent was obtained from all patients or their legal representatives prior to the study.

All the patients received 2–4 mg/h intravenous midazolam and 1–2 mg/h vecuronium bromide to assure no spontaneous breaths. Every patient was ventilated with volume control mode with Dräger Evita 4 (Dräger Medical, Lübeck, Germany). The tidal volume (V_T) was set to 6 ml/kg ideal weight, and FiO_2 and PEEP were adjusted accordingly to maintain peripheral capillary oxygen saturation (SpO_2) over 90%. If P_{plat} was >30 cmH_2O, V_T was decreased 1 ml/kg gradually until P_{plat} was <30 cmH_2O or V_T <4 ml/kg ideal weight. After 10–15 min baseline ventilation, PEEP was switched to zero end-expiratory pressure (ZEEP), and FiO_2 was increased to 100% for 3–5 min. Subsequently, PEEP was increased to 15 cmH_2O for 2 min. If the P_{plat} was <40 cmH_2O, PEEP was further increased to 20 cmH_2O for another 2 min. Decremental PEEP trial started after the RM. And FiO_2 was adjusted back to previous level before RMs, then PEEP was decreased from 20 cmH_2O or 14 cmH_2O to 5 cmH_2O in steps of 3 cmH_2O every 5–10 min unless SpO_2 less than 90% and PEEP would be never decreased further.

Measurements and data analysis

Blood gases measurements were measured by radiometer 600 series blood gas analyzers, respiratory system mechanics was measured by bedside ventilators. An EIT electrode belt with 16 electrodes was placed around the thorax in the fifth intercostal space, and one reference electrode was placed on the patients' abdomen (PulmoVista 500, Dräger Medical, Lübeck, Germany). Electrical alternating currents were applied in a sequential rotating process through adjacent electrode pairs. The resulting surface potential differences between neighboring electrode pairs were measured. The stimulation frequency and amplitude were adjusted automatically by the EIT device to minimize the influence of background noises. EIT measurements were continuously performed at 20 Hz from baseline through RM to decremental PEEP trial. Corresponding EIT data were recorded. EIT data reconstructed uses a finite element method based linearized Newton-Raphson reconstruction algorithm. Baseline of the images was referred to end-expiration of ZEEP.

Five consecutive breaths at the end of each PEEP step were selected. EIT images at end-inspiration ($I_{I,P}$) and end-expiration ($I_{E,P}$) were identified, where P denoted arbitrary PEEP levels ($P \in \{20, 17, 14,\ldots, 5\}$ cmH_2O). Corresponding images were averaged to minimize noise. We defined tidal image $I_{TV,P} = I_{I,P} - I_{E,P}$. Assuming Z_k were pixels in images with impedance value of $Z(k \in K, K = \{1, 2,\ldots, 1024\})$. Lung regions at end-expiration included pixels $m \in M$ where $Z_{m,E} \geq 25\% \times \max(Z_{k,E})$. Lung regions for tidal breathing included pixel $n \in N$ where $Z_{n,TV} \geq 20\% \times \max(Z_{k,TV})$. Regions o were considered to be overinflated, if they belong to lung regions at end-expiration but are not or minimally ventilated during tidal breathing ($o \in O$, $O = M - N$). Regions r are considered to be recruited compared to reference PEEP P1, if they belong to lung regions at end-expiration at current PEEP step but not at P1 ($r \in R$, $R = M_{Pn} - M_{P1}$, $n \neq 1$). Since the EIT images were reconstructed with zero PEEP as baseline, the amplitude of noise at low PEEPs may have the same level as impedance values at end-expiration. Therefore, we selected the end of decremental PEEP trial as P1 (2 cmH_2O) and calculated the regions o, and r at PEEP = 20, 17,…, and 5 cmH_2O. The regions o and r were further divided into four anteroposterior segments with equal height and number of recruited and over-distended pixels were calculated (denoted as 4 regions of interests [ROI], where ROI1 corresponds to most nondependent regions and ROI4 corresponds to most dependent regions).

Patients were diagnosed responders after RMs whose PaO_2 + $PaCO_2$ were more than 400 mmHg with 100% FiO_2. Recruited pixels were defined new aerated pixels when compared with ZEEP. Over-distended pixels were defined aerated pixels that did not join in tidal ventilation under the same PEEP. For studying intrapulmonary gas distribution, we separated perpendicularly EIT image into 4 equal zones from ventral to dorsal. We had still used globe inhomogeneity (GI) to evaluate gas distribution in tidal ventilation and functional residual capacity, with the nomination of GI–TV and GI–FRC individually.[14] The optimal PEEP was considered which could prevent significant derecruitment without obvious over-distention.

Statistical analysis

Statistical analyses were performed using SPSS version 21 (IBM, Chicago, IL, USA). Data were tested for normal distribution and homoscedasticity using the Kolmogorov-Smirnov test and the Brown-Forsythe test. Basal data and respiratory mechanisms, had a normal distribution values, were presented as means ± standard deviation (SD) and analysis of variance test was applied. And recruited and over-distended pixels that had an abnormal distribution were presented as the median and median interval and independent samples Kruskal-Wallis was used. All $P < 0.05$ were considered to be statistically significant.

Results

Patients and clinical data

A total of 18 ARDS patients under mechanical ventilation in Department of Critical Care Medicine of Peking Union Medical College Hospital were included in this prospective study (10 male, 8 female; age 58 ± 12 years; acute physiology and chronic health evaluation II 23 ± 8; ideal weight 62 ± 10 kg. Twelve patients were diagnosed as pneumonia, other patients were caused by extrapulmonary origins as unknown origin fever, surgery, severe acute pancreatitis, and so on.

Basal data comparison between responders and nonresponders

As shown in Table 1, 13 ARDS patients with PaO_2 + $PaCO_2$ >400 mmHg and 100% FiO_2 were diagnosed as responders after RMs, who had received less dose norepinephrine and lower V_T ventilation compared with nonresponders before RMs. In other basal parameters, there were not significant differences between responders and nonresponders. The rate of pneumonia in responders and nonresponders was not significantly different (34.8% vs. 80.0%, $P = 0.0615$).

Recruitment maneuvers

Three patients received 15 cmH_2O PEEP of RMs since their P_{plat} were higher than 40 cmH_2O. The rest of patients had received both 15 cmH_2O and 20 cmH_2O PEEP of RMs. Although there was no significant difference in PaO_2 at ZEEP between two groups, PaO_2 of responders significantly increased at PEEP 15 (302 ± 87 mmHg vs. 104 ± 75 mmHg, $P < 0.0001$) and PEEP 20 (369 ± 48 mmHg vs. 121 ± 85 mmHg, $P < 0.0001$) compared with nonresponders [Table 2].

Image of recruited pixels and over-distended pixels during positive-end-expiratory pressure titration after recruitment maneuvers in responders and nonresponders

As shown in Figure 1, during PEEP titration, recruited and over-distended pixels under different PEEP were shown from ventral (upper) to dorsal (lower). Recruited and over-distended pixels were marked in purple and white, respectively. Compared with patient no. 3 (nonresponder), much more recruited pixels were observed in dorsal regions and less over-distended pixels in ventral regions of the patient no. 1 (responder).

Changes of recruited pixels and over-distended pixels during positive-end-expiratory pressure titration after recruitment maneuvers in all patients

As shown in Table 3, the recruited pixels in all patients decreased grossly along with decremental PEEP, and the over-distended pixels were stable from PEEP 20 to PEEP 14 and decreased gradually from PEEP 14 to PEEP 8.

Recruited and over-distended pixels changed with positive-end-expiratory pressure titration in two groups

As shown in Table 4, in responders, the recruited pixels were stable grossly but decreased significantly from PEEP 20 to PEEP 14 and from PEEP 8 to PEEP 5, and the over-distended pixels were stable from PEEP 20 to PEEP 14 and decreased from PEEP 14 to PEEP 8. However, in nonresponders, no significant changes of recruited and over-distended pixels were found during PEEP titration.

Table 1: Basal data before RMs comparison between responders and nonresponders (mean ± SD)

Items	Responders ($n = 13$)	Nonresponders ($n = 5$)	Mean difference (95% *CI*)	*P*
Age (years)	57 ± 12	59 ± 13	−2.27 (−15.82–11.27)	0.726
APACHE II	23 ± 10	25 ± 6	−2.60 (−12.80–7.60)	0.591
Height (cm)	165 ± 9	172 ± 7	−6.87 (−16.58–2.82)	0.152
Ideal weight (kg)	60 ± 10	67 ± 7	−6.80 (−17.24–3.64)	0.186
NE ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	0.16 ± 0.14	0.00 ± 0.00	0.17 (0.03–0.30)	0.021
V_T (ml)	378 ± 29	412 ± 28	−33.72 (−65.74–1.70)	0.040
FiO_2 (%)	47 ± 19	55 ± 20	−8.08 (−29.37–13.21)	0.433
PaO_2 (mmHg)	115 ± 62	97 ± 26	17.80 (−51.54–87.15)	0.592
$PaCO_2$ (mmHg)	44 ± 10	51 ± 17	−7.07 (−21.52–7.38)	0.313
Compl (ml/cmH_2O)	31 ± 15	61 ± 36	−30.77 (−73.81–12.27)	0.131
PaO_2/FiO_2 (mmHg)	207 ± 51	150 ± 107	57.03 (−20.76–134.82)	0.140
PEEP (cmH_2O)	11 ± 3	11 ± 2	0.00 (−6.74–6.74)	1.000
P_{peak} (cmH_2O)	26 ± 6	31 ± 0	−4.75 (−27.14–17.64)	0.548
P_{mean} (cmH_2O)	15 ± 3	16 ± 4	−1.11 (−4.75–2.52)	0.522
P_{plat} (cmH_2O)	26 ± 5	23 ± 9	2.77 (−4.44–9.97)	0.426
HR (beats/min)	82 ± 15	102 ± 21	−20.25 (−39.06–1.44)	0.037
MAP (mmHg)	89 ± 12	85 ± 12	4.24 (−10.44–18.93)	0.541
SpO_2 (%)	97 ± 2	97 ± 2	−0.52 (−3.02–1.97)	0.659
Lactate (μmol/L)	1.60 ± 0.60	1.20 ± 0.60	0.47 (−0.31–1.24)	0.217

RMs: Recruitment maneuvers; APACHE II: Acute Physiology and Chronic Health Evaluation II; NE: Norepinephrine; V_T: Tidal volume; FiO_2: Fraction of inspired oxygen; PaO_2: Partial pressure arterial oxygen; $PaCO_2$: Partial pressure arterial carbon dioxide; Compl: Respiratory compliance; PEEP: Positive end-expiratory pressure; P_{plat}: Plateau airway pressure; P_{mean}: Mean airway pressure; P_{peak}: Peak airway pressure; HR: Heart rate; MAP: Mean arterial pressure; SpO_2: Peripheral capillary oxygen saturation; SD: Standard deviation; *CI*: Confidence interval.

Table 2: RMs between responders and nonresponders (mean ± SD)

Items	Responders (n = 13)	Nonresponders (n = 5)	Mean difference (95% *CI*)	*P*
ZEEP				
pH	7.44 ± 0.08	7.48 ± 0.06	0.90 (0.00–0.18)	0.044
Lactate (μmol/L)	1.60 ± 0.70	1.50 ± 0.50	0.05 (−0.98–1.09)	0.910
HR (beats/min)	90 ± 9	106 ± 18	−16.49 (−32.00–0.97)	0.039
MAP (mmHg)	88 ± 15	89 ± 8	−0.31 (−16.26–15.63)	0.967
P_{plat} (cmH_2O)	15 ± 4	16 ± 4	−1.28 (−5.82–3.27)	0.549
Compl (ml/cmH_2O)	41 ± 32	29 ± 9	12.23 (−20.22–44.68)	0.072
PaO_2 (mmHg)	120 ± 50	83 ± 34	37.35 (−16.42–91.12)	0.157
PEEP 15				
HR (beats/min)	91 ± 13	93 ± 13	−1.40 (−16.86–14.06)	0.848
MAP (mmHg)	78 ± 27	82 ± 7	−3.93 (−31.54–23.68)	0.762
P_{plat} (cmH_2O)	33 ± 5	37 ± 3	2.66 (−1.95–7.30)	0.230
Compl (ml/cmH_2O)	45 ± 35	31 ± 7	14.00 (−21.38–49.37)	0.406
PaO_2 (mmHg)	302 ± 87	104 ± 75	198.29 (104.30–292.28	0.000
$PaCO_2$ (mmHg)	50 ± 12	51 ± 15	−1.65 (−16.08–12.77)	0.811
PEEP 20				
HR (beats/min)	82 ± 15	98 ± 23	−16.10 (−37.12–4.92)	0.122
MAP (mmHg)	84 ± 11	80 ± 14	4.17 (−11.49–19.84)	0.569
P_{plat} (cmH_2O)	33 ± 5	36 ± 3	−3.93 (−10.27–2.40)	0.194
Compl (ml/cmH_2O)	30 ± 11	27 ± 14	2.32 (−16.11–20.74)	0.779
PaO_2 (mmHg)	369 ± 48	121 ± 85	247.80 (174.68–320.95)	0.000
$PaCO_2$ (mmHg)	50 ± 11	49 ± 17	1.17 (−14.11–16.45)	0.871

PaO_2: Partial pressure arterial oxygen; $PaCO_2$: Partial pressure arterial carbon dioxide; Compl: Respiratory compliance; PEEP: Positive end-expiratory pressure; P_{plat}: Plateau airway pressure; HR: Heart rate; MAP: Mean arterial pressure; SD: Standard deviation; *CI*: Confidence interval; ZEEP: Zero end-expiratory pressure; RMs: Recruitment maneuvers.

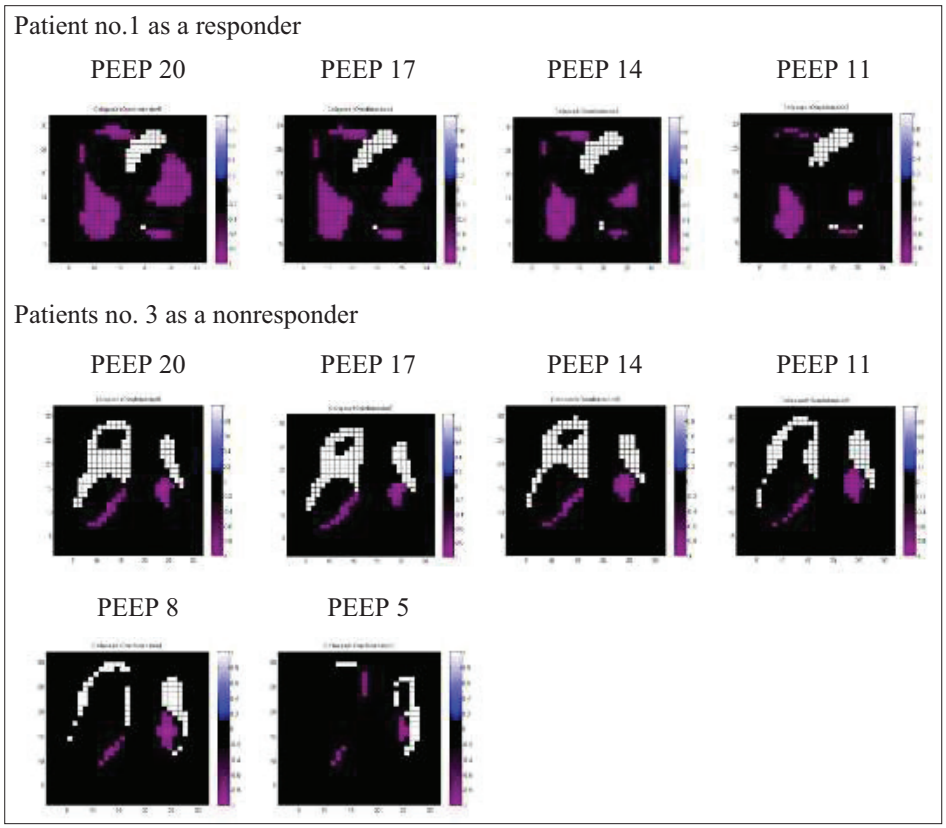

Figure 1: Image of recruited pixels and over-distended pixels during positive-end-expiratory pressure (PEEP) titration after RMs in responder and nonresponder. During PEEP titration, recruited and over-distended pixels of typical patient images under different PEEP were shown from ventral (upper) to dorsal (lower). Recruited and over-distended pixels were marked in purple and white. Compared with patient no. 3 as a nonresponders, patient no. 1 as a responder had much more recruited pixels in the dorsal region and less over-distended pixels in ventral regions.

Difference of recruited and over-distended pixels of four regions of interests with positive-end-expiratory pressure titration

As shown in Table 5, compared with nonresponders, responders had more recruited pixels in PEEP 8 ($P = 0.037$) and PEEP 5 ($P = 0.031$) and more over-distended pixels in PEEP 8 ($P = 0.05$) of ROI2.

And in responders, the recruited pixels decreased from PEEP 8 to PEEP 5, and the over-distended pixels decreased from PEEP 11 to PEEP 8 in ROI1, the over-distended pixels decreased from PEEP 14 to PEEP 8 in ROI2, and the recruited pixels decreased from PEEP 17 to PEEP 5 in ROI3. However, there was no significant difference of recruited and over-distended pixels during PEEP titration in four ROIs in nonresponders.

Globe inhomogeneity of two groups

As shown in Table 6, no significant changes of GI–TV and GI–FRC were found in nonresponders. In responders, GI–TV was improved in all PEEP levels compared with ZEEP, except PEEP 20. GI–FRC was improved in all PEEP levels except PEEP 5. During PEEP titration, there were significant changes of GI–TV from PEEP 8 to 5 and GI–FRC from PEEP 20 to 5. PEEP 11 has the lowest GI–TV of 0.39 (0.33–0.45), and PEEP 17 has the lowest GI–FRC of 0.40 (0.34–0.42).

Table 3: Changes pixels of recruited and over-distended pixels during PEEP titration after RMs in all patients

Groups	Recruited pixels	Over-distended pixels
PEEP 20 ($n = 15$)	78 (52–108)	26 (15–83)
PEEP 17 ($n = 17$)	70 (47–110)	35 (19–80)
PEEP 14 ($n = 18$)	60 (31–106)§	34 (9–64)
PEEP 11 ($n = 17$)	74 (32–101)*†	23 (6–49)*†
PEEP 8 ($n = 15$)	82 (29–99)†	15 (3–42)*†
PEEP 5 ($n = 13$)	44 (23–69)‡	33 (5–43)

*$P < 0.05$, compared with PEEP 20; $^{\dagger}P < 0.05$, compared with the neighboring upper PEEP; $^{\ddagger}P < 0.01$, compared with the neighboring upper PEEP; $^{\S}P < 0.01$, compared with PEEP 20. PEEP: Positive-end expiratory pressure; RMs: Recruitment maneuvers.

Table 4: Recruited and over-distended pixels changed with PEEP titration between two groups

Groups	Recruited pixels	Over-distended pixels
Nonresponders		
PEEP 20 ($n = 4$)	46 (30–79)	26 (15–83)
PEEP 17 ($n = 4$)	47 (29–67)	27 (10–97)
PEEP 14 ($n = 5$)	31 (22–103)	29 (6–71)
PEEP 11 ($n = 5$)	33 (20–93)	37 (7–63)
PEEP 8 ($n = 4$)	34 (19–80)	40 (15–61)
PEEP 5 ($n = 4$)	44 (23–69)	37 (25–44)
Responders		
PEEP 20 ($n = 11$)	82 (66–127)	26 (15–83)
PEEP 17 ($n = 13$)	86 (56–121)	37 (19–80)
PEEP 14 ($n = 13$)	76 (46–107)*	38 (10–65)
PEEP 11 ($n = 12$)	80 (52–101)	17 (5–54)†‡
PEEP 8 ($n = 11$)	84 (73–116)	5 (3–35)†‡
PEEP 5 ($n = 9$)	51 (33–77)†	8 (3–46)

*$P < 0.05$, compared with PEEP 20 in the same group; $^{\dagger}P < 0.05$, compared with the neighboring upper PEEP in the same group; $^{\ddagger}P < 0.01$, compared with PEEP 20 in the same group. PEEP: Positive-end expiratory pressure.

Discussion

Inhomogeneity of intrapulmonary gas distribution is the main problem for ventilation treatment in ARDS patients.[10,15] More atelectasis is present under lower PEEP, and more over-distension occurs under higher PEEP. Therefore, tidal ventilation probably happens only in some relative normal lung regions, while more stress would be introduced by involving only small part of alveoli during tidal ventilation.[16,17]

In order to improve homogeneity of ventilation distribution, RMs for opening the lung tissues would be the right choice. However, alveolar recruitment is a continuous course and behaves a pan-inspiratory phenomenon accompanied by incremental airway opening pressure. Insufficient airway opening pressure cannot achieve full alveolar recruitment and improve gas distribution. Rimensberger *et al*.[18] recommended that the lung should be maximally recruited and subsequently be maintained opening with small V_T and optimal PEEP. The criteria of "optimal" PEEP are still debatable. Hickling[19] thought the maximal change of tidal compliance during decremental PEEP after full alveolar recruitment predicted optimal PEEP. Ranieri *et al*.[20] suggested after full alveolar recruitment, the stress index between 0.9 and 1.1 indicated optimal PEEP. In our opinion, optimal PEEP is to achieve the most homogenous ventilation. At first, we had increased PEEP to 15 and 20 cmH_2O individually to implement RMs for 2 min, and secondly we titrated PEEP and monitor gas distribution dynamically with EIT.[15,21]

For studying intrapulmonary gas distribution, we divided EIT images into four ROIs perpendicularly from ventral to dorsal. It was found that PEEP mainly increased recruited pixels in ROI3 and over-distended pixels in ROI1 of responders, which coincided to our knowledge. No significant changes were found in all four ROIs of nonresponders, which indicated that RMs had little influences in nonresponders.

We had used GI–TV and GI–FRC individually to evaluate gas distribution in tidal ventilation and FRC. There were significant improvements of GI–TV and GI–FRC when compared with ZEEP and during PEEP titration after RMs in responders, which implied a more homogeneous gas distribution in tidal ventilation and FRC after RMs. Therefore, PEEP levels without significant alveolar derecruitment and over-distension could be identified individually in responders. Few changes found in nonresponders, however, again indicated that RMs had little influences in nonresponders. Hence, an optimal PEEP was difficult to decide.

One of the limitations of this study was that the P_{plat} was limited to 40 cmH_2O for safety reason. Some

Table 5: Four lung zone part difference with PEEP titration

Groups	First zone		Second zone		Third zone		Forth zone	
	Recruited pixels	Over-distended pixels	Recruited pixels	Over-distended pixels	Recruited pixels	Over-distended pixels	Recruited pixels	Over-distended pixels
Non-responders								
PEEP 20 (n = 4)	0 (0–17)	15 (4–37)	10 (1–16)	14 (3–66)	19 (10–47)	4 (1–16)	8 (5–23)	0 (0–0)
PEEP 17 (n = 4)	0 (0–18)	19 (5–25)	10 (1–17)	5 (0–61)	19 (12–43)	4 (1–15)	6 (4–15)	0 (0–0)
PEEP 14 (n = 5)	2 (0–21)	17 (3–24)	14 (3–29)	9 (1–44)	13 (8–52)	3 (2–5)	1 (0–14)	0 (0–1)
PEEP 11 (n = 5)	4 (0–21)	16 (2–23)	11 (4–24)	15 (2–37)	12 (5–49)	4 (2–6)	0 (0–13)	0 (0–1)
PEEP 8 (n = 4)	3 (0–18)	14 (4–22)	8 (5–14)	17 (6–37)	14 (2–50)	4 (2–7)	0 (0–14)	0 (0–1)
PEEP 5 (n = 4)	5 (1–10)	10 (8–19)	7 (2–14)	15 (10–24)	8 (2–35)	4 (0–9)	0 (0–12)	0 (0–2)
Responders								
PEEP 20 (n = 11)	0 (0–7)	14 (7–33)	22 (14–48)	10 (1–36)	45 (26–72)	2 (0–6)	15 (1–23)	0 (0–3)
PEEP 17 (n = 13)	0 (0–5)	10 (5–32)	25 (8–41)	17 (2–41)	45 (25–64)	0 (0–6)	11 (2–24)	0 (0–7)
PEEP 14 (n = 13)	0 (0–5)	7 (3–34)	22 (9–39)	16 (0–30)	31 (15–57)§‖	0 (0–6)	11 (0–20)	0 (0–5)
PEEP 11 (n = 12)	1 (0–14)	6 (2–13)*	29 (13–44)	6 (0–14)*†	28 (13–50)§,‖	0 (0–6)	9 (2–17)	0 (0–2)
PEEP 8 (n = 11)	3 (0–18)*	3 (1–11)*†	31 (18–49)‡	0 (0–12)*†‡	22 (9–48)*†	0 (0–4)	7 (0–14)	0 (0–1)
PEEP 5 (n = 9)	8 (0–14)*†	3 (1–9)*	26 (17–44)‡	1 (0–13)	11 (4–16)*†	4 (0–8)	3 (0–7)	0 (0–7)

PEEP: Positive-end expiratory pressure.

Table 6: Globe recruited and over-distended pixels compared with ZEEP in all patients

Groups	GI–TV	GI–FRC
Nonresponders		
ZEEP (n = 5)	0.54 (0.48–0.61)	0.92 (0.50–1.35)
PEEP 20 (n = 4)	0.36 (0.36–0.49)	0.38 (0.18–0.41)*
PEEP 17 (n = 4)	0.37 (0.33–0.48)	0.36 (0.34–0.39)
PEEP 14 (n = 5)	0.38 (0.34–0.46)*	0.35 (0.30–0.45)
PEEP 11 (n = 5)	0.42 (0.37–0.47)	0.39 (0.29–0.49)
PEEP 8 (n = 4)	0.42 (0.40–0.45)	0.40 (0.37–0.63)§
PEEP 5 (n = 4)	0.47 (0.42–0.51)	0.47 (0.37–0.96)
Responders		
ZEEP (n = 13)	0.62 (0.40–0.70)	0.84 (0.68–0.93)
PEEP 20 (n = 11)	0.42 (0.37–0.46)	0.60 (0.40–0.84)*
PEEP 17 (n = 12)	0.44 (0.37–0.46)*	0.40 (0.34–0.42)§†
PEEP 14 (n = 13)	0.40 (0.37–0.48)*	0.41 (0.36–0.48)*‡
PEEP 11 (n = 12)	0.39 (0.33–0.45)§	0.44 (0.38–0.49)§†
PEEP 8 (n = 11)	0.43 (0.33–0.45)§	0.47 (0.45–0.53)*,§
PEEP 5 (n = 9)	0.49 (0.39–0.52)*†	0.57 (0.46–0.78)†

*P < 0.05, compared with ZEEP; †P < 0.05, compared with the neighboring upper PEEP; ‡P < 0.01, compared with the neighboring upper PEEP; §P < 0.01, compared with ZEEP in same group. PEEP: Positive-end expiratory pressure; GI: Globe inhomogeneity; TV: Tidal ventilation; FRC: Functional residual capacity.

nonresponding patients had poor recruited potential, and for the rest, the P_{plat} might be not enough to achieve MAR. In further studies, measures should be taken to distinguish these two kinds of nonresponders. Another limitation of the study was that the gold-standard of identifying collapsed lung regions, namely CT scans, was missing. Due to radiation, CT is not a suitable bedside tool and indeed, there is no well-established tool available for measuring recruitment/derecruitment dynamically. The reliability of EIT has already been proven in previous studies[17,22,23] and, therefore, the findings of the present study should be reliable.

In conclusion, EIT is a useful tool to monitor regional gas distribution at bedside. PEEP titration after MAR had significantly affected intrapulmonary gas distribution, and the selection of PEEP with most homogeneous air distribution can be guided by EIT.

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