A Decremental PEEP Trial Identifies the PEEP Level That Maintains Oxygenation After Lung Recruitment

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OBJECTIVE: To assess the ability of a decremental trial of positive end-expiratory pressure (PEEP) to identify an optimal PEEP level that maintains oxygenation after a lung-recruitment maneuver. DESIGN: Prospective clinical trial. SETTING: Surgical intensive care unit of a university hospital. PATIENTS: Twenty sedated patients with acute lung injury and/or acute respiratory distress syndrome, ventilated for 1.2 ± 0.4 d. INTERVENTION: Each patient received up to 3 lung-recruitment maneuvers with continuous positive airway pressure of 40 cm H_2O sustained for 40 s to increase the ratio of P_{aO_2} to F_{IO_2} by > 20%. Following the lung-recruitment maneuver, PEEP was set at 20 cm H_2O and then the F_{IO_2} was decreased until the oxygen saturation (measured via pulse oximetry [S_{pO_2}]) was 90–94%. PEEP was then decreased in 2-cm H_2O steps until the S_{pO_2} dropped below 90%. The step preceding the drop to below 90% was considered the optimal PEEP. The lung was then re-recruited and PEEP and F_{IO_2} were set at the identified levels. The patients were followed for 4 h after the PEEP trial and the setting of PEEP and F_{IO_2}. RESULTS: After the lung-recruitment maneuver, all the patients' P_{aO_2}/F_{IO_2} increased > 50%. The mean ± SD P_{aO_2}/F_{IO_2} on the optimal decremental trial PEEP was 211 ± 79 mm Hg, versus 135 ± 37 mm Hg at baseline ($p < 0.001$), and was sustained at that level for the 4-h study period (227 ± 81 mm Hg at 4 h). F_{IO_2} at baseline was 0.54 ± 0.12 versus 0.38 ± 0.12 ($p < 0.001$) at 4 h. PEEP was 11.9 ± 3.0 cm H_2O at baseline and 9.1 ± 4.7 cm H_2O ($p = 0.011$) at 4 h. CONCLUSION: A decremental PEEP trial identifies a PEEP setting that sustains for 4 h the oxygenation benefit of a 40-cm H_2O, 40-s lung-recruitment maneuver. *Key words: lung recruitment, acute respiratory distress syndrome, ARDS, acute lung injury, positive end-expiratory pressure, PEEP, mechanical ventilation.* [Respir Care 2006; 51(10):1132–1139. © 2006 Daedalus Enterprises]

Introduction

The concept of an open-lung protective ventilation strategy during conventional ventilation of patients with acute respiratory distress syndrome (ARDS) was first articulated by Lachman in 1992.[1] This approach called for the opening of the lung with short periods of sustained high airway pressure and maintaining the lung open with appropriately set positive end-expiratory pressure (PEEP) after lung recruitment. Amato et al[2] were the first to use a lung-recruitment maneuver in a randomized controlled trial. They recruited the lung with continuous positive airway pressure (CPAP) of 40 cm H_2O for 30–40 s, followed by setting PEEP 2 cm H_2O above the lower inflection point on the inspiratory pressure-volume (P-V) curve. However, recent concern regarding information obtained from the inspiratory limb of the P-V curve of the lung[3,4] and problems with performance of the test[5] and its analysis[6] have led most clinicians to abandon the use of the inflation limb of the P-V curve for clinical care.

Recently, Hickling[4] proposed that following lung recruitment the most appropriate method of setting PEEP is a decremental PEEP trial—a PEEP trial that proceeds from a PEEP level higher than required to a PEEP level lower

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than required. The optimal PEEP is the minimum PEEP level that sustains the oxygenation benefit of the recruitment maneuver. This places the lung on the deflation limb of the P-V curve, which establishes a much greater lung volume than the same PEEP level without lung recruitment on the inspiratory limb of the P-V curve.[4]

We hypothesized that the oxygenation benefit of a lung-recruitment maneuver would be sustained for a 4-h period if post-recruitment PEEP was set with a decremental PEEP trial. We also hypothesized that lung recruitment performed early following the initial diagnosis of acute lung injury (ALI) or ARDS (by the American-European consensus-conference definition[7]) would result in a $> 20\%$ increase in the ratio of P_{aO_2} to fraction of inspired oxygen (F_{IO_2}).

Methods

This study was approved by the ethics committee of Cairo University and the New Kasr El-Aini teaching hospital, where the research was performed. Informed consent was obtained from the family of every patient prior to enrollment in the study.

Patients

Patients considered for enrollment were all located in the surgical intensive care unit (ICU) of the New Kasr El-Aini Teaching Hospital of Cairo University. To be eligible for this study, a patient had to meet the American-European consensus conference definition of ALI or ARDS[7] and require PEEP of $\geq$ 8 cm H_2O to maintain arterial oxygen saturation (measured via pulse oximetry [S_{pO_2}]) $> 90\%$. Patients were excluded if they were < 18 y old or > 75 y old; had a history of cardiac disease; had chest trauma (including lung contusion, hemothorax, or pneumothorax); had a history of severe chronic obstructive pulmonary disease; had bullae or blebs visible on chest radiograph; had a subclavian central venous line; or were hemodynamically unstable. Patients entering the ICU were screened daily, and patients who met the criteria were enrolled within 24 hours of meeting the criteria. All the patients enrolled had an arterial cannula for continuous blood-pressure monitoring and for obtaining arterial blood samples. Throughout the study, all the patients received continuous electrocardiography, pulse oximetry, and invasive blood-pressure measurement.

Protocol

On enrollment, patients were sedated with a bolus of propofol (0.25–0.75 mg/kg), until there was no evidence of spontaneous breathing effort. Sedation was maintained with a continuous infusion of propofol (10–100 μg/kg/min) during both the recruitment procedure and the subsequent decremental PEEP trial. None of the patients required paralyzing agents for performance of the protocol. Before any recruitment procedure, the patient's airways were suctioned with an in-line suction catheter. Care was exercised during the study not to disconnect the ventilator. In-line suctioning was performed as needed. Prior to performing the recruitment maneuver, baseline gas-exchange and hemodynamic data were obtained. Throughout the study period, the patients were maintained in the supine position.

Patients were then stabilized on an F_{IO_2} of 1.0 for 20 min, after which another set of blood-gas and hemodynamic data were obtained. The recruitment maneuver was performed on an F_{IO_2} of 1.0, using CPAP of 40 cm H_2O applied for up to 40 s. The recruitment maneuver was discontinued if one of the following conditions was observed: S_{pO_2} decreased to $< 88\%$; heart rate increased to > 140 beats/min or decreased to < 60 beats/min; mean arterial pressure decreased to < 60 mm Hg or decreased by > 20 mm Hg from baseline; or cardiac arrhythmia appeared. Immediately following the recruitment maneuver, mechanical ventilation was resumed with pressure-assist/control at a peak pressure of 35 cm H_2O (pressure-control setting 15 cm H_2O) and PEEP set at 20 cm H_2O, with F_{IO_2} of 1.0. After 5 min, hemodynamics and gas exchange were evaluated. If the P_{aO_2} at an F_{IO_2} of 1.0 had less than a 20% increase, the maneuver was repeated, provided the first recruitment maneuver had not been aborted because of one of the above-stated conditions. A total of up to 3 recruitment maneuvers could be performed. A $> 20\%$ P_{aO_2}/F_{IO_2} increase was targeted because we considered this a clinically important increase.

If, following the recruitment maneuver, the P_{aO_2} increased $> 20\%$, the F_{IO_2} was gradually decreased (by 0.05–0.2 every 15–20 min), until S_{pO_2} stabilized between 90% and 94%. PEEP was then lowered by 2 cm H_2O every 15–20 min until the S_{pO_2} fell below 90%. The PEEP level immediately preceding the S_{pO_2} drop to below 90% was considered the optimal PEEP to maintain the oxygenation benefit of the recruitment maneuver. Once the optimal PEEP was identified, F_{IO_2} was increased to 1.0 and a final recruitment maneuver was performed (CPAP of 40 cm H_2O for 40 s). Following the maneuver the PEEP and F_{IO_2} were set at the levels identified during the decremental PEEP trial. Fifteen to 20 min after stabilization another set of gas-exchange and hemodynamic data were obtained (initial PEEP settings). The patients were then maintained on the exact same ventilator settings, with minimal disturbance over the next 4 h. Following the setting of PEEP, the propofol infusion was decreased or stopped, and assist/control or pressure support ventilation resumed. Control of sedation at this time was determined by the staff managing the patient. Data were gathered at 1 h and 4 h after setting

Table 1. Demographic Data

Patient Number	Age (y)	Sex	Weight (kg)	Days of MV	Diagnosis	Case Type	Origin of ARDS
1	36	M	82	1	Mesenteric vascular occlusion	Surgical	Secondary
2	20	M	76	1	Perforated appendix	Surgical	Secondary
3	23	M	69	2	Intracerebral hemorrhage, septicemia	Medical	Secondary
4	47	M	93	1	Intestinal obstruction	Surgical	Secondary
5	40	M	86	1	Bleeding peptic ulcer	Surgical	Secondary
6	32	F	88	1	Septicemia after open cholecystectomy	Surgical	Secondary
7	52	F	54	2	Liver cirrhosis, hepatic coma	Medical	Secondary
8	27	M	97	1	Intracerebral and subarachnoid hemorrhage	Surgical	Secondary
9	54	M	84	2	Cancer at head of pancreas, leaking anastomosis	Surgical	Secondary
10	46	M	79	1	Intracerebral hemorrhage, craniotomy	Surgical	Secondary
11	57	F	63	1	Biliary peritonitis after cholecystectomy	Surgical	Secondary
12	29	F	58	1	Subaortic membrane resection	Surgical	Secondary
13	61	M	86	1	Leaking abdominal aortic aneurysm	Surgical	Secondary
14	27	M	68	2	Status epilepticus, aspiration	Medical	Primary
15	54	F	57	1	Perforated duodenal ulcer	Surgical	Secondary
16	65	F	53	1	Perforated gastric ulcer	Surgical	Secondary
17	60	M	71	1	Bleeding esophageal varices, aspiration	Medical	Primary
18	38	M	91	1	Pancreatitis	Medical	Secondary
19	30	M	87	1	Appendicular mass	Surgical	Secondary
20	32	M	72	1	Near-drowning	Medical	Primary

MV = mechanical ventilation

the PEEP and F_{IO_2} determined in the decremental PEEP trial.

All the patients before and during the protocol were maintained on pressure-assist/control ventilation, with a short inspiratory time ($\leq$ 1.0 s) or pressure-support with a target tidal volume of 6–7 mL/kg actual body weight. The rate was patient-determined or set to achieve a P_{aCO_2} of 35–45 mm Hg. PEEP and F_{IO_2} at baseline were set by physicians who were not involved in the study, to maintain $P_{aO_2} > 60$ mm Hg. Throughout the study period, medical management was not altered. Specifically, fluid management and diuresis were unaltered. Prior to and throughout the study, patients were maintained in the supine position. All patients were ventilated (model 7200, Puritan-Bennett, Carlsbad, California) and S_{pO_2} was monitored (model 90491, Space Labs Medical, Issaquah, Washington).

Data Gathering

Medical history, baseline physiologic data, and demographic data were obtained from all patients. Gas-exchange and hemodynamic data were obtained at baseline on F_{IO_2} of 1.0, prior to each recruitment maneuver, 5 min after each recruitment maneuver on F_{IO_2} of 1.0, 15–20 min after stabilization on the PEEP and F_{IO_2} identified during the decremental trial, and at 1 h and 4 h during the evaluation period.

Statistical Analysis

Data are expressed as mean $\pm$ standard deviation and percentages. We used the Kolmogorov-Smirnov and Lilliefors tests for normality. All data were normally distributed, except for PEEP level. Comparison of physiologic variables that were normally distributed over time were performed via analysis of variance for repeated measures. When significant differences were identified, post-hoc analysis was performed with the Newman-Keul test. Non-normally distributed data (PEEP) were compared using the nonparametric Friedman's analysis of variance (also repeated measured analysis). When significant differences were identified, post-hoc analysis was performed with the Wilcoxon matched-pairs test. A p value < 0.05 was considered significant. All statistical calculations were performed using spreadsheet software (Excel, Microsoft, Redmond, Washington) and statistics software (SPSS, Chicago, Illinois).

Results

We studied a total of 20 patients, who had not received previous recruitment maneuvers and were not requiring vasoactive drugs (Table 1). Their age range was 20–65 y (mean 41.5 $\pm$ 14 y). Their body-weight range was 53–97 kg (mean 75.7 $\pm$ 13.7 kg). Fourteen (70%) patients were

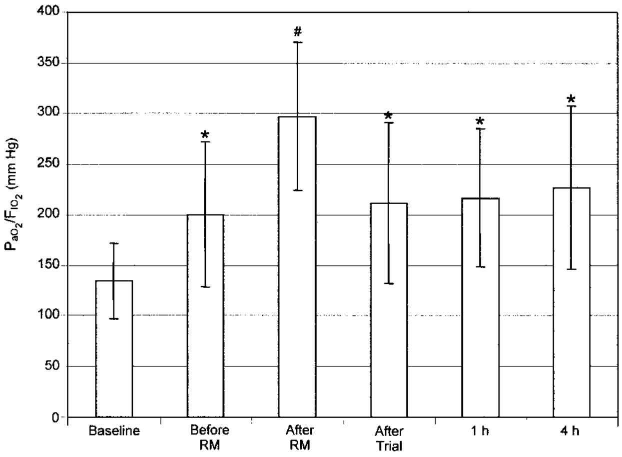

Fig. 1. Mean ± SD ratio of P_{aO_2} to fraction of inspired oxygen (F_{IO_2}). Baseline = F_{IO_2} and positive end-expiratory pressure (PEEP) levels unaltered prior to recruitment. Before RM = On F_{IO_2} of 1.0, just prior to the recruitment maneuver. After RM = On F_{IO_2} of 1.0 and PEEP of 20 cm H_2O, 5 min after the recruitment maneuver. After Trial = Fifteen to 20 min after stabilization on the PEEP and F_{IO_2} selected in the PEEP/F_{IO_2} trial. 1 h = 1 h after PEEP/F_{IO_2} trial. 4 h = 4 h after PEEP/F_{IO_2} trial. * $p < 0.05$ versus baseline. # $p < 0.01$ versus baseline.

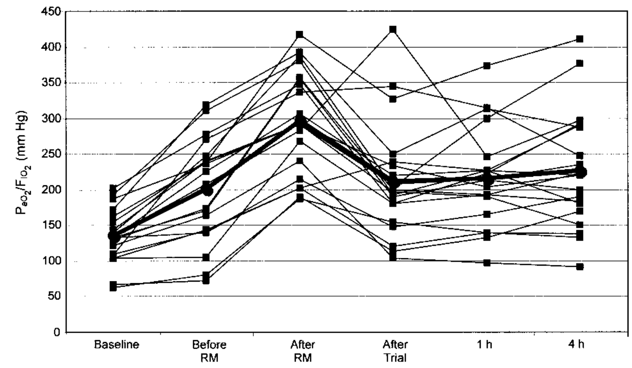

Fig. 2. Individual patient ratios of P_{aO_2} to fraction of inspired oxygen (F_{IO_2}) at all phases of the study. Baseline = F_{IO_2} and positive end-expiratory pressure (PEEP) levels unaltered prior to recruitment. Before RM = On F_{IO_2} of 1.0, just prior to the recruitment maneuver. After RM = On F_{IO_2} of 1.0 and PEEP of 20 cm H_2O, 5 min after the recruitment maneuver. After Trial = Fifteen to 20 min after stabilization on the PEEP and F_{IO_2} selected in the PEEP/F_{IO_2} trial. 1 h = 1 h after PEEP/F_{IO_2} trial. 4 h = 4 h after PEEP/F_{IO_2} trial. The bold line and dots represent mean values.

male. They were ventilated for a mean 1.2 ± 0.4 d prior to entry into the study. There were 14 surgical patients and 6 medical patients. Three had primary ARDS, and 17 had secondary ARDS. Seven of these patients had a second failing organ system. Sixteen patients were on pressure-support before entry into the protocol. No patient received a fluid bolus or additional diuretics during the study.

At baseline the mean ± SD P_{aO_2}/F_{IO_2} was 135 ± 37 mm Hg, and the S_{pO_2} was 92.7 ± 5.2%. On an F_{IO_2} of 1.0, prior to the initial recruitment maneuver, the P_{aO_2}/F_{IO_2} increased to 200 ± 72 mm Hg ($p < 0.001$) and S_{pO_2} was 98.6 ± 1.3%. Immediately after lung recruitment, at PEEP of 20 cm H_2O and F_{IO_2} of 1.0, P_{aO_2}/F_{IO_2} increased to 297 ± 73 mm Hg ($p < 0.001$) and S_{pO_2} was 99.0 ± 0.0%. Shortly thereafter, at a PEEP of 20 cm H_2O and with F_{IO_2} decreased to 0.38 ± 0.12, S_{pO_2} was 95 ± 2.3%. With 6 patients there were protocol violations; the F_{IO_2} at this step should have been decreased until S_{pO_2} was 90–94%.

Fifteen to 20 min after stabilization on the selected PEEP and F_{IO_2}, the P_{aO_2}/F_{IO_2} was 211 ± 79 mm Hg ($p = 0.001$) and the S_{pO_2} was 93.5 ± 3.4%. One hour later the P_{aO_2}/F_{IO_2} was 217 ± 69 mm Hg ($p < 0.001$) and the S_{pO_2} was 94.2 ± 3.1%. At 4 h the P_{aO_2}/F_{IO_2} was 227 ± 81 mm Hg ($p < 0.001$) and the S_{pO_2} was 94.5 ± 3.3% (Figs. 1 and 2).

The F_{IO_2} at baseline was 0.54 ± 0.12, and it was 0.38 ± 0.12 ($p < 0.001$) after recruitment and for the entire 4-h evaluation period (Table 2). Following lung recruitment, the F_{IO_2} requirement was decreased, compared to baseline, in all but 2 patients.

PEEP at baseline was 11.9 ± 3.0 cm H_2O, whereas optimal PEEP (determined in the decremental PEEP trials) was 9.1 ± 4.7 cm H_2O ($p = 0.011$), which was maintained constant throughout the 4-h evaluation period (Fig. 3). Of the 20 patients studied, the PEEP requirement increased from baseline to post-recruitment in 5 patients, remained the same in 3 patients, and decreased in 12 patients. Of the 20 patients studied, 17 required 1 recruitment maneuver, 3 required 2 recruitment maneuvers, and none required 3 recruitment maneuvers.

All the patients had chest radiography within 24 h of the study, and arterial blood pressure was continuously monitored in all patients. P_{aCO_2}, pH, heart rate, and arterial blood pressure remained stable throughout the study period (see Table 2), whereas respiratory rate decreased ($p = 0.010$). No recruitment maneuver was aborted because of an adverse event, nor was any barotrauma identified.

Discussion

The most important findings of this study are:

1. A decremental PEEP trial following a lung-recruitment maneuver identified the optimal PEEP level that sustained, for a 4-h period, the oxygenation level obtained by the recruitment maneuver.
2. All the patients responded to the lung-recruitment maneuvers, based on prespecified oxygenation criteria.
3. Some of the patients required 2 recruitment maneuvers to achieve an oxygenation response.
4. All the patients tolerated the recruitment maneuvers (40 cm H_2O for 40 s) without any adverse events.

Table 2. Gas Exchange, Ventilatory, and Hemodynamic Variables at All Stages of the Study (mean ± SD)

Variable	Baseline	Before RM	After RM	After Trial	1 Hour	4 Hours
F_{IO_2}	0.54 ± 0.12	1.00 ± 0.0*	1.00 ± 0.0*	0.38 ± 0.12*	0.38 ± 0.12*	0.38 ± 0.12*
PEEP (cm H_2O)	11.9 ± 3.0	11.9 ± 3.0	20 ± 0.0*	9.1 ± 4.7†	9.1 ± 4.7†	9.1 ± 4.7†
P_{aCO_2} (mm Hg)	34.8 ± 7.7	36.2 ± 7.7	36.2 ± 7.4	35.5 ± 7.8	35.2 ± 7	35.9 ± 7.6
pH	7.42 ± 0.1	7.40 ± 0.1	7.41 ± 0.1	7.42 ± 0.1	7.43 ± 0.1	7.43 ± 0.1
S_{pO_2} (%)	92.7 ± 5.2	98.6 ± 1.3*	99.0 ± 0.0*	93.5 ± 3.4	94.2 ± 3.1	94.5 ± 3.3
V_T (mL)	479 ± 102.7	475 ± 108.1	503 ± 141.2	497 ± 139.3	504 ± 133.1	499 ± 132.9
f (breaths/min)	25.1 ± 6.3	23.3 ± 6†	21.0 ± 3.7*	21.4 ± 4.5*	21.6 ± 4.2*	22.1 ± 4.5†
HR (beats/min)	114.4 ± 17.4	113.3 ± 17.5†	110.0 ± 16.7†	111.2 ± 20.4	110.5 ± 19.9	110.2 ± 19.0
$\dot{V}_E$ (L/min)	12.0 ± 3.7	11.0 ± 3.4†	10.5 ± 3.2*	10.5 ± 3.2†	10.9 ± 3.6	11 ± 3.6
MAP (mm Hg)	86.9 ± 12.3	84.0 ± 12.2	84.1 ± 13.0	83.1 ± 10.1	81.9 ± 12.6	83.9 ± 12.1
PIP (mm Hg)	24.9 ± 5.0	24.9 ± 5.0	35.0 ± 0.0*	24.1 ± 4.7	24.1 ± 4.7	24.1 ± 4.7

*$p < 0.01$ compared to baseline value
†$p < 0.05$ compared to baseline value
Before RM = On baseline ventilator settings with F_{IO_2} 1.0, before recruitment maneuver (RM)
After RM = F_{IO_2} 1.0 and PEEP 20 cm H_2O
PEEP = positive end-expiratory pressure
After Trial = 15–20 min after setting the PEEP and F_{IO_2}, based on the decremental PEEP/F_{IO_2} trial
1 hour = 1 hour after the PEEP/F_{IO_2} trial
4 hours = 4 hours after the PEEP/F_{IO_2} trial
F_{IO_2} = fraction of inspired oxygen
S_{pO_2} = arterial oxygen saturation measured via pulse oximetry
V_T = tidal volume
f = respiratory rate
HR = heart rate
$\dot{V}_E$ = minute volume
MAP = mean arterial pressure
PIP = peak inspiratory pressure.

5. Regardless of PEEP level or the performance of a recruitment maneuver, many ARDS patients responded with a marked increase in P_{aO_2}/F_{IO_2} when the F_{IO_2} was increased to 1.0.

Ever since Ashbaugh et al[8] first used PEEP to manage ARDS, there has been controversy over the approach to setting PEEP. Most clinicians set PEEP based on a stated or unstated algorithm that relates PEEP to F_{IO_2}.[9] Others have proposed the use of the inspiratory limb of the P-V curve.[2] And still others have adjusted PEEP to achieve an oxygenation target without hemodynamic compromise.[10,11] If the goal is to establish the minimum PEEP that maintains the improved oxygenation from a lung-recruitment maneuver, none of the above approaches is suitable. The PEEP/F_{IO_2} algorithm is not based on the patient's lung mechanics, and tends to drive PEEP to the lowest level tolerated.[9] The P-V curve is difficult to measure[5] and interpret,[6] and an accelerating PEEP trial allows for initial derecruitment by starting at a lower PEEP than is needed. The lack of sustained benefit observed by some following a recruitment maneuver may well be a result of inadequate PEEP.[12,13] As proposed by Hickling,[4] a decremental PEEP trial assures the minimum PEEP that sustains the oxygenation benefit of the recruitment maneuver.

Decremental PEEP/F_{IO_2} Trial

Our data are consistent with that of Tugrul et al,[14] who performed a similar decremental PEEP trial after lung-recruitment in 24 ARDS patients. However, they did not perform a second set of recruitment maneuvers after identifying the optimal PEEP, nor did they do multiple recruitment maneuvers, and their recruitment maneuver was with CPAP of 45 cm H_2O for 30 s. They found sustained benefit for 6 h after their recruitment maneuver. As in our study, they found no adverse effects, and the recruitment maneuvers were well tolerated.

Contrary to our study and the study by Tugrul et al,[14] others have not found a sustained benefit from lung-recruitment maneuvers.[12,13,15,16] The major difference between those protocols and ours is the method of setting PEEP, which explains our ability to sustain the oxygenation benefit. We and Tugrul et al[14] used a decremental PEEP trial that identifies the specific PEEP needed after recruitment. The ARDS Network[15] used its PEEP/F_{IO_2} table and never increased PEEP after recruitment, instead focusing only on the lowest possible PEEP and F_{IO_2}. Oczenski et al[16] performed an incremental PEEP trial before the recruitment maneuver, instead of a decremental trial after recruitment. Grasso et al[13] used exactly the same PEEP before and after recruitment, without a PEEP trial.

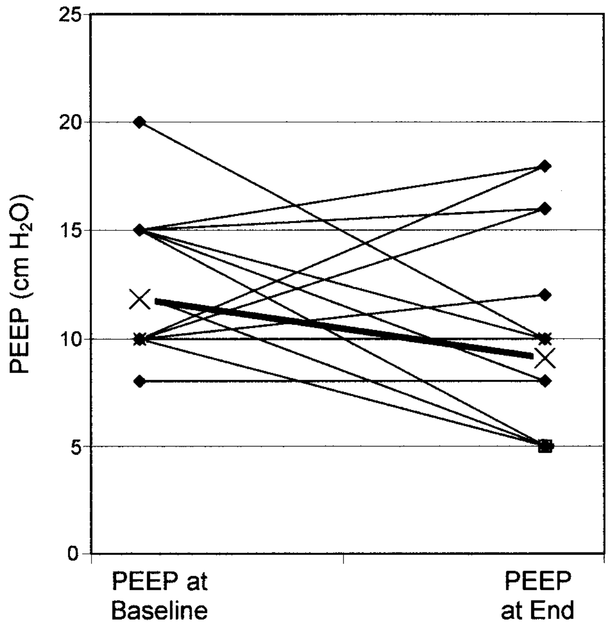

Fig. 3. Individual values for baseline and decremental-trial positive end-expiratory pressure (PEEP) with all 20 patients studied. The bold line and ×s represent mean values.

Lapinsky et al[12] used the same PEEP following the initial recruitment maneuver; but when the recruitment benefit was lost, the lungs were again recruited and PEEP set at a higher level. They used as many as 3 recruitment maneuvers, with increasing PEEP after each maneuver. The key to sustaining the oxygenation benefit is to determine the post-recruitment PEEP required in each patient.

Effect of 100% Oxygen

We set the F_{IO_2} at 1.0 prior to and during the recruitment maneuver to provide a margin of safety if the recruitment maneuver caused marked hemodynamic instability. Increasing the F_{IO_2} above 0.5 in ARDS may markedly improve the P_{aO_2}/F_{IO_2}.[17–19] This effect is based on the ventilation-perfusion relationship, cardiac output, and hemoglobin level. The baseline P_{aO_2}/F_{IO_2} (at F_{IO_2} 0.54) increased on average 48% simply by increasing the F_{IO_2} to 1.0. Of the 20 patients studied, only 3 did not have a P_{aO_2}/F_{IO_2} increase > 20% when we increased F_{IO_2} to 1.0. The mean F_{IO_2} of these patients was 0.63 ± 0.15, and their P_{aO_2} at baseline was 60.6 ± 6.1 mm Hg, versus 105.6 ± 33.0 mm Hg at F_{IO_2} of 1.0. After lung recruitment, decreasing the F_{IO_2} from 1.0 to 0.38, with the PEEP maintained at 20 cm H_2O, resulted in an S_{pO_2} of 95.2%. As emphasized by others,[19] this effect of F_{IO_2} on P_{aO_2}/F_{IO_2} in ARDS may have profound effects on enrolling patients into clinical trials.

Lung Recruitment

At an F_{IO_2} of 1.0, the recruitment maneuver with CPAP of 40 cm H_2O increased the average P_{aO_2}/F_{IO_2} by approximately 50%. This allowed a 31% decrease from the original F_{IO_2} (from 0.54 ± 0.1 to 0.38 ± 0.1) and a 23% decrease from the original PEEP (from 11.9 ± 3.0 cm H_2O to 9.1 ± 4.7 cm H_2O). We expected to be able to decrease the F_{IO_2} following the recruitment maneuver, but were surprised by the decrease in PEEP. On close examination (see Fig. 3), some patients may have been on excessive PEEP prior to the recruitment maneuver. In 6 patients, PEEP was decreased ≥ 5 cm H_2O after the lung recruitment. This overall PEEP decrease was greater than the small PEEP increases in the other 14 patients. This clearly shows the benefit of placing lung volume on the deflation limb of the P-V curve following lung recruitment. On the deflation limb, PEEP levels similar to those on the inflation limb result in the maintenance of improved oxygenation.[4,20,21] We presume that this oxygenation improvement was a result of lung-volume recruitment, since no change in hemodynamics was observed. Our data are consistent with those of the recruitment-responsive group in the study by Grasso et al.[13] That is, our patients were recruited early in their ventilator course (1.2 ± 0.4 d) and shortly after their diagnosis of ARDS/ALI. In addition, the only difference we found between patients who required 2 recruitment maneuvers and those who required only one was that all 3 patients who required 2 maneuvers were in their 2nd day of ARDS/ALI.

Many approaches to lung-recruitment maneuvers have been published.[22–24] We chose to be conservative in the recruitment pressure we applied, to avoid hemodynamic compromise and barotrauma. Not a single recruitment maneuver was aborted and no patient developed a pneumothorax. We may have been able to recruit a greater lung volume had we used higher recruitment pressure, but that could have caused hemodynamic compromise and barotrauma. Our use of multiple recruitment maneuvers may have offset in some patients the lack of higher recruitment pressure. Most likely, the combination of time and pressure determines the success of a recruitment maneuver; that is, the higher the recruiting pressure, the shorter the recruiting time necessary to achieve a similar level of alveolar recruitment. In addition, the patients studied were ideally suited to respond to a recruitment maneuver; they were mostly postoperative, in their first or second day of ventilatory support, hemodynamically stable, and were suctioned prior to the recruitment maneuver. Patients outside of those conditions may not respond in a similar manner.

Although there were no adverse reactions during the lung-recruitment maneuvers we conducted, clearly there is the potential for hemodynamic compromise and barotrauma. Recent animal data from Lim et al[25] clearly show depressed cardiac output during lung recruitment. Similar concerns were raised by Nielsen et al,[26] for cardiac surgical patients, and by Grasso et al,[13] for patients who are ventilated for a lengthy period before the performance of a recruitment maneuver. However, if the patients are appropriately fluid managed, we and others have not observed a marked hemodynamic effect during lung recruitment.[1,2,12,13,20,21,27,28]

Limitations

The primary limitation to this study is that it is not a randomized controlled trial, so we are not able to make any conclusions regarding outcome. Another important limitation is that the post-recruitment-maneuver observation period was only 4 h, because of which we cannot comment on the ability of this PEEP-setting method to sustain the benefit of a lung-recruitment maneuver for a longer period. We also used 100% oxygen to stabilize patients before and during the recruitment maneuver, so we cannot be sure that this did not induce atelectasis. Also, varying the F_{IO_2} during the protocol may have directly affected P_{aO_2}/F_{IO_2}. However, at optimal PEEP, P_{aO_2}/F_{IO_2}, F_{IO_2}, and PEEP were all significantly better than baseline values, which indicates that the post-recruitment response was not simply the reversal of induced atelectasis. In addition, we did not measure static lung compliance at each phase of the study.

The use of pulse-oximetry values (S_{pO_2}) instead of P_{aO_2} measured from arterial blood may have caused us to select an inappropriate PEEP level in some patients. The accuracy of the pulse oximeter is $\pm$ 4–5% at 2 standard deviations,[29] which may have prevented us from identifying the optimal PEEP in the 4 patients whose P_{aO_2}/F_{IO_2} decreased over the 4-h evaluation period (see Fig. 1). In addition, we waited about 15 min between the decremental PEEP steps, which may have been too short a period to ensure stability of oxygenation at individual steps in some patients.

Additionally, we cannot state that it is better to first adjust F_{IO_2} then PEEP, or PEEP first then F_{IO_2}. We decreased F_{IO_2} to the lowest level that placed S_{pO_2} in our target range, to ensure we could rapidly identify a change in S_{pO_2} as PEEP was decreased. Also, setting PEEP at 20 cm H_2O after recruitment and then slowly decreasing PEEP may have assisted in lung recruitment. During the application of 16–20 cm H_2O PEEP, peak pressure was above 30 cm H_2O, which might have furthered recruitment. Additional work needs to be performed on the exact approach to a decremental PEEP/F_{IO_2} trial.

The patients studied were all from a surgical ICU, although some did have pneumonia and sepsis, so our data should be cautiously generalized to the overall population of patients in a medical ICU.

Finally, we cannot be sure that alveolar recruitment actually occurred, versus redistribution of airway/alveolar fluid,[30] since lung volume was not measured. However, our ability to sustain this benefit for a 4-h period at a PEEP level $\leq$ prerecruitment PEEP argues for alveolar recruitment. In addition, oxygenation as a surrogate outcome measure has been questioned.[9,31,32] Although improvements in arterial blood gases are often perceived as reflecting improvement in disease, there are multiple examples in the literature of strategies that yield oxygenation benefit without improvement in outcome.[9,31,32]

Future Directions

Additional study of lung-recruitment maneuvers is needed. The best approach to performing a lung-recruitment maneuver and a decremental PEEP trial, and the expected and potential complications of recruitment maneuvers need to be determined. Most importantly, appropriately designed randomized controlled trials need to be performed to assess the role of recruitment maneuvers on patient outcome.

Conclusion

In summary, a decremental PEEP/F_{IO_2} trial following a lung-recruitment maneuver can identify the optimal PEEP/F_{IO_2} that sustains the oxygenation benefit of a recruitment maneuver for 4 h. Lung recruitment, when used early in the course of ARDS/ALI, results in a large increase in P_{aO_2}/F_{IO_2}.

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