Critical Review Form
Therapy

PGY-3

Fuller BM, Ferguson IT, Mohr NM, et al. Lung-Protective Ventilation Initiated in the Emergency Department (LOV-ED): A Quasi-Experimental, Before-After Trial. Ann Emerg Med. 2017 Mar 1. pii: S0196-0644(17)30028-8.

Objectives: **"to evaluate the effectiveness of an ED-based lung-protective mechanical ventilation protocol on reducing the incidence of pulmonary complications." (p. 2)**

Methods: **This before-and-after study was conducted at the Barnes-Jewish Hospital ED in St. Louis, MO. Patients in the "before" period were identified retrospectively from September 2009 to January 2014. Following an approximately 6-month run-in period, during which a lung-protective ventilation protocol was implemented in the ED, consecutive patients were prospectively enrolled in the "after" group between October 2014 and March 2016, twenty-four hours a day. Adult patients aged 18 years or older requiring mechanical ventilation through an endotracheal tube were included in both groups. Exclusion criteria were death or discontinuation of mechanical ventilation within 24 hours, long-term mechanical ventilation, presence of a tracheostomy, transfer to another hospital, or fulfillment of acute respiratory distress syndrome (ARDS) criteria during the ED stay.**

The intervention being studied consisted of lung-protective tidal volume (6-8 mL/kg ideal body weight), appropriate positive end-expiratory pressure (≥5 cm H_2O, set according to BMI), rapid weaning of oxygen, and head-of-bed elevation. Following intubation in the ED, the respiratory therapist measured the patient's height and set tidal volume accordingly. While ventilators were initially set according to protocol, changes could be made at the discretion of the treating clinicians.

ICU ventilator settings were followed for 2 weeks, and all patients were followed until death or hospital discharge. The primary outcome was a composite of ARDS (defined by the Berlin definition) and "ventilator-associated conditions" defined according to the Centers for Disease Control and Prevention criteria. Secondary outcomes included ventilator-free, hospital-free, and ICU-free days, and hospital mortality.

Propensity-score matching was used, with multivariable logistic regression, to create two groups (before and after) balanced with respect to APACHE II score, BMI, vasopressor use, sepsis, trauma, and age. A total of 1192 patients met inclusion criteria during the pre-intervention period, while 513 eligible patients were identified in the intervention period. Propensity matching resulted in 490 pairs of patients. The mean age in the propensity matched pre-intervention and intervention groups was 58.2 and 58.0 years, respectively. The majority of patients in both groups were male (55.3% and 58.8%).

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	No. This was a quasi-experimental before and after trial, subject to all of the inherent biases associated with such study design. In particular, it is impossible to control for all other potential changes in patient management over time, and some of these changes could affect the outcomes being studied.
2.	Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	N/A. This was not a randomized trial. Patient allocation was based on whether the ED visit occurred during the before or after phase of the study.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. Although there was no randomization, patients were analyzed according to which time frame their presentation occurred in, regardless of whether or not they received lung-protective ventilation (intention to treat analysis).
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. For the two groups (before propensity matching) there were significant differences with regards to several variables, including history of HIV, blood product administration, and vasopressor infusion. Following propensity matching, there remained significant differences between the pre-intervention and post-intervention groups with regards to dialysis dependence (13.3% vs. 6.1%) and intubation for CHF or pulmonary edema (7.6% vs. 2.2%).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Yes and no. There was no blinding involved in this study, but as all enrolled patients were intubated, it is unlikely that they would be aware of group allocation or intervention. It is unlikely that there would be any risk of performance bias on the part of the patients.
2.	Were clinicians aware of group allocation?	Yes. This was a non-blinded, before and after study, and clinicians were aware of group allocation. It is possible (though unlikely) that performance bias on the part of the clinicians could have affected outcomes.

3.	Were outcome assessors aware of group allocation?	No. As stated in the report: "Adjudicators of acute respiratory distress syndrome status were blinded to all clinical variables, including ventilator settings and treatment period." (p. 4)
4.	Was follow-up complete?	Yes. All of the interventions were measured during the hospital stay, and hence outcome data was available for all patients included in the analysis.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• For all patients enrolled, there was a significant reduction in median tidal volume (8.1 mL/kg to 6.3 mL/kg; difference -1.8, 95% CI -1.9 to -1.7) and median FiO_2 (80% to 40%) in the ED between the pre- and post-intervention periods, with a significant increase in mean PEEP (5.4 cmH_2O to 6.5 cmH_2O; difference 1.1, 95% CI 0.9 to 1.3) and mean respiratory rate (15.3 to 20.9; difference 5.6, 95% CI 5.3 to 5.9). • In the propensity-matched analysis, there was an absolute reduction in the risk of the primary outcome of 7.1%, with an adjusted OR of 0.47 (95% CI 0.31 to 0.71). • There was an increase in ventilator-free days (mean difference 3.7; 95% CI 2.3 to 5.1), ICU-free days (mean difference 2.4, 95% CI 1.0 to 3.7), and hospital-free days (mean difference 2.4, 95% CI 1.2 to 3.6) associated with the intervention. • There was an absolute reduction in mortality of 14.5% associated with the intervention (OR 0.47, 95% CI 0.35 to 0.63).
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Yes. This study was, in fact, conducted at our institution, using our patients.
2.	Were all clinically important outcomes considered?	Yes. The authors considered pulmonary complications of high tidal volume ventilation (including ARDS), mortality (which has been shown to be associated with ARDS), and various measures of hospital stay (including days free of the ventilator and days out of the ICU). They did not address cost or quality of life.
3.	Are the likely treatment benefits	Yes. While this study has some limitations (before

	worth the potential harm and costs?	and after study design, use of propensity matching as a surrogate for randomization, lack of blinding), it does demonstrate a fairly significant reduction in pulmonary complications and mortality with a simple, low-cost intervention that is not itself associated with any morbidity. It therefore makes sense to implement a protocol utilizing lung-protective ventilation strategies for intubated patients in the ED.

Limitations:

1. **This was not a randomized controlled trial, but was an observational study utilizing a before and after study design, in which it is impossible to control for simultaneous interventions that could affect the outcomes (i.e. changes in methods of sedation, sepsis management protocols, or use of blood products).**

2. **The authors used propensity score matching as a surrogate for randomization, which attempts to control for known or observed confounders. Unfortunately, it is never possible to control for all unknown or unobserved confounders using such a method.**

3. **The clinicians in this study were not blinded, opening the study to the possibility of performance bias.**

Bottom Line:

In this before and after study evaluating the effect of implementing a protocol for lung-protective ventilation in the ED, after propensity matching to balance known confounders, there was a significant reduction in the risk of pulmonary complications (adjusted OR 0.47, 95% CI 0.31 to 0.71) and mortality (OR 0.47, 95% CI 0.35 to 0.63). Despite some methodological issues, this study clearly demonstrates both the feasibility and effectiveness of lung-protective ventilation in the ED.