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Mechanical Ventilation and ARDS in the ED

A Multicenter, Observational, Prospective, Cross-sectional Study

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BACKGROUND: There are few data regarding mechanical ventilation and ARDS in the ED. This could be a vital arena for prevention and treatment.

METHODS: This study was a multicenter, observational, prospective, cohort study aimed at analyzing ventilation practices in the ED. The primary outcome was the incidence of ARDS after admission. Multivariable logistic regression was used to determine the predictors of ARDS.

RESULTS: We analyzed 219 patients receiving mechanical ventilation to assess ED ventilation practices. Median tidal volume was 7.6 mL/kg predicted body weight (PBW) (interquartile range, 6.9-8.9), with a range of 4.3 to 12.2 mL/kg PBW. Lung-protective ventilation was used in 122 patients (55.7%). The incidence of ARDS after admission from the ED was 14.7%, with a mean onset of 2.3 days. Progression to ARDS was associated with higher illness severity and intubation in the prehospital environment or transferring facility. Of the 15 patients with ARDS in the ED (6.8%), lung-protective ventilation was used in seven (46.7%). Patients who progressed to ARDS experienced greater duration in organ failure and ICU length of stay and higher mortality.

CONCLUSIONS: Lung-protective ventilation is infrequent in patients receiving mechanical ventilation in the ED, regardless of ARDS status. Progression to ARDS is common after admission, occurs early, and worsens outcome. Patient- and treatment-related factors present in the ED are associated with ARDS. Given the limited treatment options for ARDS, and the early onset after admission from the ED, measures to prevent onset and to mitigate severity should be instituted in the ED.

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ABBREVIATIONS: APACHE = Acute Physiology and Chronic Health Evaluation; IQR = interquartile range; LIPS = Lung Injury Prediction Score; LOS = length of stay; PBW = predicted body weight; PI = principal investigator; SOFA = Sequential Organ Failure Assessment; VALI = ventilator-associated lung injury

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The frequency of critically ill patients in the ED and the severity of illness have increased.[1] The need for mechanical ventilation is one of the most common indications for ICU admission and has also increased in incidence.[2,3] Initiation of mechanical ventilation in the ED is common, and because of the long ED length of stays (LOSs) for critically ill patients, mechanical ventilation hours provided have also increased.[4-13] Despite these trends, there remain relatively few data on ED-based mechanical ventilation practices.[14]

ARDS exacts a significant toll on patients who are mechanically ventilated in terms of mortality, long-term survivor morbidity, and health-care use.[15,16] Compared with those in the ICU, ARDS data in the ED population are sparse. The ED prevalence of ARDS and knowledge of the early factors that may promote its development and modify its severity are incomplete. Observational studies indicate an ARDS prevalence of approximately 9% in patients receiving mechanical ventilation in the ED.[14,17,18] Most of these data, however, are restricted to a narrow cohort of patients (ie, those with sepsis) and are single-center investigations.

In patients with ARDS, unequivocal data exist that harmful ventilator settings cause ventilator-associated lung injury (VALI) and worsen outcome.[19-21] In patients without ARDS but at risk of the syndrome, there are mounting data to suggest that the mechanical ventilator contributes to ARDS development.[22-31] Most relevant to the ED, the pathophysiology triggered by VALI can occur within hours, and progression to ARDS in at-risk patients typically occurs shortly after admission.[29,32-35] We hypothesize that modifiable patient characteristics and treatment variables can influence clinical outcome during this most proximal time window. In the future, the ED could, therefore, be a vital arena for the treatment and clinical investigation of patients who are mechanically ventilated to (1) further refine predictive variables of outcome, (2) improve the quality of mechanical ventilation delivered during the early stages of respiratory failure, (3) decrease the incidence of ARDS, and (4) decrease mortality and long-term survivor morbidity.

The objectives of this study were to (1) further characterize ED mechanical ventilation practices, (2) determine the incidence of ARDS after admission and the risk factors associated with this outcome, (3) determine the prevalence of ARDS in the ED and assess ED compliance with lung-protective ventilation, and (4) assess outcome differences between patients with ARDS and those without ARDS.

Materials and Methods

This was a multicenter, prospective, observational, cross-sectional study conducted at four academic EDs. For each center, data were collected during four temporally distinct 1-month time periods (July 10, 2012, to August 10, 2012; September 1, 2012, to October 2, 2012; January 21, 2013, to February 22, 2013; and July 2, 2013, to August 3, 2013). The study, therefore, spanned a total of 13 months. This observational study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies.[36] The institutional review boards at each site approved the study under waiver of informed consent (e-Appendix 1).

Eligible patients were all patients receiving mechanical ventilation in the ED and aged ≥ 18 years. Exclusion criteria were as follows: (1) death in the ED, (2) ED LOS < 1 h, (3) total mechanical ventilation duration < 1 h, and (4) elective extubation while in the ED. To ensure uniform data collection and accuracy, all variables were defined a priori and were recorded in a standardized format during the data collection process.

The baseline patient characteristics included age, sex, race, weight, height, predicted body weight (PBW), BMI, ED LOS, patient comorbidities, home medications, vital signs, hemodynamics, and laboratory values. Modified APACHE (Acute Physiology and Chronic Health Evaluation) II and Sequential Organ Failure Assessment (SOFA) scores and the Lung Injury Prediction Score (LIPS) were determined.[37-41] PBW in kilograms was calculated according to the following formula: men, 50 + 2.3 (height [inches] – 60); women, 45.5 + 2.3 (height [inches] – 60).[42] Process of care variables in the ED (IV fluid, blood products, etc) were collected, as were all ventilator-related variables. All these data were collected prospectively by research assistants and principal investigators (PIs) at each site.

Definitions

Definitions of comorbid conditions are provided in e-Appendix 2. Severe sepsis and septic shock were defined as described previously.[43,44] Lung-protective ventilation was defined as the use of tidal volume of < 8 mL/kg PBW, because this was the upper limit of tidal volume allowed by previous investigations of low tidal volume ventilation in ARDS.[19] We did not include a pressure limit to define lung protective, because previous data suggest monitoring of inspiratory plateau pressure is rare in intubated patients in the ED.[14]

Outcomes

All patients were analyzed for ED mechanical ventilation practices. The primary outcome variable of interest was the development of ARDS after admission, and it was defined according to the Berlin definition.[45] It was assessed by site PIs at least once daily (based on frequency of chest radiographs and arterial blood gas measurements). Given the focus of this investigation on ED-based factors associated with ARDS development, and data suggesting that the majority of ARDS cases develop in the first 5 days after admission, assessment of the primary outcome was

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restricted to day 5 after ICU admission (or death if occurring prior to day 5).[40] In patients without an arterial blood gas measurement, the oxygenation criteria was determined using the pulse oximeter to F_{IO_2} ratio as described previously.[46] When more than one value was present, the worst value was selected.

A detailed description of our standard operating procedure for adjudicating ARDS status is provided in e-Appendix 3. Secondary analyses of interest included clinical outcome differences between patients with ARDS and those without ARDS. These outcomes were assessed daily by research assistants and site PIs until hospital discharge.

Analysis

Descriptive statistics, including mean ± SD, median (interquartile range [IQR]), and frequency distributions were used to assess the characteristics of the patient cohort. The Spearman correlation coefficient (r) was used to assess the relationship between ED and ICU tidal volume. To assess predictors of progression to ARDS, continuous and categorical variables were compared using an unpaired t test, Wilcoxon test, χ^2 test, or Fisher exact test, as appropriate. Variables that were statistically significant in univariate analyses at a $P \leq .10$ level were candidates for inclusion in a bidirectional, stepwise, multivariable logistic regression analysis. The stepwise regression method selected variables for inclusion or exclusion from the model in a sequential fashion based on the significance level of .10 for entry and .15 for removal. Statistical interactions and collinearity were assessed. The model used variables that contributed information that was statistically independent of the other variables in the model. The model's goodness of fit was assessed with the Hosmer-Lemeshow test. Adjusted ORs and corresponding 95% CIs are reported for variables in the multivariable model, adjusted for all variables in the model. To assess clinical outcomes based on ARDS status, χ^2 and Kruskal-Wallis tests were used to compare groups. The Kaplan-Meier method was used to compare mortality difference. All tests were two-tailed, and a P value $< .05$ was considered statistically significant. A sample size calculation was not performed a priori, because the primary analysis was descriptive and was to further characterize mechanical ventilation in the ED. Based on previous existing data, our sample size was recognized as likely to be adequate for investigation of ED-based parameters associated with progression to ARDS.[14,47] The analysis was conducted in consultation with a biostatistician.

Results

Characteristics of Study Subjects

A total of 259 patients received mechanical ventilation in the ED during the study period (Fig 1); the final study population totaled 219 patients. All patients were assessed for mechanical ventilation practices and clinical outcomes. Fifteen patients (6.8%) had ARDS while in the ED and were excluded from the analysis of risk factors for ARDS progression after ED admission. Table 1 shows the baseline characteristics of the study population. For the entire cohort, the median ED LOS was 3.4 h (IQR, 2.2-5.4 h), with a range of 1.1 to 18.3 h.

Ventilator Characteristics

Ventilator variables are presented in Table 2. The preferred mode of ventilation across centers was assist-control, volume-control ventilation (65.3%). The median tidal volume delivered was 7.6 mL/kg PBW (IQR, 6.9-8.9 mL/kg PBW), with a range of 4.3-12.2 mL/kg PBW. Figure 2 shows the distribution of tidal volume in the ED. Lung-protective ventilation was used in 122 patients (55.7%),

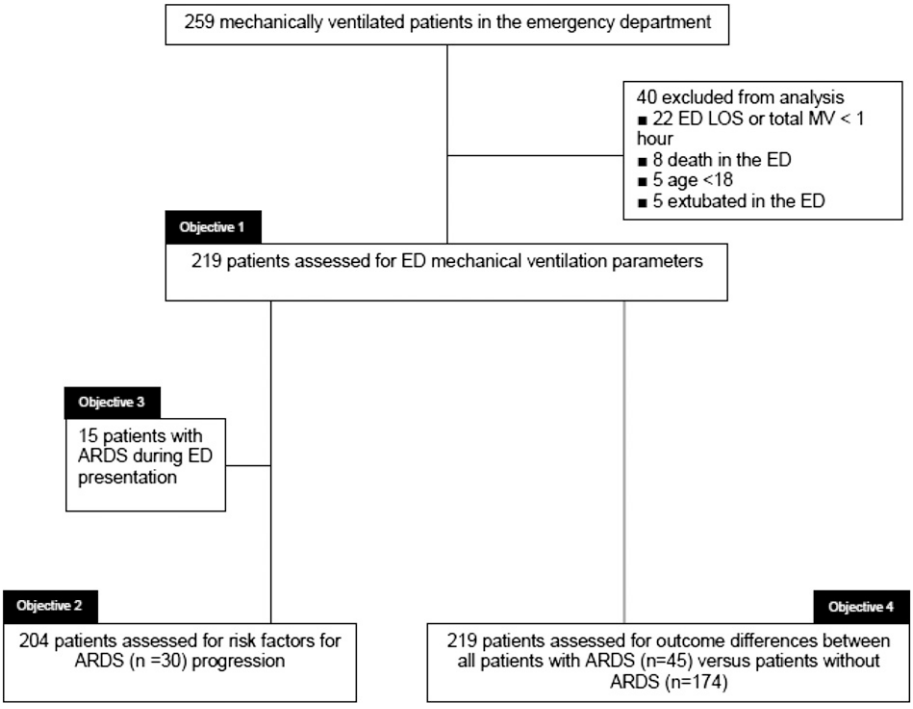

Figure 1 – *Flow diagram depicting the patients analyzed to achieve each objective of the study. LOS = length of stay; MV = mechanical ventilation.*

TABLE 1] Characteristics of Patients Receiving Mechanical Ventilation in the ED

Characteristics and Variables	Patients in the ED (N = 219)
Baseline characteristics	
Age, y	55.6 ± 19.9
Male sex	128 (58.4)
Race	
White	152 (69.4)
Black	59 (26.9)
Other	8 (3.7)
Comorbidities	
Diabetes	47 (21.5)
Cirrhosis	13 (5.9)
CHF	20 (9.1)
CKD	17 (7.8)
Dialysis	10 (4.6)
Malignancy	26 (11.9)
COPD	42 (19.2)
Immunosuppression	19 (8.7)
Alcohol abuse	11 (5.0)
AIDS	6 (2.7)
Home medications	
Corticosteroids	13 (5.9)
Aspirin	55 (25.1)
Statin	55 (25.1)
H2 blocker/PPI	46 (21.0)
Height, inches	67.0 ± 4.3
Weight, kg	79.3 ± 23.1
PBW, kg	64.2 ± 11.5
BMI	27.4 ± 7.4
Temperature, °C	36.3 ± 1.2
HR	98.6 ± 29.1
RR	20.2 ± 6.9
SBP	130.8 ± 38.8
DBP	75.1 ± 23.9
Spo_2	99.0 (96.0-100)
Pao_2 to Fio_2 ratio (n = 168)	236.5 (130.0-368.0)
Lactate (n = 168)	2.6 (1.6-4.8)
Creatinine	1.0 (0.76-1.5)
Hemoglobin	12.6 ± 3.4
WBC	14.6 ± 8.0
Platelet	232.0 ± 94.9
INR	1.4 ± 1.3
Total bilirubin	0.78 ± 1.2
pH (n = 205)	7.3 ± 0.16
Albumin (n = 151)	3.5 ± 0.82
APACHE II[a]	15.7 ± 7.6
SOFA score[a]	3.0 (2.0-5.0)
LIPS	5.4 ± 2.9
Location of intubation	
ED	146 (66.7)
Prehospital	45 (20.6)
Transferring facility	28 (12.8)
Cause for initiation of mechanical ventilation	
Medical	167 (76.3)
Trauma	52 (23.7)
Sepsis	42 (19.2)
Admit location	
Medical ICU	88 (40.2)
Surgical/trauma ICU	80 (36.5)
Neurologic ICU	27 (12.3)
Cardiac ICU	16 (7.3)
Other	8 (3.7)
ED LOS, h	3.4 (2.2-5.4)
Process of care variables	
Antibiotics	77 (35.2)
Appropriate antibiotic[b]	58 (75.3)
Time to antibiotic administration, min	96.0 (53.0-155.0)
IV fluids in ED, L	1.0 (0-2.0)
Vasopressor infusion	37 (16.9)
Dose, μg/min	20 (10-30)
Blood product administration	31 (14.2)

Variables are reported as No. (%), mean ± SD, or median (interquartile range). APACHE = Acute Physiology and Chronic Health Evaluation; CHF = congestive heart failure; CKD = chronic kidney disease; DBP = diastolic BP; H2 = histamine-2 receptor; HR = heart rate; INR = international normalized ratio; LIPS = Lung Injury Prediction Score; LOS = length of stay; PBW = predicted body weight; PPI = proton pump inhibitor; RR = respiratory rate; SBP = systolic BP; SOFA = Sequential Organ Failure Assessment; Spo_2 = pulse oximetry.
[a]Modified score, which excludes Glasgow Coma Scale.
[b]Refers to the 77 patients who received antibiotics while in the ED.

and 25 patients (11.4%) were ventilated with a tidal volume > 10 mL/kg PBW. Of the 97 patients ventilated with non-lung-protective ventilation in the ED, 31 (32%) had their settings changed to protective settings upon ICU arrival. ED tidal volume was significantly correlated to ICU tidal volume ($rs = 0.60$, $P < .001$). In the subgroup of patients exposed to non-lung-protective ventilator while in the ED, ED tidal volume

TABLE 2] Ventilator Variables and Care in the ED

Ventilator Settings	Entire Cohort (N = 219)	No ARDS in ED (n = 204)	ARDS in ED (n = 15)	Developed ARDS After Admission (n = 30)
Ventilator mode				
VC-AC	143 (65.3)	133 (65.2)	10 (66.7)	21 (70.0)
VC-SIMV	36 (16.4)	34 (16.7)	2 (13.3)	8 (26.7)
PC-AC	28 (12.8)	25 (12.3)	3 (20.0)	1 (3.3)
Other	12 (5.5)	12 (5.9)	0 (0.0)	0 (0)
Tidal volume, mL	500 (450-520)	500 (450-520)	500 (475-500)	500 (500-550)
Tidal volume, mL/kg PBW	7.6 (6.9-8.9)	7.6 (6.9-8.9)	8.2 (7.2-9.0)	7.5 (6.7-9.1)
Lung protective ventilation	122 (55.7)	115 (56.4)	7 (46.7)	20 (66.7)
PEEP	5.3 ± 1.3	5.2 ± 1.1	6.1 ± 2.9	5.5 ± 1.5
F_{IO_2}	88.0 ± 21.2	87.8 ± 21.3	90.0 ± 20.7	92.0 ± 18.8
Peak pressure, cm H_2O (n = 208)	24.0 (20.0-32.0)	24.0 (20.0-32.0)	28.0 (25.0-37.0)	29.0 (21.5-35.5)
Plateau pressure, cm H_2O (n = 78)	18.0 (16.0-23.0)	18.0 (16.0-22.0)	21.5 (20.0-24.5)	18.5 (17.3-20.8)
Ventilator parameters changed in ED	150 (68.5)	139 (68.1)	11 (73.3)	21 (70.0)
Head of bed elevated in ED	79 (36.1)	74 (36.2)	5 (33.3)	15 (50.0)
Exposure to F_{IO_2} 100%, min	27.5 (0-106.5)	43.5 (0-117.0)	99.0 (60.0-198.0)	36.0 (0-140.0)
First ICU setting same as last ED setting	91 (41.6)	86 (42.2)	5 (33.3)	12 (40.0)
Exposure to same tidal volume for 24 h	61 (27.9)	58 (28.4)	3 (20.0)	12 (40.0)

Variables are reported as No. (%), mean ± SD, or median (interquartile range). There was no significant difference in any variable when comparing patients with ARDS in the ED and those without ARDS in the ED. AC = assist control; PC = pressure control; PEEP = positive end-expiratory pressure; SIMV = synchronized intermittent mandatory ventilation; VC = volume controlled. See Table 1 for expansion of other abbreviation.

remained significantly correlated to ICU tidal volume ($rs = 0.46$, $P < .001$). Inspiratory plateau pressure was recorded in 78 patients (35.6%). At least one ventilator parameter was changed in 150 patients (68.5%) during their ED stay. The head of bed was elevated in 79 patients (36.1%) while receiving mechanical ventilation in the ED.

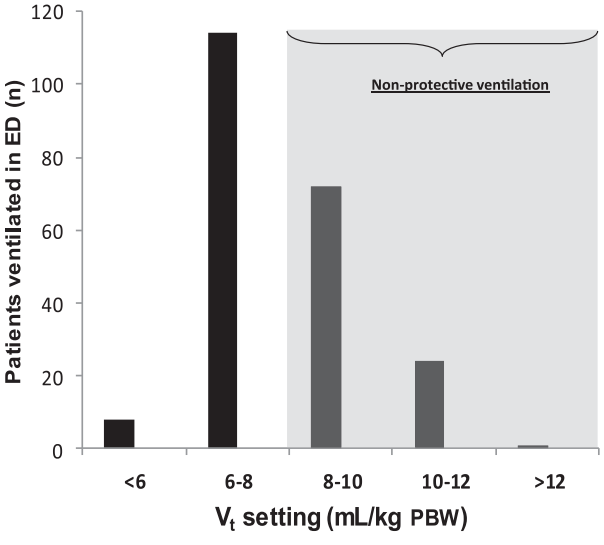

Figure 2 – *Delivered V_t in the ED. Of the 219 patients mechanically ventilated in the ED, 122 (55.7%) received lung-protective ventilation (< 8 mL/kg PBW) and 25 (11.4%) were ventilated with a tidal volume > 10 mL/kg PBW. PBW = predicted body weight; V_t = tidal volume.*

Analysis of ARDS

The incidence of ARDS after admission from the ED was 14.7% (n = 30), with a mean ± SD onset of 2.3 ± 1.2 days (Fig 3). There were no differences in the ED ventilator variables in these patients (Table 2). Multivariable logistic regression analysis demonstrated that higher ED APACHE II scores and LIPS were associated with progression to ARDS, as was a higher SOFA score (persistent organ failure) on ICU day 2. Intubation occurring prehospital or from a transferring facility was associated with an increased risk of ARDS compared with ED intubation (Table 3).

Fifteen patients (6.8%) had ARDS during their stay in the ED. Median tidal volume was 8.2 mL/kg PBW (IQR, 7.2-9.0 mL/kg PBW), compared with 7.6 mL/kg PBW (IQR, 6.9-8.9 mL/kg PBW) in patients without ARDS ($P = .37$). Lung-protective ventilation was used in seven patients with ARDS (46.7%). Inspiratory plateau

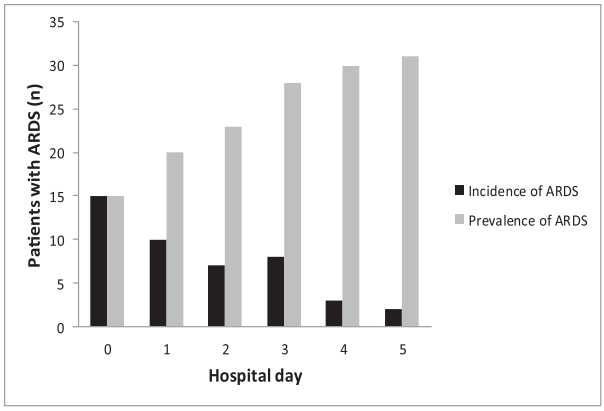

Figure 3 – *Hospital d 0 refers to the ED. Incidence of ARDS represents the development of new cases of ARDS on an individual hospital day (eg, seven new cases of ARDS development on hospital d 2). Prevalence of ARDS represents the total number of ARDS cases present on an individual hospital d, excluding those cases experiencing death.*

pressure was monitored in six patients with ARDS in the ED (40%). Exposure to F_{IO_2} of 1.0 in patients with ARDS in the ED was 99.0 min (IQR, 60-198 min) compared with 43.5 min (IQR, 0-117.0 min) in patients without ARDS in the ED. Compared with patients without ARDS, patients who progressed to ARDS experienced a greater duration of organ failure and ICU LOS, and higher mortality (Fig 4, Table 4).

Discussion

Our first objective was to characterize further the use of mechanical ventilation in the ED across a heterogeneous patient population in multiple centers. To summarize, based on our analysis, mechanical ventilation in the ED is delivered using (1) higher than recommended tidal volumes and infrequent lung-protective ventilation regardless of ARDS status, (2) high F_{IO_2} and low positive end-expiratory pressure, (3) infrequent monitoring of inspiratory plateau pressure, and (4) the supine, flat position.

Previous work in patients with severe sepsis and septic shock (database from 2005 to 2010) showed a median tidal volume of 8.8 mL/kg PBW (IQR, 7.8-10.0 mL/kg PBW),

TABLE 3] Multivariate Analysis for Factors Associated With Development of ARDS

Variable	aOR	95% CI	*P* Value
ED APACHE II	1.08	1.0-1.17	.05
SOFA score on ICU d 2	1.29	1.07-1.57	.009
ED LIPS	2.8	1.01-7.75	.04
Location of intubation[a]	0.23	0.07-0.73	.01

aOR = adjusted OR. See Table 1 for expansion of other abbreviations.
[a]Refers to intubation in the ED vs prehospital/transferring facility.

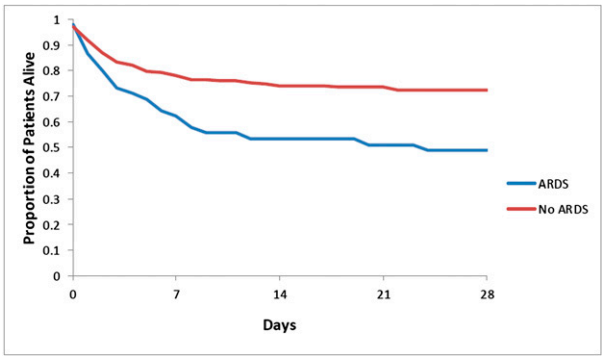

Figure 4 – *Probability of survival to hospital discharge in patients mechanically ventilated in the ED.*

ranging as high as 14.6 mL/kg PBW.[14] The current investigation shows a decrease of about 1 mL/kg PBW and overall less variability in practice. However, a significant percentage of patients remain exposed to high tidal volumes while in the ED. Based on three systematic reviews and meta-analyses, non-lung-protective ventilation seems to be associated with VALI and the development of ARDS.[29,31,48]

Our results highlight the infrequency with which positive end-expiratory pressure is titrated in the ED, in favor of delivery of high levels of oxygen. Increasing evidence suggests excessive oxygen exposure has adverse effects in various conditions, such as cardiac arrest, ARDS, COPD, and acute myocardial infarction.[49-53] Providing an optimal environment for lung protection, however, probably requires attention to not only tidal volume, but also appropriate lung recruitment and oxygen exposure.

TABLE 4] Clinical Outcomes Comparing All Patients Who Progressed to ARDS With Those With No ARDS Progression

Outcome	ARDS (n = 45)	No ARDS (n = 174)	*P* Value
Δ SOFA score on ICU d 2	0.3 ± 2.3	−0.8 ± 2.5	.01
Vasopressor duration, d	2.0 ± 3.9	0.4 ± 1.4	< .0001
Mechanical ventilation duration, d	6.8 ± 7.2	3.6 ± 6.6	.0002
ICU LOS, d	8.0 ± 7.9	4.8 ± 5.4	.002
HLOS, d	9.8 ± 8.1	8.6 ± 9.5	.25
Mortality, No. (%)	23 (51.1)	49 (28.2)	.004

Variables are reported as mean ± SD unless indicated otherwise. Δ refers to the change in SOFA score from ED baseline to 48 h. A negative value reflects an improvement in organ function. HLOS = hospital length of stay. See Table 1 for expansion of other abbreviations.

Only one-third of the study cohort had their head of bed elevated while undergoing mechanical ventilation in the ED. Supine head position during the first 24 h of mechanical ventilation is an independent risk factor for pneumonia.[54] This is an immediately modifiable process of care variable that could reduce complications in patients receiving mechanical ventilation admitted from the ED.

Prior work showed an ARDS prevalence of 8.8% in patients receiving mechanical ventilation with severe sepsis in the ED and septic shock.[14] This current investigation of a heterogeneous ED population demonstrated an ARDS prevalence of 6.8%, which is similar to the findings of work examining ARDS in patients receiving mechanical ventilation in the ED.[14,17,18] Combining data from these studies provides some epidemiologic insight into an ED ARDS prevalence of approximately 8.4% in intubated patients. As in previous work, adherence to lung-protective ventilation in patients with ARDS was low (46.7%). With a conservative estimate of 240,000 patients who receive ED mechanical ventilation annually, the sheer number of patients exposed to potentially harmful ventilation presents an opportunity to reexamine clinical practice and to study these patients further.[6]

VALI and ARDS can evolve quickly.[22,24,26,32,33,47,55,56] The ED represents a period of early critical illness during which protective interventions can influence the complications of critical illness.[57] However, our data cannot answer the question of whether altering ED ventilator practices will decrease ARDS or mitigate its severity, and our study did not show any association with ventilator variables and incidence of ARDS.[57,58] This may indicate that our study was underpowered to detect a small difference that does exist, that there is a true lack of association between ED ventilator management and downstream complications, or that the ED exposure is too short to impact the outcome. However, our data do suggest that ED tidal volume settings influence those delivered in the ICU. This remained true for patients exposed to non-lung-protective ventilation in the ED and suggests that even suboptimal ventilator settings were continued forth into early ICU care. Furthermore, although tidal volume often exceeded 8 mL/kg PBW, rarely did it exceed the levels shown in prior trials to be injurious in patients with established ARDS (ie, 12 mL/kg PBW) or at risk of the syndrome (ie, 10 mL/kg PBW [11.4% of patients in this study]).[19,25] Therefore, in a study of this size, deviations of this magnitude may not be enough to cause a measurable clinical difference, both in terms of ARDS mortality and ARDS development. A lack of association between ventilator variables and ARDS incidence may also reflect the fact that the cause of ARDS is heterogeneous; the most appropriate ED intervention may be a bundled, quality-based approach to address ventilator and nonventilator treatments.[57]

The incidence of ARDS development in this heterogeneous cohort was 14.7%; a previous investigation of patients with severe sepsis and septic shock (perhaps the highest risk cohort for ARDS) showed an ARDS incidence of 27.5% after ED admission.[14] This provides further evidence that ARDS prevention strategies should be considered a priority in emergency research and quality initiatives. Clinical ARDS research has historically been confined to the ICU, but as additional preventive therapies are proposed, ED-based trials will be critical to treat high-risk patients early in the course of disease. The results of our multivariable analysis coincide with the findings of prior research and suggest that these high-risk patients are identified by higher illness severity scores (APACHE II) and LIPS.[40] Our results also suggest that two potential non-ventilator-related variables could be targets for future ARDS prevention: reversal of early organ failure and prehospital intubation.

This study has important limitations. This was a cross-sectional study conducted over a single time period (ie, 1 month) at each center. ED mechanical ventilation practice patterns and incidence of ARDS may vary in association with seasonal respiratory illnesses such as H1N1 influenza. However, there is a lack of data to support seasonal variation of ARDS, and our study months were temporally distinct and varied seasonally across centers. This temporal distribution offers some assurance that our data represent a national longitudinal sample.[59]

This was a relatively small study and, therefore, prone to random error. However, our results are consistent with prior evidence. This study was restricted to academic medical centers. It is, therefore, possible that these data are not truly representative of ED-based mechanical ventilation practices and ARDS prevalence in the community as a whole. The multicenter trial design, consistency with the small amount of previously published data, and inclusion of all mechanically ventilated patients do improve the external validity of our results.

Adjudicating ARDS status can be difficult and will always have a subjective component. This potentially exposes the study to ascertainment bias. Our adjudication protocol was systematic, rigorous, and objective. Our event rate for ARDS was also consistent with that of

previous investigations. We are, therefore, confident that we adjudicated the syndrome accurately for the purposes of this investigation.

Finally, the trained research assistants played no role in the clinical care of the patients, and the physicians were unaware of our study hypotheses. However, the possibility that the presence of bedside research assistants influenced clinical care and ventilator settings cannot be excluded completely (ie, Hawthorne-like effect). Our findings, particularly suboptimal adherence to best-practice guidelines such as protective lung ventilation strategies and head-of-bed elevation, speak against this possibility.

Conclusions

This multicenter study of patients with respiratory failure in the ED demonstrates a significant opportunity to improve ED-based mechanical ventilation practices. This includes delivery of lung-protective ventilation, monitoring of inspiratory plateau pressure, and head-of-bed elevation. Across a heterogeneous intubated population in the ED, progression to ARDS is a common occurrence, occurs early after ICU admission, and leads to significant negative clinical consequences. Modifiable patient- and treatment-related variables exist that could prevent or mitigate ARDS severity, and the ED and prehospital environments should be investigated further.

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Additional information: The e-Appendixes can be found in the Supplemental Materials section of the online article.

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