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The Relative Impacts of Various Positive End-Expiratory Pressure Selection Techniques on Adult Patients' Deaths, Who Have Sever or Moderate Acute Respiratory Distress Syndrome; Systematic Review

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Review Article

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Abstract – ***Background:*** Studies contrasting higher and lower PEEP in individuals with ALI have not been sufficiently powered to examine differences or identify subtle but potentially significant impacts on mortality. Our objective was to evaluate the association between high versus low PEEP and patient-important outcomes in individuals with ALI receiving low TVs ventilation. ***Method:*** The PRISMA statement was followed in the course of this systematic review investigation. Randomized trials that qualified for this review examined higher and lower PEEP levels in critically ill patients diagnosed with ALI. To locate relevant trials, we performed an electronic search of MEDLINE, Cochrane, and EMBASE (all from 2000 to 2011). We only included English-language randomized controlled trials. ***Results:*** Four trials yielded 2394 patients met our eligibility criteria. In the Assessment of Low TV and Elevated End-Expiratory Pressure to ALI and the Lung Open Ventilation to Reduce Mortality in the ARDS, PEEP levels were titrated to oxygenation using equivalent PEEP to FIO2 charts. The Expiratory Pressure Study's experimental strategy titrated PEEP levels based on plateau pressure data, regardless of the effect on oxygenation. ***Conclusion:*** Higher PEEP levels associated with a lower hospital death rate in patients with ARDS. Additionally, our findings suggest that this is unlikely to be beneficial for patients with less severe lung injuries; in fact, treating these patients with high PEEP levels may be harmful.

Keywords – Acute lung injury, Positive End-Expiratory Pressure, Tidal volume, acute respiratory distress syndrome.

INTRODUCTION

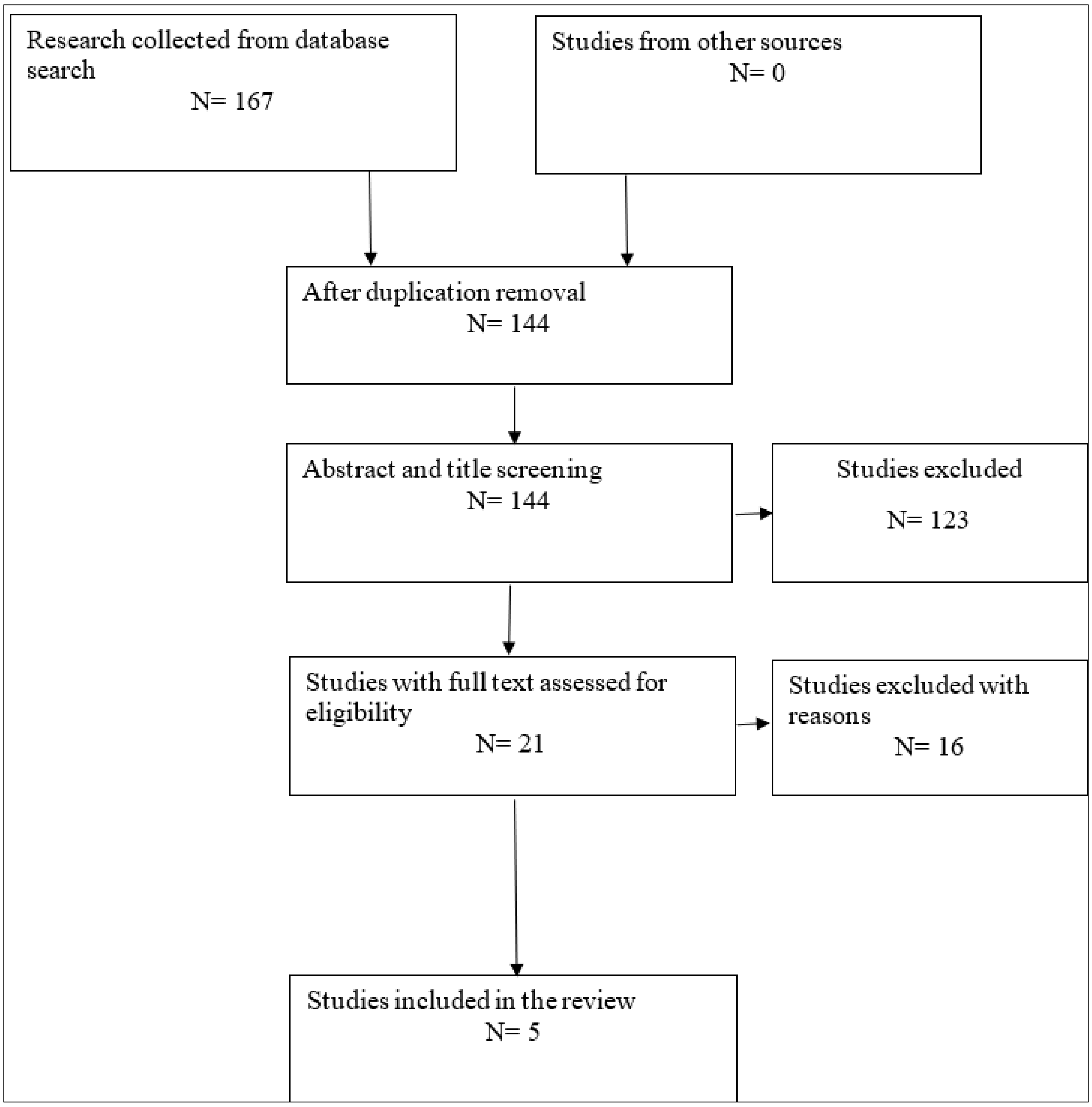
Recent modifications in the technique of mechanical breathing have improved acute respiratory distress syndrome patients survival, but mortality remains high. While it is evident that patients with ARDS benefit from reduced tidal volumes, it is unclear how to select a PEEP (1). The ideal mechanical ventilation system should minimize lung damage caused by over-distention or recurrent alveolar collapse by maintaining a trans-pulmonary pressure that is high enough to maintain oxygenation (2). Trans-pulmonary pressures, at a given amount of PEEP, can vary predictably from patient to other because to the considerable variability in abdominal pressure and pleural pressures across critically sick patients (3,4). Esophageal balloon catheter method has been shown effective in both healthy humans and animals, but it hasn't been routinely used on patients in an intensive care unit. PEEP may be modified based on the unique chest-wall and lung mechanics of each patient (5,6). The purpose of this study was to assess the relative impact of several PEEP selection techniques on mortality in adult patients with moderate-to-severe acute respiratory distress.

METHOD

The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement extension for network meta-analysis was followed in conducting the systematic review (7). In order to find randomized clinical studies that were recruiting adult patients with ARDS, we performed a thorough search of the literature between 2004 and 2011. Trials assessing PEEP selection techniques and their impact on mortality from all causes were included in our study.

We conducted a thorough search of the following electronic bibliographic databases: Embase, Cochrane Central, and MEDLINE. In two rounds, two reviewers independently assessed the eligibility of the research. Consensus was used to settle disputes. Search terms included; ARDS; mortality; PEEP; hypoxemic respiratory failure; lung recruitment maneuver.

Data was collected in a pre-designed Google Form and all authors were added to the form to insure accessibility and avoid information duplication or missing. Information collected include; (citation, intervention, sample size, outcome, study aim, method and main findings).



RESULTS AND DISCUSSION

We included 5 trials in this systematic review (Fig 1). Patients with PaO2:FiO2 less than 300 mm Hg were included in 2 trials (8,9). The following comparisons had direct evidence available: Pes-guided against lower PEEP strategy (10), greater PEEP without LRM versus lower PEEP strategies (8,9), higher PEEP with longer LRM versus lower PEEP strategies (11), higher PEEP with brief LRM versus lower PEEP strategies (12) (Table 1). For higher PEEP with extended LRM against higher PEEP without LRM techniques, as well as higher PEEP with brief LRM versus higher PEEP without LRM strategies, there were no head-to-head comparisons available. The majority of studies used follow-up durations ranging from hospital discharge to 28 days to evaluate death as their primary endpoint.

The heterogeneity of the patients, lower post-RM PEEP level, small sample size, and the possibility that for some patients the CPAP level of RM was insufficient to open the collapsed alveolar were some of the reasons why the Xi et al. (12) trial did not demonstrate a statistically significant benefit in hospital mortality and 28-day mortality. On the other hand, they discovered that ARDS patients' ICU mortality was reduced and their survival with independent breathing was enhanced when low tidal volume combined with periodic RM was used. They attribute the improved results to decreased rates of organ dysfunction and greater rates of ventilator weaning (Table 2).

The main cause of death for individuals with ARDS and a significant determinant of prognosis is the degree of organ failure (13). The Xi et al. study demonstrated that the intervention group's nonpulmonary organ failure-free days were considerably longer than those of the control group. Slutsky et al. (13) investigated the possibility that mechanical ventilation might have a major impact on mortality and be crucial in the start and/or spread of a systemic inflammatory response that results in multi-organ dysfunction syndrome. The ability of individuals with ARDS to survive may be significantly impacted by improvements in organ function.

The opening of previously collapsed lung units due to a rise in transpulmonary pressure is referred to as recruitment, a dynamic process. By doing this, the cyclic opening and closure of unstable lung units is prevented, which would otherwise induce shear stress at the alveolar wall epithelium (14,15). Previous studies have demonstrated that lung protective breathing techniques are linked to decreased blood levels of inflammatory mediators and cytokines as well as a diminished systemic and local cytokine response in ARDS patients (16,17). The Xi et al investigation revealed that while there was no statistically significant difference between the two groups, patients in the RM group had lower plasma concentrations of IL-6.

It seems beneficial to recruit ARDS patients' lungs and avoid further lung recruitment by maintaining an open lung, as proposed by Lachmann more than a decade ago (18,19). Using greater or lower PEEP levels in the ALVEOLI study did not affect the clinical results (9). The greater PEEP technique, which was table-based like the one in the current research and matched on the oxygenation target independent of any patient-related characteristic, was the issue with the ALVEOLI trial. Preserving the PEEP-induced reopening of atelectatic zones and preventing PEEP-induced lung over-inflation constitute a suitable strategy for figuring out the right amount of PEEP. Finding the right PEEP level appears to be possible when using lung-recruiting exercises in conjunction with higher than usual PEEP levels (20).

According to experimental findings, ARM's effects on alveolar recruitment are only temporary if the PEEP levels that before the maneuver are kept constant (21). Higher PEEP levels are necessary to maintain alveolar aeration once they have been recruited (22). The effectiveness of the ARM depends on maintaining the proper amount of PEEP as an anti-derecruiting factor.

According to Huh et al., daily decremental PEEP titration following ARM did not enhance respiratory mechanics during a week and only exhibited an initial increase in oxygenation when compared to the table-based PEEP approach. For the first week in the decremental PEEP titration group, they conducted the ARM and PEEP titration every day. On the other hand, there were no discernible variations in the 28-day mortality, ICU stay, or 60-day mortality. An enhanced survival rate was not linked to the earlier improvement in oxygenation, despite the fact that the responder rate was greater in the decremental PEEP titration group than in the control group (11).

According to Talmor et al. (10) it is possible to get esophageal pressure readings repeatedly with sufficient fidelity and quality for use in treating patients who need mechanical breathing. When treated in this manner, patients with acute lung damage or ARDS showed considerable improvements in respiratory system compliance and oxygenation, as shown by the PaO2:FiO2 ratio. Furthermore, substantial gains were made without raising trans pulmonary pressure above the physiological range during end inhalation. In the group of critically ill patients, there was a tendency toward increased 28-day survival that was correlated with these improvements in lung function.

Even when tidal volume or peak pressure is regulated, lowering end-expiratory lung volume or pressure can be harmful, as demonstrated by a number of studies on acute lung damage (23). Increasing PEEP may be protective in these models (24,25). Effective PEEP modification to the unique physiological characteristics of each patient has proven challenging in ARDS patients, nevertheless. For instance, PEEP and FiO2 were modified in accordance with arterial oxygenation in the ARDS Net research of reduced tidal volume, without taking into account lung mechanics or the chest wall (17).

Table 1: Characteristics of the Included Studies

Study	Comparison	Sample size	Intervention	Mortality measurement time
Xi 2010 (12)	Low PEEP vs High PEEP with LRM	125	Vt 4 to 8 ml/kg CPAP + PBW + PEEP per Sp_{O2}	28 days
Mercat	Low PEEP vs	767	PEEP + PBW + Vt 6	28 days

2008 (8)	High PEEP without LRM		ml/kg PBW	
Huh 2009 (11)	Low PEEP vs High PEEP with LRM	61	LRM + PBW + high PEEP Vt 6 to 8 ml/kg	28 days
Talmor 2008 (10)	low PEEP vs Esophageal pressure guidance	61	PEEP + Vt 6 ml/kg PBW	28 days
Brower 2004 (9)		549	High PEEP Vt 6 ml/kg PBW	After hospital discharge

Table 2: Main Findings of the Included Studies

Study	Main findings
Xi 2010 (12)	One and two days after RM, the PaO2/FiO2 in the RM group was considerably higher than baseline at 120 minutes. On day 28, there were no discernible changes in hospital mortality or ventilator-free days between the RM and control group. The RM group was favored by ICU mortality, the rate of survival with unaided breathing for at least 48 hours on day 28, and days free of nonpulmonary organ failure on day 28. The mean blood pressure and heart rate before RM and 30, 60, and 120 minutes after RM did not differ significantly.
Mercat 2008 (8)	In the group with limited distension, the 28-day mortality rate was 31.2%, whereas in the group with higher recruitment, it was 27.8%. In the group with limited distension, the hospital death rate was 39.0%, whereas in the group with greater recruitment, it was 35.4%. In comparison to the minimum distension group, the enhanced recruitment group experienced a greater median number of organ failure and ventilator-free days.
Huh 2009 (11)	Between the control and decremental PEEP titration groups, there were no appreciable differences in the baseline parameters. The decremental PEEP titration group saw a greater improvement in initial oxygenation than the control group. During the first week, the two groups' dynamic compliance, tidal volume, and PEEP were comparable. The decremental PEEP titration and control groups did not substantially vary in terms of the length of time spent using paralyzing or sedative medications, mechanical ventilation, hospitalization in the intensive care unit, or death at 28 days.
Talmor 2008 (10)	After enrolling 61 participants, the trial reached its stopping point and was closed. In the esophageal-pressure-guided group, the ratio of the partial pressure of arterial oxygen to the percentage of inspired oxygen at 72 hours was 88 mm Hg greater than in the control group. Throughout the whole duration of the follow-up, the effect persisted. In the esophageal-pressure-guided group, respiratory system compliance was also considerably better after 24, 48, and 72 hours.
Brower 2004 (9)	On days 1 through 4, the lower PEEP group's mean PEEP value was 8.3 cm of water, whereas the higher PEEP group's mean value was 13.2 cm of water. Prior to hospital release, the mortality rates were 24.9 percent and 27.5 percent, respectively. Breathing was done without assistance for a mean of 14.5 days in the lower-PEEP group and 13.8 days in the higher-PEEP group from day 1 to day 28.

CONCLUSION

Whether lower or higher PEEP levels are employed, the clinical results are the same in patients with acute lung damage and ARDS receiving mechanical ventilation with a tidal-volume objective of 6 ml per kilogram of projected body weight and an end-inspiratory plateau-pressure limit of 30 cm of water. A ventilator technique that estimates the trans-pulmonary pressure using esophageal pressures increases oxygenation and compliance greatly when compared to the current standard of care. Mechanical ventilation with a smaller tidal volume than is customary in patients with acute lung damage and acute respiratory distress syndrome reduces mortality and lengthens the period of time without ventilator usage.

List of abbreviations

PEEP; Positive end-expiratory pressure
PaO2, partial pressure of oxygen in arterial blood
FiO2, inspiratory oxygen concentration
LRM, Lung recruitment maneuvers
RM, recruitment maneuvers
CPAP, Continuous positive airway pressure
ARM, alveolar recruitment manoeuvre

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