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Recognition and Appropriate Treatment of the Acute Respiratory Distress Syndrome Remains Unacceptably Low*

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Clinical trials published in 1998 and 2000 convincingly showed mechanical ventilation with low tidal volumes provides a clear mortality benefit to patients with the acute respiratory distress syndrome (ARDS) (1, 2). Soon after publication, however, evidence mounted that low tidal volume ventilation (LTVV), a form of lung protective ventilation, was difficult to implement in clinical practice (3, 4). In this issue of *Critical Care Medicine*, more than 15 years after these landmark studies were published and after redefinition of ARDS (5), Weiss (6) provide a contemporary report of LTVV compliance, demonstrating that the vast majority of patients with ARDS still do not receive lung protective tidal volumes while receiving mechanical ventilation.

The study examined the electronic health records (EHRs) of one academic and three community hospitals and identified 362 patients meeting the Berlin definition of ARDS. Among this cohort, the authors assessed LTVV compliance, which was defined as the receipt of a tidal volume less than 6.5 mL/kg of predicted body weight at any point during mechanical ventilation. Under this definition, the authors found that only 20% of patients with ARDS received LTVV at any point while receiving mechanical ventilation. Under a looser definition of 8 mL/kg predicted body weight, they found only 54% of ARDS patients received LTVV.

A few aspects of the study's approach should be recognized as one considers the surprisingly low compliance rate reported. The authors performed a retrospective review of EHR data to identify ARDS patients and assess LTVV compliance. They developed a protocol for identifying Berlin ARDS criteria, using the clinical notes of attending physicians to identify ARDS risk factors and radiographic reports to identify bilateral infiltrates on imaging.

*See also p. 1515.

Key Words: acute lung injury; adult respiratory distress syndrome; diagnosis; mechanical ventilation; quality improvement

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Although their approach was carefully designed, and based in part on a previously validated algorithm for identifying ARDS from radiology reports (7), it has not been validated outright. The author's point out that ARDS was documented in the clinical chart among patients they identified with ARDS just 12.4% of the time. Potentially, this could mean that the algorithm they used for identifying ARDS was highly inaccurate—an unlikely prospect given its careful design. More likely, it could mean physicians underrecognize ARDS when it is present.

Poor compliance with LTVV has prompted a number of studies to examine barriers preventing universal utilization, citing perceptions of patient contraindications to LTVV by providers, concerns with patient discomfort, and failure to recognize the patients for whom it is indicated (8, 9). Additional studies examined factors linked to higher compliance with therapy, including the use of a written protocol for LTVV delivery (10), and a closed ICU staffing model (11). Yet, despite this growing literature, the study by Weiss et al (6) suggests that very little progress with LTVV compliance has been made.

One approach to spur improvement would be to make LTVV compliance a performance measure tied to hospital reimbursement. There are several reasons why LTVV compliance might be a worthy performance measure for the Center for Medicare and Medicaid Services (CMS) to adopt. First, in contrast to some current CMS performance measures, it has a strong underlying evidence basis and a clear link to patient outcomes (12). Second, as suggested in the study by Weiss et al (6), current LTVV compliance is remarkably low, providing a high ceiling for improvement. Finally, evidence suggests that tidal volumes can be reduced by quality improvement initiatives that utilize audit and feedback (13).

A major barrier to developing an ARDS performance measure, however, is the need for a protocol that reliably identifies a cohort from which to assess LTVV compliance. Similarly, a major barrier to ARDS patient care is the high-frequency ARDS is missed or recognized late. The study by Weiss et al (6) is not the first to suggest that recognition of ARDS by bedside clinicians is poor. A study at the Mayo clinic in 2009 found that ARDS was documented in the clinical charts by bedside clinicians only 26.5% of the time it was present (7). Importantly, when ARDS was documented, patients received significantly lower tidal volumes. LTVV compliance cannot improve without new approaches to help physicians identify ARDS, and an ARDS performance measure cannot succeed without a rigorously identified ARDS cohort to evaluate performance.

The article by Weiss et al (6) shows that identification of ARDS using EHR data is feasible and, once validated, could serve as model to design a LTVV performance measure. Yet, this approach still requires a careful review of the medical record by trained reviewers, a costly and time-consuming endeavor. It also does not solve the problem of assisting bedside clinicians with ARDS recognition at the point of care. Automated algorithms that scan EHR systems for patients with ARDS features may be a potential solution. Such systems could perform natural language processing of clinical notes, scan laboratory values, and vital signs and may provide more reliable methods for ARDS identification. Although systems that can integrate all the data available in EHRs may still be years away, early efforts suggest that even simple systems that search blood gas values and the text of radiographic reports can be reasonably accurate ARDS screeners (7, 14).

Ultimately, "smart" EHR systems could help physicians identify patients as ARDS develops and identify these patients for performance measurement. Healthcare systems have made major investments in EHRs, which have been touted as a key tool for improving the quality of healthcare. However, some feel that these systems have yet to live up to this potential (15). New approaches are needed to address the problem of inadequate ARDS care, and ARDS recognition systems built into EHRs may provide a missing link toward improvement.

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Low Tidal Volume Ventilation Use in Acute Respiratory Distress Syndrome*

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***See also p. 1611.**

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Objective: Low tidal volume ventilation lowers mortality in the acute respiratory distress syndrome. Previous studies reported poor low tidal volume ventilation implementation. We sought to determine the rate, quality, and predictors of low tidal volume ventilation use.

Design: Retrospective cross-sectional study.

Setting: One academic and three community hospitals in the Chicago region.

Patients: A total of 362 adults meeting the Berlin Definition of acute respiratory distress syndrome consecutively admitted between June and December 2013.

Measurements and Main Results: Seventy patients (19.3%) were treated with low tidal volume ventilation (tidal volume < 6.5 mL/kg predicted body weight) at some time during mechanical ventilation. In total, 22.2% of patients requiring an F_{IO_2} greater than 40% and 37.3% of patients with F_{IO_2} greater than 40% and plateau pressure greater than 30 cm H_2O received low tidal volume ventilation. The entire cohort received low tidal volume ventilation 11.4% of the time patients had acute respiratory distress syndrome. Among patients who received low tidal volume ventilation, the mean (SD) percentage of acute respiratory distress syndrome time it was used was 59.1% (38.2%), and 34% waited more than 72 hours prior to low tidal volume ventilation initiation. Women were less likely to receive low tidal volume ventilation, whereas sepsis and F_{IO_2} greater than 40% were associated with increased odds of low tidal volume ventilation use. Four attending physicians (6.2%) initiated low tidal volume ventilation within 1 day of acute respiratory distress syndrome onset for greater than or equal to 50% of their patients, whereas 34 physicians (52.3%) never initiated low tidal volume ventilation within 1 day of acute respiratory distress syndrome onset. In total, 54.4% of patients received a tidal volume less than 8 mL/kg predicted body weight, and the mean tidal volume during the first 72 hours after acute respiratory distress syndrome onset was never less than 8 mL/kg predicted body weight.

Conclusions: More than 12 years after publication of the landmark low tidal volume ventilation study, use remains poor. Interventions that improve adoption of low tidal volume ventilation are needed. (*Crit Care Med* 2016; 44:1515–1522)

Key Words: acute respiratory distress syndrome; critical care; implementation science; knowledge translation; mechanical ventilation; quality improvement

Acute respiratory distress syndrome (ARDS), including the commonly used term acute lung injury, is a clinical syndrome of acute severe hypoxemia due to bilateral noncardiogenic pulmonary edema (1). ARDS is commonly diagnosed in critically ill patients and is associated with high mortality and morbidity (1–3). Low tidal volume ventilation (LTVV) is the most extensively investigated ARDS therapy that improves mortality in patients with ARDS (4–8). The target of LTVV is a tidal volume of 6 mL/kg predicted body weight (PBW) (some definitions include a target pressure during an end-inspiratory hold maneuver, or plateau pressure [P_{Plat}], ≤ 30 cm H_2O) (4, 9).

Despite strong clinical trial evidence of its effectiveness (4–6, 10) and its inclusion in at least one major clinical practice guideline (11), LTVV remains underused (5, 6, 12–18). Many studies reporting low LTVV use come from the same ARDS Network (ARDSNet) institutions that first studied the LTVV intervention (5, 6, 13, 14); less is known about LTVV adoption in other hospitals. In addition, prior studies have important limitations. Either they were conducted more than 8 years ago, used an outdated definition of ARDS, evaluated LTVV utilization only once or twice daily, or did not thoroughly examine predictors of LTVV use.

We conducted this study to analyze the current rate of LTVV use for ARDS in several non-ARDSNet academic and community medical centers using the Berlin Definition of ARDS, continuous ventilator data, and an expanded list of LTVV predictors (1). We hypothesized that implementation of LTVV would be low despite conducting this study more than one dozen years after the publication of the landmark ARDSNet study (4).

MATERIALS AND METHODS

Study Design

We performed a retrospective cross-sectional study of patients admitted to the ICUs at one academic (hospital A) and three community hospitals (hospitals B–D) in the Chicago, IL, region (**Table S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). None of these hospitals used a LTVV protocol or order set at the time of the study. The study was approved by the Institutional Review Boards of Northwestern University and the participating community hospitals.

We screened all patients greater than or equal to 18 years old consecutively admitted to a participating hospital's ICU between June 24, 2013, and December 31, 2013, who received mechanical ventilation via an endotracheal tube or tracheostomy. We included patients if they met the Berlin Definition of ARDS (1). We addressed some limitations in Berlin Definition specificity in the following ways: 1) we required qualifying Pao_2/Fio_2 ratios and infiltrates to occur within 48 hours of each other (ARDSNet trials generally required enrollment within 36–48 hr after ARDS onset) (14); 2) we developed criteria to identify bilateral infiltrates based on radiologists' reports, and ARDS risk factors and cardiac failure based on attending physician notes; and 3) we developed criteria for the objective assessment of cardiac failure based on echocardiographic findings and β-natriuretic peptide measurement (for cohort development, see **Supplemental Methods**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803).

We excluded patients receiving noninvasive ventilation because of concerns regarding the accuracy of tidal volume measurements. ARDS onset was defined as the later time of Pao_2/Fio_2 less than or equal to 300 mm Hg or bilateral infiltrates on chest imaging.

Measurements

Data were collected from the electronic health records at participating hospitals. We recorded continuous ventilator settings during mechanical ventilation. The primary outcome was the percentage of patients with ARDS with at least one LTVV ventilator setting between ARDS onset and the earliest of extubation, ICU discharge, or death. LTVV was defined as tidal volume (V_T) less than 6.5 mL/kg PBW, consistent with the cutoff chosen by ARDSNet when evaluating LTVV adherence (14). LTVV without consideration of P_{Plat} was chosen as the primary outcome because P_{Plat} was not recorded at hospitals C and D.

Secondary ventilator outcomes included: the percentage of time patients received LTVV from ARDS onset to the earliest of extubation, ICU discharge, or death; among patients treated with LTVV, the time from ARDS onset to initial LTVV; the percentage of patients who had P_{Plat} less than or equal to 30 cm H_2O at all times after LTVV initiation; and the percentage of time after LTVV initiation that patients had P_{Plat} less than or equal to 30 cm H_2O. We determined the percentage of patients who received V_T less than 8 mL/kg PBW, a more lenient definition of LTVV that includes the upper 95% CI for the low tidal volume arm of the ARDSNet study (19).

Clinical characteristics included patient demographic and clinical characteristics, ICU type (for hospital A), ARDS severity (per Berlin Definition) (1), ARDS risk factor, and the attending physician on each day a patient had ARDS. We constructed univariate and multivariate models to determine whether clinical, demographic, or severity of illness variables were associated with the delivery of LTVV (20–22).

Subgroup analyses were conducted for the primary and secondary outcomes for two subgroups of ARDS patients: 1) patients requiring Fio_2 greater than 40% at least once after ARDS onset and 2) patients with both Fio_2 greater than 40% and P_{Plat} greater than 30 cm H_2O at least once after ARDS onset. For these two subgroups, the relevant timeframe for analysis

was the time a patient received F_{IO_2} greater than 40% between ARDS onset and the earliest of extubation, ICU discharge, or death. Also, we conducted a sensitivity analysis to identify whether ARDS duration less than 12 hours or whether P:F ratio/infiltrates interval less than or equal to 24 hours affected the primary outcome.

Statistical Analysis

Data are presented as mean (SD), median (interquartile range [IQR]) for nonnormal data, or frequency (%). We used Fisher exact test to compare categorical variables and Student *t* test or Kruskal-Wallis test to compare continuous variables, as appropriate. The relationship between time to LTVV and ARDS severity was analyzed by Spearman rank correlation coefficient. Logistic regression results are expressed as odds ratios (ORs) with 95% CI.

We anticipated a priori that 42.3% of patients with ARDS would receive LTVV based on prior studies (13, 14, 23). Inclusion of 353 patients would be sufficient to determine this utilization rate ± 5% with 95% CI. All tests are two tailed, and a *p* value of less than 0.05 was considered significant. Analyses were performed with SAS (SAS Institute Inc, Cary, NC) (24).

RESULTS

A total of 1,628 adult intubated patients were screened for inclusion, and 362 met inclusion criteria (**Fig. 1**). Demographic and clinical characteristics are shown in **Table 1** and **Table S2** (Supplemental Digital Content 1, http://links.lww.com/CCM/B803); 20.7% of the cohort had severe ARDS. The most common ARDS risk factors were sepsis (49.5%) and pneumonia (48.9%); 84.2% of patients had at least one risk factor, and 16.8% had cardiac failure in addition to ARDS. Compared with hospital A (the academic urban hospital), patients from the three community hospitals were older, were more likely to be Hispanic (specifically hospital D), had a shorter time from intubation to ARDS onset, were less likely to have sepsis and shock, and were more likely to have pneumonia, aspiration, or F_{IO_2} greater than 40% at any time after ARDS onset.

Seventy patients (19.3%) were treated with LTVV at any point after ARDS onset (**Table 2**). LTVV use was 22.2% for patients who had at least one F_{IO_2} greater than 40% after ARDS onset, and 37.3% for those who had at least one F_{IO_2} greater than 40% and one P_{Plat} greater than 30 cm H_2O after ARDS onset. LTVV utilization did not differ significantly between the academic hospital and the three community hospitals. More patients with severe ARDS were treated with LTVV (26.7%) than moderate or mild ARDS (18.1% and 16.8%, respectively), although this difference was not statistically significant ($p = 0.21$) (Table 2). In none of the subgroups analyzed (e.g., sepsis, pneumonia, individual hospital) did more than half of patients receive LTVV (**Tables S3** and **S4**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). Results were similar when we included only patients whose P:F ratio/infiltrates interval was less than or equal to 24 hours (19.6% overall utilization, 22.6% in the $F_{IO_2} > 40\%$ subgroup), or when we excluded patients who had ARDS for less than 12 hours.

The entire 362 patient cohort received LTVV 11.4% of the time patients had ARDS, which increased to 20.7% for those who had at least one F_{IO_2} greater than 40% and one P_{Plat} greater than 30 cm H_2O after ARDS onset. Among the 70 patients who received LTVV, the mean (SD) percentage of time that they received LTVV was 59.1% (38.2%). This percentage was similar in the F_{IO_2} greater than 40% and F_{IO_2} greater than 40% plus P_{Plat} greater than 30 cm H_2O subgroups (**Table S5**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). The median proportion of time that patients received LTVV that was daytime (7:00 AM to 6:59 PM) was 0.50 [0.48–0.53].

The mean (SD) tidal volume (mL/PBW) in patients who received LTVV was not less than 6.5 mL/kg PBW but was lower than those who did not receive LTVV (6.62 mL/kg PBW [0.68 mL/kg PBW] vs 8.84 mL/kg PBW [1.50 mL/kg PBW]; $p < 0.001$). The distribution of tidal volumes for the first 3 days after ARDS onset is illustrated in **Figure S1** (Supplemental

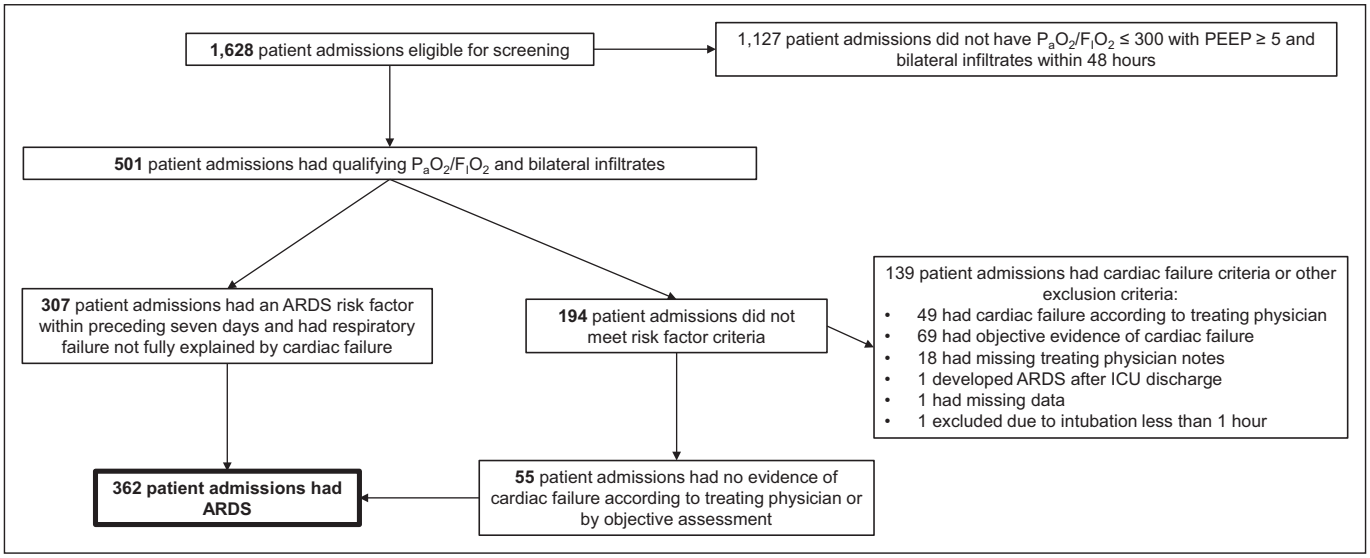

Figure 1. Flow diagram for patient inclusion. ARDS = acute respiratory distress syndrome, PEEP = positive end-expiratory pressure.

TABLE 1. Demographic and Clinical Characteristics of Acute Respiratory Distress Syndrome Cohort

Characteristic	Overall (*n* = 362)	Hospital A[a] (*n* = 282)	Hospitals B–D[a] (*n* = 80)
Age (yr), mean (SD)	60.8 (16.4)	59.1 (16.2)	66.7 (16.0)
Female, *n* (%)	154 (42.5)	112 (39.7)	42 (52.5)
Race, *n* (%)			
White	197 (54.4)	150 (53.2)	47 (58.8)
Black	93 (25.7)	80 (28.4)	13 (16.3)
Hispanic	37 (10.2)	23 (8.2)	14 (17.5)
Asian	12 (3.3)	10 (3.6)	2 (2.5)
Other, declined or unable to answer	23 (6.4)	19 (6.7)	4 (5.0)
Ethnicity, *n* (%)			
Hispanic	32 (9.8)	20 (7.1)	12 (26.1)[b]
Non-Hispanic	265 (80.8)	231 (81.9)	34 (73.9)[b]
Unable or declined to answer	31 (9.5)	31 (11.0)	0[b]
ARDS severity, *n* (%)			
Severe (Pao_2:FIO_2 ≤ 100)	75 (20.7)	55 (19.5)	20 (25.0)
Moderate (100 < Pao_2:FIO_2 ≤ 200)	144 (39.8)	116 (41.1)	28 (35.0)
Mild (200 < Pao_2:FIO_2 ≤ 300)	143 (39.5)	111 (39.4)	32 (40.0)
ARDS risk factor, *n* (%)[c]			
Sepsis	179 (49.5)	151 (53.6)	28 (35.0)
Pneumonia	177 (48.9)	126 (44.7)	51 (63.8)
Aspiration	58 (16.0)	37 (13.1)	21 (26.3)
Shock	134 (37.0)	119 (42.2)	15 (18.8)
Drug overdose	2 (0.6)	1 (0.4)	1 (1.3)
Trauma	5 (1.4)	4 (1.4)	1 (1.3)
Pancreatitis	6 (1.7)	6 (2.1)	0
Burn	0	0	0
Transfusion-related acute lung injury	1 (0.3)	1 (0.4)	0
Any one risk factor (*n* = 360)	303 (84.2)	230 (82.1)	73 (91.3)
Cardiac failure, *n* (%)[d]	60 (16.8)	42 (15.1)	18 (22.5)
Time from intubation to ARDS onset (d), median [interquartile range]	0.7 [0.3–1.5]	0.8 [0.5–1.7]	0.2 [0.05–1.0]
Patients with FIO_2 > 40% at any time during ARDS, *n* (%)	252 (69.6)	187 (66.3)	65 (81.3)
Patients with P_{Plat} > 30 cm H_2O at any time during ARDS, *n* (%) (*n* = 304)	74 (24.3)	69 (24.5)	5 (22.7)[e]
P_{Plat} (cm H_2O) from ARDS onset to the earlier of extubation, death, or ICU discharge, mean (SD)	21.1 (4.9)	21.1 (5.0)	21.0 (3.4)[e]

ARDS = acute respiratory distress syndrome, P_{Plat} = plateau pressure.
[a]Hospital A is an academic hospital, and hospitals B–D are community hospitals.
[b]Ethnicity was not reported separately at hospital C.
[c]Patients may have had more than one risk factor.
[d]Missing four patients.
[e]Plateau pressure not recorded at hospitals C and D.

TABLE 2. Low Tidal Volume Ventilation Use for Acute Respiratory Distress Syndrome Patients

Proportion of Patients Who Received Low Tidal Volume Ventilation	All Patients		$F_{IO_2} \geq 40\%$		F_{IO_2} and Plateau Pressure ≥ 30 cm H_2O[a]	
	n (%)[b]	*p*[c]	*n* (%)[d]	*p*[c]	*n* (%)[d]	*p*[c]
Overall	70 (19.3)		56 (22.2)		22 (37.3)	
Academic (hospital A)	59 (20.9)	0.20	47 (25.1)	0.08	22 (40.0)	0.29
Community (hospitals B–D)	11 (13.8)		9 (13.8)		0	
Acute respiratory distress syndrome severity[e]						
Severe	20 (26.7)	0.21	18 (25.7)	0.58	8 (40.0)	0.99
Moderate	26 (18.1)		24 (19.7)		10 (37.0)	
Mild	24 (16.8)		14 (23.3)		4 (33.3)	

[a]Plateau pressure not recorded at hospitals C and D.
[b]Between acute respiratory distress syndrome (ARDS) onset and the earlier of extubation, death, or ICU discharge.
[c]Fisher exact test.
[d]Between ARDS onset and the earlier of extubation, death, or ICU discharge and during which $F_{IO_2} > 40\%$.
[e]Severe: $Pa_{O_2}:F_{IO_2} \leq 100$, moderate: $100 < Pa_{O_2}:F_{IO_2} \leq 200$, mild: $200 < Pa_{O_2}:F_{IO_2} \leq 300$.

Digital Content 2, http://links.lww.com/CCM/B804; legend, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). The weighted mean (SD) tidal volumes (mL/kg PBW) were 8.44 mL/kg PBW (1.66 mL/kg PBW) zero to 24 hours after ARDS onset, 8.35 mL/kg PBW (1.61 mL/kg PBW) 24–48 hours after ARDS onset, and 8.36 mL/kg PBW (1.58 mL/kg PBW) 48–72 hours after ARDS onset.

Thirty-eight patients (54%) who received LTVV were already receiving LTVV at ARDS onset. In patients for whom LTVV was initiated after ARDS onset, the median time from ARDS onset to LTVV was 22.1 hours [IQR, 5.4–125.2 hr] (**Table S6**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). In the F_{IO_2} greater than 40% subgroup, a lower percentage of patients (43%) were receiving LTVV at ARDS onset; for those who were not, median time to LTVV was 26.1 hours [IQR, 9.5–155.1 hr] (Table S6, Supplemental Digital Content 1, http://links.lww.com/CCM/B803). In the F_{IO_2} greater than 40% subgroup (but not the overall cohort), patients with more severe ARDS had a shorter median time to LTVV initiation (severe ARDS: 7.0 hr [IQR, 3.2–11.8 hr], moderate ARDS: 41.3 hr [IQR, 20.4–166.0 hr], mild ARDS: 72.6 hr [IQR, 21.4–249.2 hr]; Spearman's $\rho = 0.41$; $p = 0.019$). Of 56 patients who received LTVV who had P_{Plat} recorded after ARDS onset, 14 (25%) had at least one P_{Plat} greater than 30 cm H_2O during LTVV administration; the mean percentage of time P_{Plat} greater than 30 cm H_2O was 44.4% (SD 29.9%).

In multivariable regression modeling (**Table 3**), women were less likely to receive LTVV (adjusted OR, 0.31; 95% CI, 0.17–0.56; $p < 0.001$). Sepsis and F_{IO_2} greater than 40% were both associated with increased odds of LTVV (adjusted OR, 1.85; 95% CI, 1.07–3.20; $p = 0.028$; and adjusted OR, 2.21; 95% CI, 1.15–4.24; $p = 0.017$, respectively). Mean (SD) height was lower for women than men (63.4 ± 3.2 vs 69.2 ± 3.7 inches; $p < 0.001$).

Sixty-five attending physicians cared for a median of 5 [IQR, 2–10] patients within 1 day of ARDS onset and who were eligible but not already receiving LTVV. Four physicians (6.2%) initiated LTVV within 1 day of ARDS onset for 50% or more of their eligible patients, whereas 34 physicians (52.3%) never initiated LTVV within 1 day of ARDS onset (including

TABLE 3. Predictors of Low Tidal Volume Ventilation[a]

Variable	Crude OR (95% CI)	Univariate *p*[b]	Adjusted OR (95% CI)	Multivariate *p*[b]
Female gender	0.33 (0.18–0.61)	< 0.001	0.31 (0.17–0.56)	< 0.001
$F_{IO_2} > 40\%$ during acute respiratory distress syndrome	1.96 (1.04–3.70)	0.038	2.21 (1.15–4.24)	0.017
Sepsis	1.70 (1.00–2.88)	0.051	1.85 (1.07–3.20)	0.028

OR = odds ratio.
[a]The following variables were not predictors of low tidal volume ventilation (LTVV): age, race, ethnicity, hospital, acute respiratory distress syndrome (ARDS) severity, mean F_{IO_2}, time from intubation to ARDS onset, plateau pressure (P_{Plat}) during ARDS, Acute Physiology Score on day of ARDS onset, Acute Physiology and Chronic Health Evaluation IV (20, 21) predicted mortality, Sequential Organ Failure Assessment (22) score on the day of ARDS onset, ARDS risk factors (other than sepsis), pH < 7.30, and pH < 7.15. The highest P_{Plat} on the day of ARDS onset was associated with LTVV at hospitals A and B (adjusted odds ratio [95% CI], 1.10 [1.03–1.17]; $p = 0.002$).
[b]Wald chi-square test.

15 physicians who cared for five or more eligible patients) (**Table S7**, Supplemental Digital Content 1, http://links.lww.com/CCM/B803).

One hundred ninety-seven patients (54.4%) received V_T less than 8 mL/kg PBW at least once after ARDS onset, of whom 156 (79.2%) were already receiving V_T less than 8 mL/kg PBW at ARDS onset. The percentage was no different in the F_{IO_2} greater than 40% subgroup (54.8%).

The mean (SD) percentage of time that the entire 362 patient cohort received V_T less than 8 mL/kg PBW was 44.6% (46.7%), which was similar for the F_{IO_2} greater than 40% subgroup (46.7% [47.2%]). Among the 197 patients who received V_T less than 8 mL/kg PBW, the mean percentage of time that they received it was 81.9% (SD 30.8%). This percentage was similar in the F_{IO_2} greater than 40% subgroup (85.3% [27.8]).

DISCUSSION

Although LTVV improves outcomes in patients with ARDS and has been recommended in practice guidelines, we found that adoption of LTVV remains poor: LTVV was administered to less than 20% of 362 ARDS patients admitted to four hospitals. Even for the most severe cases of ARDS, LTVV was administered to no more than 40% of patients at some time while on mechanical ventilation. For those who did receive LTVV, LTVV was used less than 60% of the time patients were eligible and was often started after significant delay. Although a majority were initiated on LTVV within 24 hours of ARDS onset, 34% waited more than 72 hours. Furthermore, many of the patients who received LTVV had plateau pressures above 30 cm H_2O.

Women had lower odds of receiving LTVV, consistent with previous studies (5, 6). A possible explanation is that if patients are treated with a default tidal volume that is not gender-based (e.g., 450 or 500 mL), women who are on average shorter than men (also demonstrated in our cohort) would have required a greater tidal volume change from this default range than men.

LTVV utilization rates in our study are similar to those reported in studies from the time of the original ARDSNet study more than a dozen years prior (**Fig. 2**). Although the criteria used to define LTVV differ among these studies, the low rate of LTVV use is remarkably consistent. The exception is Needham et al (5, 6) who demonstrated LTVV use between 63% and 70%. These studies are the exception to the overall trend of LTVV utilization and may be due to unique characteristics of the providers and institutions where they were conducted.

Several characteristics of our study are unique compared with previous studies. First, patients in our study were admitted in 2013, 8 years after the most recent comparably large studies (5, 6). Second, we employed the Berlin Definition of ARDS, which addresses several limitations of the American-European Consensus Conference on ARDS definition used

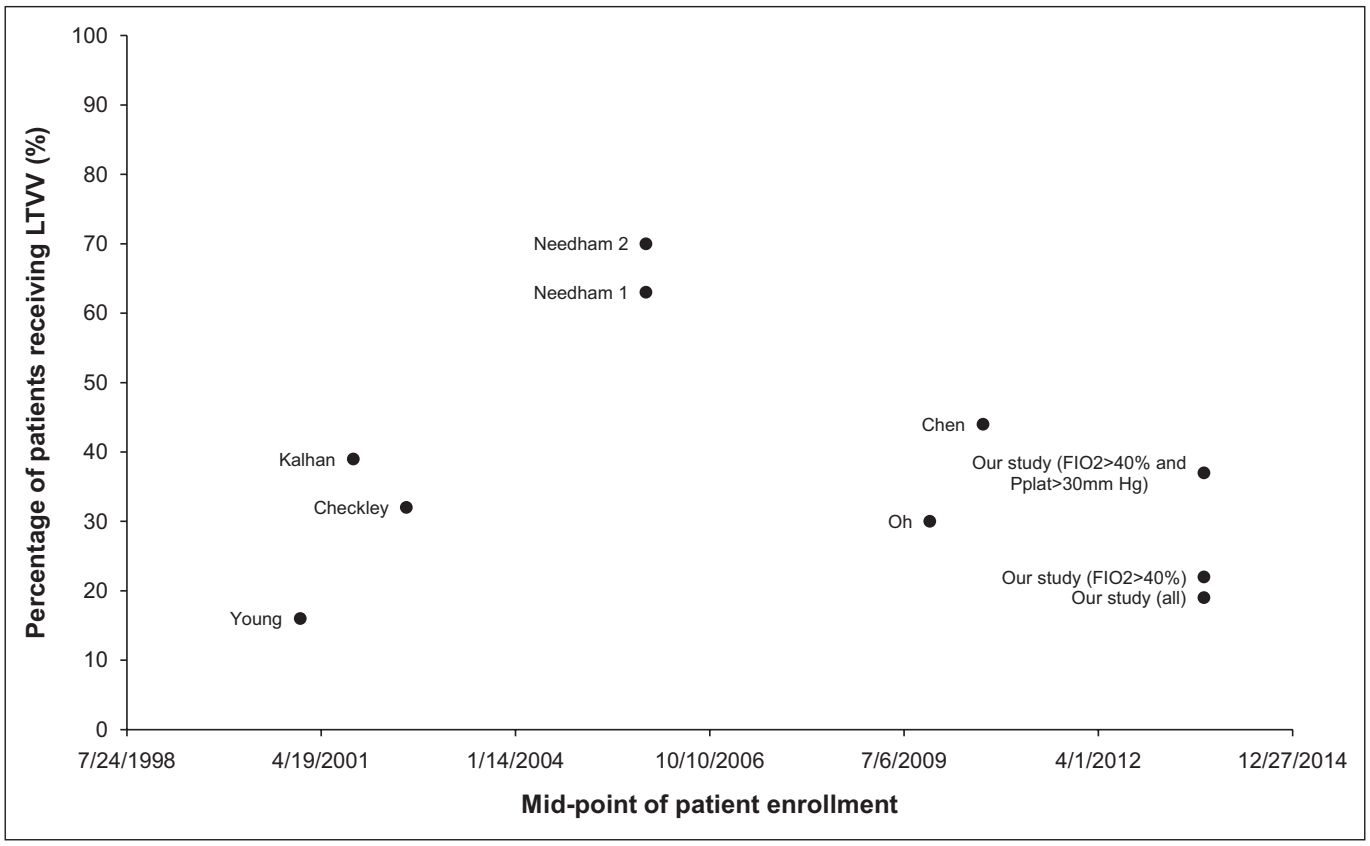

Figure 2. Low tidal volume ventilation (LTVV) utilization since Acute Respiratory Distress Syndrome Network (ARDSNet) study. Studies are listed according to last name of first author and placed along the *x*-axis according to the midpoint between the first and last patient enrollment (from published articles and publicly available information). Each study had slightly different LTVV criteria. Needham 1 and Needham 2 were separate analyses and published articles from the same cohort (5, 6, 12–14, 16, 17). P_{Plat} = plateau pressure.

in previous studies, and has better predictive validity (1, 25). Third, our study was conducted in non-ARDSNet settings. Fourth, we analyzed physician-specific utilization and found LTVV use to be consistently poor. Finally, by obtaining continuous ventilator settings instead of once- or twice-daily settings, we were able to examine the degree to which actual LTVV use corresponded to recommended variables.

The reasons why LTVV remains poorly implemented are unclear. LTVV is part of one of few convincingly proven therapies in critical care medicine shown to reduce mortality in randomized controlled trials and subsequent observational studies. It is part of at least one clinical practice guideline (11). Some perceived barriers to implementation of LTVV include poor physician recognition of ARDS, unwillingness of physicians to use a protocol, and perceptions of contraindications to LTVV (26). In our study, the consistently poor use of LTVV among physicians may be due to difficulty with ARDS recognition (only 12.4% of the cohort were identified by attending physicians as having ARDS) or other system barriers that may be impeding implementation. Negative attitudes are also possible: a clinician survey in this study is ongoing to explore these issues. If barriers can be identified, interventions should be designed to provide real-time diagnostic information to improve the recognition of ARDS (27, 28) and the sustained delivery of LTVV, and to address perceptions of providers reluctant to adopt LTVV. On a policy level, operationalizing LTVV use in ARDS as a performance measure could greatly assist in its implementation.

This study has several potential limitations. First, as stated in the *Methods* section, the Berlin Definition criteria lack some clarity, especially regarding the identification of and temporal relationship among ARDS diagnostic criteria and the objective criteria for assessing cardiac failure. These raise the possibility of misclassification bias, leading to the concern that our ARDS cohort is not truly representative of the ARDS phenotype. We addressed these limitations by adapting the ARDSNet trials' enrollment criteria and previous literature (14, 28), and through expert opinion. Also, the validity of our diagnostic process should have been increased through the use of highly conservative inclusion criteria (especially concerning the objective assessment of cardiac failure). Second, our algorithm for identifying qualifying radiographic infiltrates, ARDS risk factors, and cardiac failure has not been validated. Third, we relied on attending physician identification of ARDS risk factors. Although misclassification could have occurred because these are subjective data, we believe it was important to reflect whether practicing physicians were themselves identifying ARDS risk factors, and therefore identifying their patients who would be eligible for LTVV. Fourth, our results from only four sites in a single metropolitan area may not be generalizable to the United States at large or other countries' experience with LTVV implementation. However, our study was conducted in a large academic medical center and three community hospitals in geographically and socioeconomically diverse communities, and in ICUs with varying high- and low-intensity critical care structures; these factors potentially enhance the generalizability of our results.

Fifth, some controversy exists as to what constitutes lung-protective ventilation, specifically whether achieving a plateau pressure less than or equal to 30 cm H_2O is at least as important as achieving a low tidal volume (11, 18, 29, 30), although other evidence suggests that low tidal volumes improve outcomes regardless of whether P_{plat} is above or below this threshold (9). In any case, the ARDSNet ventilator protocol clearly requires the initial stepwise reduction of tidal volume to a goal of 6 mL/kg PBW (4); only after this target tidal volume is achieved can tidal volume potentially be increased based on P_{plat} or patient dyspnea. Even using a generous definition of LTVV as any one tidal volume less than 6.5 mL/kg PBW, LTVV was still used in a minority of patients in our cohort with at least one P_{plat} greater than 30 cm H_2O.

Finally, it is possible that V_T less than 8 mL/kg PBW may be more realistic for provider adherence, and sufficiently less than the 12 mL/kg PBW in the ARDS Network lower tidal volume trial control group to be considered lung protective (4). Our finding that 54% of patients received V_T less than 8 mL/kg PBW at least once could suggest some clinician movement in the direction of lower tidal volumes for ARDS, or it could represent the evolution of the standard for tidal volumes for intubated patients. However, the mean tidal volume during the first 72 hours after ARDS onset was never less than 8 mL/kg PBW. The sensitivity analyses we conducted address concerns with plateau pressure and the tidal volume threshold, demonstrating poor LTVV use even when plateau pressure was above 30 cm H_2O and under the most lenient definition of low tidal volume.

CONCLUSIONS

We demonstrate that LTVV, a well-supported therapy that reduces mortality in patients with ARDS, remains poorly implemented. Researchers, individual providers, hospitals, and policymakers should work to design and evaluate interventions and develop systems and standards that address both the complexity and importance of LTVV.

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