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Rate of low tidal volume ventilation use remains low in patients with acute respiratory distress syndrome despite improvement efforts at a single center

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ABSTRACT

Purpose: Low tidal volume ventilation (LTVV) reduces mortality in acute respiratory distress syndrome (ARDS) patients. Understanding local barriers to LTVV use at a former ARDS Network hospital may provide new insight to improve LTVV implementation.
Methods: A cohort of 214 randomly selected adults met the Berlin definition of ARDS at Harborview Medical Center between 2008 and 2012. The primary outcome was the receipt of LTVV (tidal volume of ≤6.5 mL/kg predicted body weight) within 48 h of ARDS onset. We constructed a multivariable logistic regression model to identify factors associated with the outcome.
Results: Only 27% of patients received tidal volumes of ≤6.5 mL/kg PBW within 48 h of ARDS onset. Increasing plateau pressure (OR 1.11; 95% CI 1.03 to 1.19; *p*-value <0.01) was positively associated with LTVV use while increasing PaO_2:F_IO_2 ratio was negatively associated (OR 0.75, 95% CI 0.57 to 0.98; *p*-value 0.03). Physicians documented an ARDS diagnosis in only 21% of the cohort. Neither patient height nor gender were associated with LTVV use.
Conclusions: Most ARDS patients did not receive LTVV despite significant institutional efforts to improve utilization, which suggests that ARDS remains under-recognized and untreated.
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1. Introduction

Acute respiratory distress syndrome (ARDS) is a common and devastating form of respiratory failure that affects 190,000 patients annually in the United States and has a mortality rate of 39% [1]. Despite 30 years of clinical trials and drug research, only a handful of interventions reduce mortality in ARDS patients [2,3]. In 2000, the ARDS Network published the results of the landmark randomized controlled trial that demonstrated a 9% absolute reduction in mortality utilizing a low tidal volume ventilation (LTVV) strategy, defined as ≤6 mL per kilogram (kg) of predicted body weight (PBW) with a goal plateau pressure (P_{plat}) ≤30 cm H_2O [4]. This ventilation strategy is now termed "lung protective ventilation" and has become the standard of care for patients with ARDS [5]. Many studies have confirmed the benefits of LTVV, and have suggested a time-dependent mortality benefit from early utilization of LTVV [5-10]. New evidence also suggests that LTVV may prevent incident ARDS in critically ill patients at risk [11,12].

The adoption of lung protective ventilation strategies in clinical practice has been slow despite convincing evidence of the benefits of LTVV [13-19]. Studies performed in the initial five years of the ARDS Network trial demonstrated only 40% of ARDS patients received appropriate LTVV therapy [20,21]. Low rates of compliance with LTVV have prompted further examination of barriers to utilization. Several barriers to LTVV use have already been described and include mismeasurement or missing documentation of patient height used to calculate predicted body weight, concern for patient discomfort or perceived need for greater doses of sedating medications, and physician failure to recognize ARDS [13,20,22,23]. Studies of sedation practices in the LTVV era have not found an association between LTTV and increased sedation use in either dose or duration [24,25]. Factors associated with higher utilization of LTVV in prior studies include a written protocol for delivery of appropriate ventilator settings and a closed ICU staffing model [20,26].

Abbreviations: ARDS, Acute Respiratory Distress Syndrome; APACHE, Acute Physiology, Age and Chronic Health Evaluation; F_IO_2, fraction of inspired oxygen; ICU, Intensive Care Unit; LTVV, Low Tidal Volume Ventilation; PaO_2, partial pressure of arterial oxygen; P_{plat}, plateau pressure; PEEP, positive end-expiratory pressure.

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This analysis was conducted at Harborview Medical Center, an academic hospital with a level one trauma designation and a former ARDS Network contributing site. Our hospital is a unique location as a contributing site in the original ARDS Network trial and we have already adopted several mechanisms to increase utilization of LTVV. Our institution has implemented written ventilator protocols and uses a ventilator order set for LTVV [27,28]. We also operate in a "closed" ICU staffing model, which has been associated with delivery of lower tidal volumes [26]. Our primary aim was to describe patient and physician factors associated with the use of LTVV in patients meeting the Berlin Definition of ARDS [29], over ten years since the original trial. We hypothesized that the proportion of ARDS patients who receive LTVV remains low at our academic center, despite significant institutional efforts to increase utilization.

2. Methods

The University of Washington institutional review board approved this study with waiver of informed consent.

2.1. Study population: ARDS cohort

We conducted a retrospective cohort study using a pre-existing registry of mechanically ventilated patients admitted to a Harborview Medical Center (HMC) intensive care unit (ICU) between January 1, 2008 and December 31, 2012. We identified patients who received mechanical ventilation via an endotracheal tube for at least 48 h and included patients meeting the Berlin Definition of ARDS [29]. We required a PaO_2:F_IO_2 ratio ≤ 300 mm Hg on two consecutive arterial blood gas (ABG) measurements to meet criteria for hypoxemia in our study. We then selected a random sample of the hypoxemic patients and evaluated chest radiographs obtained within 24 h of the qualifying ABG. Study authors blinded to ventilator settings analyzed each radiograph, and 10% of the total radiographs were reviewed by two readers (LJS and CLH). A qualifying chest radiograph met Berlin criteria with demonstration of bilateral infiltrates. ARDS onset was defined as the latter time of either the second qualifying ABG or qualifying chest radiograph.

2.2. Definition of LTVV

We defined our primary outcome of LTVV as ventilation with tidal volumes (V_T) ≤6.5 mL/kg of predicted body weight (PBW) from values charted by respiratory therapists in our electronic medical record. A V_T of 6.5 mL/kg PBW is consistent with the cutoff chosen by the ARDS Network when evaluating LTVV adherence, and permits for slight deviations from the goal of 6.0 mL/kg PBW that can happen due to miscalculations or rounding in practical use [20]. LTVV use was not dependent on ventilator mode in our study and thus patients receiving ventilation via a pressure controlled mode met criteria for LTVV if the delivered tidal volume was ≤6.5 mL/kg PBW. We also collected plateau pressures from values charted by respiratory therapists. We measured the number of cases that received a low tidal volume at the time of the first qualifying ABG, and then again at 24 h and 48 h after ARDS onset. Patients met criteria for our primary outcome if they received LTVV at any of those three time points.

2.3. Collection of covariates

We abstracted electronic medical record charts to obtain demographic data, physiologic variables, lab values, ventilator data and ICU type. We reviewed admission and daily notes in the first 48 h after ARDS onset to identify the underlying ARDS risk factor(s). We also reviewed physician notes to assess for documentation of concurrent acute brain injury as a potential contraindication to the use of LTVV or acute cardiac events that could call an ARDS diagnosis into question. We did not exclude patients with chart documentation of acute cardiac events. We also reviewed progress notes for interpretation of ABG and/or chest radiographs, documentation of respiratory failure and/or of an ARDS diagnosis by physicians and trainees. Documentation of Acute Lung Injury and the more general, "lung injury," were also considered equivalent to an ARDS diagnosis as this cohort existed prior to the current Berlin definition [29].

2.4. Statistical analysis

We computed descriptive statistics for all study variables including binomial confidence intervals for proportions. Difference testing between groups was performed using two-tailed *t*-tests for means, Mann-Whitney nonparametric tests for medians, and chi-square tests for proportions, as appropriate. A *p*-value of <0.05 was considered significant. We used SAS statistical software for all analyses (SAS version 9.4; SAS Institute, Inc., Cary, NC).

We built a multivariable logistic regression model using five factors selected a priori (age, type of ICU, sepsis/pneumonia; PaO_2: F_IO_2 ratio; P_{plat}) to examine associations with the receipt of LTVV at any time within 48 h of ARDS onset. There are potential contraindications to the use LTVV per the ARDS Network trial protocol including a pH <7.15, PaO_2 < 55 mm Hg, RR >40 breaths per minute, and/or co-morbid acute brain injury. We examined the subset of patients without these potential contraindications, collected at ARDS onset, to assess for the possible effect of these contraindications on the use of LTVV at our center.

3. Results

From 31,722 patients admitted to an ICU at Harborview Medical Center between 2008 and 2012, we randomly selected 700 adult patients (≥18 years of age) for evaluation (Fig. 1). Of those, 255 patients (36%) were intubated for at least 48 h and had two consecutive ABG measurements with a PaO_2:F_IO_2 ratio ≤ 300 mm Hg, meeting our criteria for possible ARDS. We excluded fourteen patients with chronic respiratory failure, three with brain death on arrival, four with missing radiographs, and 20 with radiographs inconsistent with ARDS. The final study cohort included 214 patients.

The cohort had a mean age of 55 ± 16 years, was mostly male (71%) and predominately white race (83%) as shown in Table 1. We identified at least one ARDS risk factor in 95% of patients. At ARDS onset, 211 patients (99%) were on assist control, volume-cycled ventilation. Patients had a mean PaO_2:F_IO_2 of 199 ± 68, a mean P_{plat} of 22.7 ± 5 mm Hg, and received a mean tidal volume of 8.0 ± 0.96 mL/kg PBW. At ARDS onset, only 16 patients (7.5%) received a tidal volume of ≤6.5 mL/kg PBW, while 24 patients (11.2%) received tidal volumes >9 mL/kg PBW (Fig. 2). At 24 h, LTVV use increased to 30 of 200 cases with tidal volumes reported (15.0%). At 48 h, LTVV use again increased to 45 of 214 patients (21.0%). Overall, only 58 patients (27.1%) ever received LTVV within 48 h after ARDS onset. Only 28 (13%) patients had a potential contraindication to LTVV use (pH <7.15, PaO_2 < 55, RR >40, acute brain injury). Among the remaining 186 patients without a potential contraindication, 38 (20%) received LTVV within 48 h of ARDS onset.

The ARDS Network lung protective ventilation strategy included a goal P_{plat} < 30 cm H_2O in addition to a low tidal volume. Of the 58 patients who received a tidal volume ≤ 6.5 mL/kg PBW in this study, 30% ($N = 18$) had P_{plat} above the goal of 30 cmH_2O. Per the lung protective protocol, additional decreases in tidal volume should be undertaken to reach a goal P_{plat} < 30 cm H_2O in ARDS patients. Only 6 (33%) of the 18 patients had the recommended decrease in tidal volume to meet the goal plateau pressure.

Patient demographic and clinical characteristics significantly differed by outcome at ARDS onset in unadjusted analyses are shown in Table 1. Patients who did receive LTVV were an average of seven years younger, were more than twice as likely to be admitted to a medical ICU, and were twice as likely to have severe ARDS with a PaO_2:F_IO_2

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