Stepwise PEEP Elevation with Determination of the Alveolar Collapsing Pressure versus Sustained Lung Inflation as a Recruitment Maneuver in Patients with ARDS

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ABSTRACT: In patients with acute respiratory distress syndrome (ARDS), protective lung strategy and positive end expiratory pressure (PEEP) therapy should be started as early as possible to avoid lung damage by high pressures, volumes and fraction of inspired oxygen (FiO_2). Recruitment is a strategy aiming at re-expanding the collapsed lung tissue and then maintaining an adequate level of PEEP to prevent subsequent de-recruitment. The objective of this study was to compare safety and efficacy of two lung recruitment maneuvers (RM): stepwise PEEP elevation with determination of the alveolar collapsing pressure versus sustained lung inflation in ARDS patients. A prospective randomized comparative interventional study, conducted in units of the department of Critical Care Medicine of Alexandria Main University hospital, Egypt, included 24 ARDS patients mechanically ventilated with lung protective strategy. Patients were enrolled under two equal groups. Lung recruitment was performed using sustained lung inflation in group I and stepwise PEEP elevation in group II. Arterial blood gases (ABG), hypoxic index and compliance (Cs) were measured. Heart rate (HR), and blood pressure (BP) were monitored and signs of barotraumas were documented. Lung injury score (LIS) was calculated. Results: Hypoxic index, static compliance and lung infiltration improved significantly in group II compared to group I. Significant hypoventilation occurred in group II during RM. Recruitment was successful in 41.7% of patients in group I and in 83.3% of group II. The survival rate was 33.3% in group I and 66.7% in group II. Conclusion: Stepwise elevation of PEEP with determination of optimal PEEP according to alveolar collapsing pressure is a more effective RM than sustained lung inflation, however, hypoventilation, tachycardia and hypotension are likely to occur.
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1. Introduction

In patients with ARDS, protective lung strategy and PEEP therapy should be started as early as possible to avoid lung damage by high pressures, volumes and FiO_2 [1]. The low tidal volumes and pressures advocated for lung protective ventilation has been found to cause progressive de-recruitment of the lung leading to worsening of the hypoxemia. This de-recruitment can be reversed by RM to open the collapsed alveoli followed by application of a high level of PEEP to keep the alveoli open [2,3].

Recruitment is a strategy aiming at re-expanding the collapsed lung tissue through application of a high pressure sufficient to exceed the critical opening pressure of the affected lung tissue [3]. A wide variety of RM has been described. The most relevant are sustained inflation maneuvers [4,5], high pressure controlled ventilation [6,7], incremental PEEP [6,8], and intermittent sighs [9-13]. However, the best recruitment maneuver technique is currently unknown and may vary according to the specific circumstances [4,5].

Therefore, our aim was to evaluate the safety and efficacy of stepwise PEEP elevation with determination of the optimal PEEP according to the alveolar collapsing pressure as a RM in comparison with the sustained lung inflation maneuver in ARDS patients ventilated with the lung protective strategy.

2. Patients and Methods

This prospective randomized comparative study included 24 patients admitted to the Critical Care Medicine Department of Alexandria Main University Hospital fulfilling the diagnostic criteria of ARDS. Consents for inclusion were taken and the study was approved by the local ethical committee.

Patients with hemodynamic instability, cardiac, previous lung diseases, or barotraumas (till insertion of intercostal tube) were excluded. Patients were enrolled at random into two equal groups. Lung recruitment was performed using sustained lung inflation or stepwise PEEP elevation for groups I and II, respectively. The effect of recruitment was evaluated using the hypoxic index, lung Cs and radiological infiltrations in the chest X-ray.

Complications, success rate and outcome were documented.

All patients were ventilated according to the lung protective strategy [14]. Every selected patient had an arterial line for ABG sampling. Chest X-ray was done to exclude pneumothorax and evaluates parenchymal infiltrates. Just before and during each maneuver every patient was sedated using propofol infusion and relaxed using atracurium.

Group I, patients were managed by sustained lung inflation using CPAP mode with a PEEP level of 30 cmH_2O for 30 seconds at FiO_2 of 1.0 then they were switched back to their previous setting of PEEP and FiO_2 [15], the maneuver was repeated after 6 hours. Failure of the maneuver was considered if PaO_2 remained less than 250 mmHg after performing the maneuver twice.

Group II, patients in this group were managed by a stepwise elevation of PEEP. This RM is a modification of previously published maneuver [16,17]. The maneuver was performed using pressure controlled ventilation with end-inspiratory minus end-expiratory pressure of 15 cmH_2O, respiratory rate of 10-15 breaths / min, I: E ratio of 1:1 and FiO_2 of 1.0.

The maneuver was composed of two parts. Part 1 (the recruitment phase) at which PEEP was increased by 5 cmH_2O every 2 minutes. If paO_2 reached 250 mmHg at PEEP level of 25 cmH_2O, the lung was considered recruited and that PEEP level was considered the recruitment pressure (the recruiting PEEP). However, PaO_2 of 250 mmHg was not achieved at PEEP level of 25 cmH_2O in five patients, therefore, part 1 of RM was extended. The PEEP level was increased successively to 30, 35 and 40 cm H_2O for 2 minutes for each step. The end point was either a PaO_2 of $\geq$ 250 mmHg (3 patients) or reaching a PEEP of 40 cmH_2O (2 patients).

After the end of part 1, part 2 (determining the alveolar collapsing pressure) was initiated. PEEP was progressively reduced in steps of 2 cmH_2O every 2 minutes. ABG was analyzed after each decrement starting from the PEEP level of 20 cmH_2O. The PEEP level at which recruitment PaO_2 dropped by a 10% or more was considered the alveolar collapsing pressure. Subsequently, PEEP was reincreased to the recruiting level for 2 minutes to reopen the alveoli that have collapsed then PEEP was maintained 2 cmH_2O above the alveolar collapsing PEEP level, Figure 1. Afterward, ventilatory parameters were reset according to the clinical situation not exceeding a plateau pressure of 30 cmH_2O. Maintenance PEEP was kept for 12 to 24 hours then weaning of PEEP was allowed by decreasing PEEP by 2 cmH_2O every 1 to 2 hours guided by ABG.

Measurements and timing

For group I, ABG analysis, hypoxic index and Cs were monitored before and 30 min after the 1st maneuver then before, 30 min and 6 hours after the 2nd maneuver. For group II, ABG analysis and hypoxic index were monitored before recruitment, following steps of PEEP increment during the recruitment phase, with every step during the alveolar collapsing phase starting from the PEEP level of 20 cmH_2O, 30 min and 6 hours after the maneuver. The Cs was measured before recruitment, when reaching the recruiting PEEP level, 30 min after and 6 hours after the RM.

Statistical analysis

SPSS version 13.0 software was used for data entry and analysis. All tests were two sided and the cut off value for statistical significance was $P < 0.05$. Descriptive statistics were used as indicated. Prior to statistical analysis, the normality of the distribution of quantitative variables was tested. As the distributions were skewed, non-parametric tests were employed. Comparison between the studied groups was performed using the Mann-Whitney test while comparison among stages was performed using the Friedman test. Wilcoxon Signed Ranks test was used for comparison between paired observations. Odds ratio (OR) and 95% confidence limits (95%CL) were used to measure the risks of failure and mortality among the studied groups. Fisher's exact P and Chi-square test were used for comparison between proportions in case of small frequency [18].

3. Results

At time of inclusion, both groups were comparable regarding age, gender, etiology of ARDS, preexisting pneumothorax, intercostal tubes, and LIS; hypoxic index, compliance, PEEP, and chest X-ray quadrants infiltrations (Table 1). The mean values of the hypoxic index in group I increased significantly after 30 min and 6 hours from the first RM and reached its maximum 30 min after the second RM ($P = 0.021$), while Cs showed no significant changes (Table 2). In group II, hypoxic index and Cs improved significantly during and after 30 min and 6 hours following stepwise PEEP RM ($P = 0.000$ and 0.005, respectively) table 3. The hypoxic index and Cs after 6 hours from end of RM and the LIS after 24 hours from RM were more significantly improved in group II than group I (Table 4).

After 24 hours of RM among group I patients, 3 patients (25%) showed complete resolution of CXR infiltrate, 2 patients (16.7%) showed 1quadrant infiltrations, while 3 patients (25%) had 3 quadrants infiltrations, and 4 patients (33.3%) had 4 quadrants

infiltrations. The difference was insignificant (P 0.06).

In group II, 24 hours following RM, 6 patients (50%) showed complete resolution, 4 patients (33.3%) had 1quadrant infiltrations, while still 1 (8.3%) had 3 quadrants infiltrations and 1 patient (8.3%) had 4 quadrants infiltrations. The difference was statistically significant (P 0.004). In comparison to group I, stepwise PEEP elevation produced significant improvement in chest X-ray infiltration.

In group I, the duration of the RM was very short (30 seconds), in contrast, the duration of the RM in group II was ≥ 16 minutes during which significant tachycardia as well as hypoventilation occurred, however, these effects were rapidly reversed 30 min after RM (Table 5). During RM in group II, 6 out of 12 patients (50%) had hypotension and 10 out of 12 (83.3%) had hypoventilation. Hypotension and hypoventilation were not reported in any patient of group I. this difference was highly significant (Table 6).

Three patients (25%) had comparable recruitment related barotraumas in each group (Table 6). Using stepwise PEEP recruitment above 25 cm H_2O was associated with significant increase in the number of patients who developed hypotension and barotraumas in group II patients (Table 7).

Significantly more number of patients were successfully recruited by stepwise PEEP RM (10 out of 12) in comparison to sustained lung inflation RM (5 out of 12). Comparable survival rate was found in both groups (Table 8).

Comparing patient outcome in relation to the success of recruitment denoted that 4 out of the 5 patients who responded successfully to the RM in group I (80%) survived, while all the 7 patients who failed to respond (100%) died, showing a significant difference (P=0.010). In group II, 8 out of 10 patients who responded successfully to recruitment (80%)

4. Discussion

The goal of using unproven therapies for severe ARDS are to sustain life, minimize additional lung injury, and avoid placing the patient at excess risk for other non-pulmonary complications [19]. Several studies recommend the adjunction of RMs to mechanical ventilation to limit alveolar derecruitment induced by low VT [20-22]. When PEEP applied at appropriate levels, it can prevent de-recruitment of the alveolar units previously recruited during the inspiratory phase [23]. However, as demonstrated in many studies, increasing levels of PEEP, at a fixed tidal volume, increased levels of end-inspiratory pressure and end-inspiratory volume. In this way, stepwise increases in PEEP levels can be used as a means of alveolar recruitment [24-26]. Single or repeated recruitment maneuvers can result in a statistically significant improvement in oxygenation. Adverse hemodynamic effects and/or barotraumas were reported in various studies. [16,17,27].

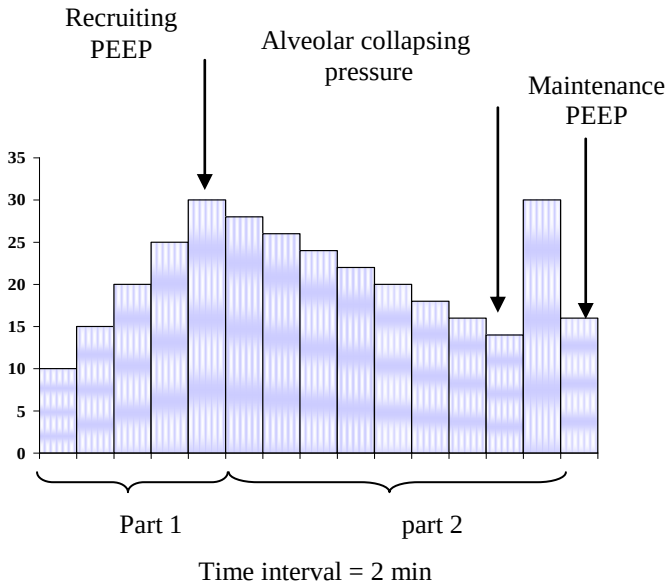

Figure 1. Steps of recruitment and selection of the optimal PEEP.

In the present study, we used the alveolar collapsing pressure rather than lower inflection point (LIP) to determine the optimum PEEP in group II. It was originally believed that LIP represented the opening up of the majority of collapsed alveoli. It is now understood that alveoli open continually along the entire slope of the curve. Evaluation of LIP is subjected to considerable variations among observers. Also, LIP cannot be identified in some patients. [25,26,28,29]. Moreover several studies using computed tomography (CT) have suggested that the right level of PEEP should be selected according to the specific lung morphology of each individual patient [30-33].

In agreement with our results, Rimensberger *et al.* [15] and Grasso *et al.* [34] reported that sustained lung inflation RM produced a significant mean increase of the hypoxic index of 63.9 ± 37.4 and 72.8 ± 41.5, an increase of Cs by 1.9 ± 8.2 and 3.6 ± 6.00 ml/ cmH_2O and a 62.5% and a 66.6% improvement of radiological infiltration, respectively. Similarly, Povoa *et al.* [16] and Borges *et al.* [17] reported that stepwise PEEP RM induced a significant mean increase of hypoxic index of 136.9 ± 16.8 and 142.6 ± 29.2, an increase of Cs of 10.1 ± 1.3 and 12.5 ± 0.9 mL/cmH_2O and 100% and 92.3% improvement of the radiological infiltrations, respectively.

The difference between both groups in this study could be explained by the long duration of high PEEP

therapy used during stepwise PEEP elevation as well as the use of the proper level of maintenance PEEP which was determined according to the alveolar collapsing pressure (14.10 ± 2.02 cmH_2O in group II versus 10.2 ± 0.45 cmH_2O in group I).

Significant but transient hypoventilation occurred in group II during stepwise PEEP RM, it returned to baseline 30 min after the maneuver. This is in agreement with other studies [17,18]. This transient hypoventilation was the result of the prolonged (16 - 35 min) and significantly low minute volumes delivered to the patients because of the low set frequency (10-15 cpm).

During RM, almost all patients of group II showed significant degree of tachycardia. All patients required a recruiting PEEP of more than 25 cmH_2O showed hypotension while only one among those were recruited at a PEEP of 25 cmH_2O had hypotension. Tachycardia can be explained as a response to hypotension and/or hypoventilation. Hypoventilation produces tachycardia through stimulation of sympathetic nervous system and catecholamine release [35]. In agreement, Borges *et al.* [17] observed comparable transient hemodynamic effects without major clinical consequences during stepwise PEEP elevation. They observed hypotension in cases recruited by PEEP of >30 cmH_2O and tachycardia was documented in all cases.

In the present study, sustained lung inflation used in group I caused no hypoventilation and nearly no effect on hemodynamic most probably due to the very short duration of RM. The same was reported by others studies [15, 34]. In contrast, Constantin *et al.* [12] compared RM using CPAP of 40 cm H2O for 40 seconds versus extended sigh (eSigh) consisted of increasing PEEP 10 cm H2O above the LIP for 15 min during volume-controlled ventilation. The only significant hemodynamic change was a decrease in mean arterial pressure during CPAP in non-responders from 86 ± 12 to 70 ± 16 mm Hg (P = 0.0081), the decrease in blood pressure during eSigh was not significant. However, later on Constantin *et al.* [5] reported a transient decrease in blood pressure only in one out of 20 patients had recruitment by CPAP of 40 cmH2O for 30 sec. This was partly explained by the fluid challenge administered before intubation and RM.

Following recruitment, three patients in each group of the present study (25%), developed barotrauma. Accordingly, the stepwise elevation of PEEP did not increase the risk of barotrauma compared to sustained lung inflation despite using high levels of PEEP over a long period of time (16-35 minutes). It is important to note that patients developed barotrauma in group II were 3 out of the 5 patients required a recruiting PEEP of > 25 cmH_2O. So, the risk of barotrauma could be related to the level of applied PEEP.

Grasso *et al.* [34] studied sustained lung inflation (CPAP 40 cm/ H_2O) and reported 18.5% risk of barotrauma in the form of subcutaneous emphysema (11.1%) and pneumomediastinum (7.4%). Additionally, Borges *et al.*[17] studied stepwise PEEP elevation and reported 19.2% risk of barotrauma in the form of subcutaneous emphysema (11.5%) and pneumothorax (7.7%). Conversely, Rimensberger *et al.* [15] who studied sustained lung inflation using a PEEP level of 30 cmH_2O have reported no barotrauma. In addition, Povoa *et al.* [16] who studied stepwise PEEP elevation with recruiting PEEP of 25 to 45 cmH_2O have showed no barotraumas directly related to RM. However, in these studies, recruitment was performed while putting patients in the prone position which has a protective effect against barotraumas [36].

In the present study, stepwise elevation of PEEP showed a significantly higher success (83.3%) than did the sustained lung inflation (41.7%). Concurring, Rimensberger *et al.* [15] and Grasso *et al.* [34] studied sustained lung inflation and reported a success rate of 62.5% and 66.6%, respectively. While Povoa *et al.* [16] and Borges *et al.* [17] who studied stepwise elevation of PEEP reported 100% and 92.3% success rate, respectively. Conversely, Richards *et al.* [37] and Halbertsma *et al.* [38] studied sustained lung inflation and reported 80% and 86.7% success rate respectively. However, they used a fixed maintenance PEEP of 15 cmH_2O.

All patients with failure of recruitment in both groups died and most of the successful cases have survived till weaning from mechanical ventilation and discharge out the ICU. This denotes that recruitment can improve prognosis of patients with ARDS.

Conclusion:

Proper lung recruitment can improve the outcome of patients with ARDS. Stepwise elevation of PEEP with determination of the optimal PEEP according to the alveolar collapsing pressure is more effective and has a higher success rate than sustained lung inflation and risk of barotrauma is similar in both maneuvers. Reversible non- harmful short lived hypoventilation and hypotension are likely to occur with stepwise elevation of PEEP.

Limitation of the study:

- Small number of patients included
- Patients were randomized one by one into both groups without a proper method of randomization, however, both groups were comparable at time of inclusion,

Table 1. Characteristics of patients in both groups at time of inclusion

	Group I n= 12	Group II n= 12	P
Age (years): range	18- 49	18- 50	0.563
(mean ± SD)	29.58 ± 11.05	31.50 ± 11.14	
Gender : number (%)			
Male	6 (50.0 %)	7 (58.3 %)	0.682
Female	6 (50.0 %)	5 (41.7 %)	
Aetiology: number (%)			
Pulmonary ARDS	5 (41.7 %)	6 (50.0 %)	
Extrapulmonary ARDS	7 (58.3 %)	6 (50.0 %)	0.682
Lung injury Score: range	2.75- 3.750	2.75- 4	
mean ± SD	3.13 ± 0.41	3.13 ± 0.43	0.976
Hypoxic index: range	75- 130	75- 140	
mean ± SD	109.08 ± 17.54	111.83 ± 21.65	0.583
Static compliance: (mL/cm H2O): range	11- 30	13- 51	
mean ± SD	21.08 ± 6.5	21.67 ± 5.8	0.931
PEEP: (cm H2O): range	9- 15	9- 15	
mean ± SD	11.33 ± 2.23	11.58 ± 2.43	0.906
Chest X-ray quadrants: number (%)			Fisher's
2 quadrants	1 (8.3 %)	0.0	Exact P
3 quadrants	10 (83.3 %)	11 (91.7 %)	1.000
4 quadrants	1 (8.3 %)	1 (8.3 %)	
Pneumothorax on presentation: number (%)			Fisher's
Unilateral	4 (33.3 %)	2 (16.7 %)	Exact P
Bilateral	1 (8.3 %)	2 (16.7 %)	1.000

Table 2. Values of hypoxic index and static compliance before and thirty minutes after 1st maneuver. Then before, thirty minutes and six hours after the 2nd maneuver in patients of group I.

		First RM			Second RM		Friedman test	P
		Before	After 30 min.	After 6 hours	Before	After 30 min.	After 6 hours		
Hypoxic index	Range	75-130	80-250	71-210		78-345	69-334	11.60	0.021*
	Mean	109.08	153.42	121.25		183.67	162.58		
	± SD	17.54	60.76	45.27		111.03	94.33		
Static compliance (ml/cm H_2O)	Range	11-30	12-31	10-33		9-36	7-40	1.87	0.725
	Mean	21.08	21.50	21.66		22.58	23.08		
	± SD	6.50	6.80	7.80		10.04	13.6		

Table 3. Values of hypoxic index and static compliance before, during, and thirty minutes and six hours after the recruitment maneuver in patients of group II.

		Before	During	After 30 min	After 6 hrs	Friedman	P
Hypoxic index	Range	75-140	160-310	73-310	60-300	20.58	0.000 *
	Mean	111.83	268.58	249.25	239.58		
	± SD	21.65	48.11	80.41	84.38		
Static compliance (ml/cm H_2O)	Range	13-31	12-37	12-36	10-41	16.67	0.005 *
	Mean	21.67	29.6	27.08	31.00		
	± SD	5.80	7.90	6.74	9.98		

Table 4. Mean values (mean ± SD) and the mean change of hypoxic index, static compliance and lung injury score before and six hours after the end of recruitment in both groups

			Before recruitment	End of recruitment	Change
Hypoxic index	Group I	Mean ± SD	109.08±17.54	162.58±94.33	53.5±82.61
	Group II	Mean ± SD	111.83±21.65	239.58±84.38	127.75±68.61
		Z	0.46	2.03	2.51
		P	0.644	0.043*	0.012*
Static compliance (ml/cm H_2O)	Group I	Mean ± SD	21.08±6.50	23.17±13.06	2.00±7.10
	Group II	Mean ± SD	21.67±5.80	31.00±9.98	9.33±5.88
		Z	0.09	0.96	2.70
		P	0.931	0.340	0.007*
Lung Injury Score [a]	Group I	Mean ± SD	3.13± 0.41	2.71± 1.18	0.42± 1.93
	Group II	Mean ± SD	3.13± 0.43	2.08± 0.60	1.05± 0.71
		Z	0.03	0.10	2.63
		P	0.976	0.045*	0.012*

Z = Mann-Whitney test * P < 0.05 (Significant) a= before and after 24 hours of recruitment

Table 5. Values of systolic and diastolic blood pressures (mmHg), heart rate (bpm) and $PaCO_2$ (mmHg) before, during and 30 minutes after RM in group II patients.

		Before	During	After 30 min	P	Friedman test
SBP (mmHg)	Range	100-140	80-140	90-125	0.62	0.93
	Mean ± SD	111.67± 11.93	103.75± 25.06	113.33± 9.61		
DBP (mmHg)	Range	60-90	40-90	60-80	0.73	0.61
	Mean ± SD	72.08± 10.76	65.75± 20.48	74.58± 6.56		
HR (bpm)	Range	90-120	106-140	88-115	0.00 *	20.67
	Mean ± SD	105.25± 9.30	125.17± 11.52	101.83± 7.87		
$PaCO_2$ (mmHg)	Range	35.0-43.1	44.3-67.0	37.0-50.0	0.000*	28.3
	Mean ± SD	39.39± 2.70	53.36±7.70	41.83±4.37		

SBP= systolic blood pressures; DBP = diastolic blood pressures; HR = heart rate.

Table 6. Incidence of recruitment related barotraumas, hypoventilation and hypotension in both groups

		Group I		Group II		Fisher's Exact P
		N	%	n	%	
Barotrauma:	Absent	9	75.0	9	75.0	1.000
	Emphysema	2	16.7	2	16.7	
	Pneumomediastinum.	-	0.0	1	8.3	
	Pneumothorax	1	8.3	-	0.0	
Hypoventilation:	No	12	100.0	2	16.7	0.000*
	Yes	-	0.0	10	83.3	
Hypotension:	No	12	100.0	6	50.0	0.014*
	Yes	-	0.0	6	50.0	

Table 7. Relationship between the recruiting PEEP level and incidence of complications in group II.

		25 cmH_2O (n=7)		>25cmH_2O (n=5)		Fisher's exact P
		N	%	N	%	
Barotraumas	No	7	100	2	40	
	Yes	0	0	3	60	0.045*
Hypoventilation	No	2	28.6	0	0	
	Yes	5	71.4	5	100	0.470
Hypotension	No	6	85.7	0	0	
	Yes	1	14.3	5	100	0.015*

Table 8. Rates of success and Outcome of patients of the two groups of patients

	Group I		Group II		OR	95% CL
	N	%	N	%		
Successful	5	41.7	10	83.3	7.00*	1.04-46.95
Failed	7	58.3	2	16.7		
Survivors	4	33.3	8	66.7	4.00	0.73-21.84
Non-survivors	8	66.7	4	33.3		

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References

1. Villar J, Kacmarek RM, Hedenstierna G (2004). From ventilator-induced lung injury to physician-induced lung injury: why the reluctance to use small tidal volumes? Acta Anaesthesiol Scand, 48:267- 74.
2. Christophe R, Salvatore M, Jordi M, Laurent B (2001). Influence of tidal volume on alveolar recruitment. Am J Respir Crit Care Med., 163:1609-13.
3. Gattinoni L, Mehta S, Ranieri M (2002). Lung recruitment in respiratory failure: New insights. Am J Respir Crit Care Med., 159:872- 80.
4. Tusman G, Bohm SH, Vazquez de Anda GF(1999). Alveolar recruitment strategy improves arterial oxygenation during general anaesthesia. Br J Anaesth., 82:8- 22.
5. Constantin JM, Futier E, Cherprenet AL, Chanques G, Guerin R, Cayot-Constantin S, Jabaudon M, Perbet S, Chartier C, Jung B, Guelon D, Jaber S, Bazin JE (2010). A recruitment maneuver increases oxygenation after intubation of hypoxemic intensive care unit patients: a randomized controlled study. Crit Care, 14 (4):R76.
6. Susan P (2006). Improving oxygenation and management of ARDS. In: Mechanical ventilation physiological and clinical applications. 4th ed. Florida, Elsevier, 14:295-333.
7. Matos G, Borges J, Okamoto V, Carvalho C, Amato M, Barbas C (2010). Maximal recruitment strategy minimizes tidal recruitment in severe ARDS: a CT scan study. Critical Care, 14(Suppl 1): P186.
8. Nemer SN, Barbas C, Caldeira J, Coimbra C, Azeredo L, Silva V, Santos R, Carias T, Souza P (2009). A comparison of three alveolar recruitment maneuver approaches in acute lung injury and acute respiratory distress syndrome. Critical Care, 13(Suppl 3): P44.
9. Pelosi P, Cadringher P, Bottino N, Panigada M, Carrieri F, Riva E, Lissoni A, Gattinoni L (1999). Sigh in acute respiratory distress syndrome. Am J Respir Crit Care Med., 159:872- 80.
10. Foti G, Cereda M, Sparacino ME (2000). Effects of lung recruitment on gas exchange and respiratory mechanics in ALI/ ARDS patients. Intensive Care Med., 26:501- 11.
11. Lim CM, Koh Y, Park W (2001). Mechanistic scheme and effect of "extended sigh" as a recruitment maneuver in patients with ARDS: a preliminary study. Crit Care Med., 29:1255- 8.
12. Constantin JM, Jaber S, Futier E, Cayot-Constantin S, Verny-Pic M, Jung B, Bailly A, Guerin R, Bazin JE (2008). Respiratory effects of different recruitment maneuvers in acute respiratory distress syndrome. Crit Care, 12(2):R50.
13. Huh JW, Jung H, Choi HS, HongS-B, Lim CM, Koh Y (2009). Efficacy of positive end-expiratory pressure titration after the alveolar recruitment manoeuvre in patients with acute

respiratory distress syndrome. Critical Care, 13:R22.
14. The National Heart, Lung, and Blood Institute ARDS (2004). Clinical Trials Network: Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med., 351:327- 39.
15. Rimensberger PC, Cdx PN, Frundova H (1999). The open lung during small tidal volume ventilation: concepts of recruitment and "optimal" positive end-expiratory pressure. Crit Care Med., 27: 1946- 52.
16. Povoa P, Almeida E, Femandes A, Mealha R, Moreira P, Sabino H (2004). Evaluation of a recruitment maneuver with positive inspiratory pressure and high PEEP in patients with severe ARDS. Acta Anaesthesiol Scand, 48:287- 93.
17. Borges B, Okamoto N, Gustava F, Ropert M (2006). Reversibility of lung collapse and hypoxemia in early ARDS. Am J Respir Crit Care Med., 174:268- 78.
18. Norman GR, Streiner DL (2000). Biostatistics, the bare essential. 2nd edition; Hamilton, London: B.C.Decker Inc:.
19. Diaz JV, Brower R, Calfee CS, Matthay MA (2010). Therapeutic strategies for severe acute lung injury. Crit Care Med., 38:1644- 50.
20. Lapinsky SE, Mehta S (2005): Bench-to-bedside review: Recruitment and recruiting maneuvers. Crit Care, 9:60- 5.
21. Rouby JJ, Lu Q (2005). Bench-to-bedside review: Adjuncts to mechanical ventilation in patients with acute lung injury. Crit Care, 9:465- 71.
22. Barbas CS, de Mattos GF, Borges Eda R (2005). Recruitment maneuvers and positive end-expiratory pressure/tidal ventilation titration in acute lung injury/acute respiratory distress syndrome: translating experimental results to clinical practice. Crit Care, 9:424- 6.
23. Borges J, Carvalho C, Amato M (2006). Lung recruitment in patients with ARDS. N Engl J Med., 355: 319- 21.
24. Levy M, Richard J (2004). PEEP in ARDS. N Engl J Med., 351:389- 91.
25. Ranieri M, Eissa NT, Corbeil C (2003). Effects of PEEP on alveolar recruitment and gas exchange in patients with ARDS. Crit Care Med., 31:318- 20.
26. Brochard L, Vandelet P (2003). Respective effects of end-expiratory and end-inspiratory pressures on alveolar recruitment in acute lung injury. Crit Care Med., 31:89- 92.
27. Moran I, Mancebo J, Suarez F (2002). Possible adverse effects of recruitment maneuves in patients with ARDS. Am J Respir Crit Care Med., 163:31- 2.
28. Vieillard A, Prin S, Schmitt J (2002). Pressure-volume curves in acute respiratory distress syndrome. Am J Respir Crit Care Med., 165:1107- 11.
29. Rouby J, Goldstein I (2002). Selecting the right level of PEEP in patients with ARDS. Am J Respir Crit Care Med., 165:1182- 4.
30. Vieira SR, Nieszkowska A, Lu Q, Elman M, Sartorius A, Rouby JJ (2005). Low spatial resolution computed tomography underestimates lung overinflation resulting from positive pressure ventilation. Crit Care Med., 33:741- 9.
31. Rouby JJ, Lu Q, Vieira S (2003). Pressure/volume curves and lung computed tomography in acute respiratory distress syndrome. Eur Respir J Suppl.; 42:27s- 36s.
32. Rouby JJ, Constantin JM, Roberto De AGC, Zhang M, Lu Q (2004). Mechanical ventilation in patients with acute respiratory distress syndrome. Anesthesiology, 101:228- 34.
33. Rouby JJ, Puybasset L, Nieszkowska A, Lu Q (2003). Acute respiratory distress syndrome: lessons from computed tomography of the whole lung. Crit Care Med., 31:S285- S95.
34. Grasso S, Mascia L, Turco M (2002). Effects of recruiting maneuver in patients with ARDS ventilated with protective ventlatory strategy. Anesthesiology, 96:795- 802.
35. Guyton C (2006). Heart muscle; the heart as a pump and functions of the heart valves. In: Textbook of Medical Physiology. Edited by Guyton C, Hall E. 11th ed. Philadelphia: Elsevier Saunders, 9:103-15.
36. Villar J, Lu Q (2006). Patient positioning in ARDS. Crit Care Med., 60:55- 9.
37. Richards G, White H, Schalkwyk J (2006). A new strategy of lung recruitment in ARDS. Crit Care Med., 65:105- 9.
38. Halbertsma J, Hoeven G (2005). Lung recruitment during positive pressure ventilation in the patients with ARDS. Anaesthesia Journal, 60:779- 82.