The Association Between the Mechanical Ventilator Pressures and Outcomes in a Cohort of Patients with Acute Respiratory Failure

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ABSTRACT

BACKGROUND: Pressures measured during mechanical ventilation provide important information about the respiratory system mechanics and can help predict outcomes.

METHODS: The electronic medical records of patients hospitalized between 2010 and 2016 with sepsis who required mechanical ventilation were reviewed to collect demographic information, clinical information, management requirements, and outcomes, such as mortality, ICU length of stay, and hospital length of stay. Mechanical ventilation pressures were recorded on the second full day of hospitalization.

RESULTS: This study included 312 adult patients. The mean age is 59.1 ± 16.3 years; 57.4% were men. The mean BMI was 29.3 ± 10.7. Some patients had pulmonary infections (46.2%), and some patients had extrapulmonary infections (34.9%). The overall mortality was 42.6%. In a multi-variable model that included age, gender, number of comorbidities, APACHE 2 score, and PaO_2/FiO_2 ratio, peak pressure, plateau pressure, driving pressure, and PEEP all predicted mortality when entered into the model separately. There was an increase in peak pressure, plateau pressure, and driving pressure across BMI categories ranging from underweight to obese.

CONCLUSIONS: This study demonstrates that ventilator pressure measurements made early during the management of patients with acute respiratory failure requiring mechanical ventilation provide prognostic information regarding outcomes, including mortality. Patients with high mechanical ventilator pressures during the early course of their acute respiratory failure require more attention to identify reversible disease processes when possible. In addition, increased BMIs are associated with increased ventilator pressures, and this increases the complexity of the clinical evaluation in the management of obese patients.

KEYWORDS: Mechanical ventilation, sepsis, acute respiratory failure, plateau pressure, driving pressure, body mass index, outcomes

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Introduction

Patients with sepsis and acute respiratory failure have complex presentations and frequently have multiorgan failure. Clinicians use several indices to classify these patients and to predict prognosis. In patients requiring mechanical ventilation, gas exchange indices, such as the PaO_2/FiO_2 ratio, and intrathoracic pressures, such as the plateau pressure and driving pressure, can help classify patients and provide estimates of prognosis. Intrathoracic pressures during mechanical ventilation reflect disease in the lung parenchyma, pleural space, chest wall, and abdomen.[1] Premorbid conditions, such as COPD, congestive heart failure, and obesity, influence the severity of any acute presentation. In addition, obesity has potential effects on both the lung parenchyma and the chest wall.[2] Monitoring intrathoracic pressures provides an overall parameter, which is affected by ongoing acute and chronic medical problems in any particular patient. In addition, pressures, such as a plateau pressure and the driving pressure, warrant attention because elevations in these pressures indicate the need for patient reassessment and possibly adjustments in the ventilation.[3]

In this study we evaluated the association between intrathoracic pressures and outcomes in a heterogeneous group of patients requiring mechanical ventilation for the management of acute respiratory failure associated with sepsis. In addition, we evaluated the potential association between obesity defined by body mass index categories and ventilator pressures.

Methods

We conducted an Institutional Review Board (IRB) approved retrospective review of existing data for patients admitted with diagnosis of severe sepsis or septic shock to the medical intensive care unit (MICU) at University Medical Center in Lubbock, Texas, between March 1, 2010 and March 31, 2016. The charts were initially identified by discharge codes (ICD codes 995.91 and 785.52) and then reviewed to determine whether or not the patients met study criteria. The diagnosis

was based on the Third International Consensus Definitions for Sepsis and Septic Shock.[4] We included adults 18 years or older, intubated for a minimum of 24 hours, and admitted into the MICU with the diagnosis of severe sepsis or septic shock. We excluded all patients younger than 18 years and older than 89 years, all other types of shock, and patients requiring mechanical ventilation for less than 24 hours. Our IRB restricts retrospective studies to patients less than or equal to 89 years, and all information was deidentified. We extracted the following information from the electronic medical records (EMRs): gender, age, BMI based on the admission weight and height, initial vital signs (either in the emergency department or the MICU), the first available laboratory tests (hemoglobin, white blood cell counts, lactate, BUN, creatinine, albumin, pH, $PaCO_2$, bicarbonate), APACHE II score on admission to the MICU, source of sepsis (respiratory, gastrointestinal, urinary, skin and subcutaneous tissue, neurologic, bloodstream, bone, endocarditis, mixed), in-hospital mortality, ICU length of stay (LOS), hospital LOS, length of mechanical ventilation (MV), comorbidities (specifically diabetes, end stage renal disease [ESRD], chronic obstructive pulmonary disease [COPD], chronic heart failure [CHF], obesity hypoventilation syndrome [OHS], liver disease), initial chest x-ray results (clear lung fields, pleural effusion, focal or bilateral infiltrates, pneumothorax), renal replacement therapy during MICU management, and vasopressor support. We used the following classification for BMI: BMI $<$ 18.49 kg/m^2, underweight; BMI 18.5 to 24.9 kg/m^2, normal weight; BMI 25 to 29.9 kg/m^2, overweight; BMI 30 to 34.9 kg/m^2, obese class I; BMI 35 to 39.9 kg/m^2, obese class II; BMI $>$ 40 kg/m^2, obese class III. Patients in obese class I, obese class II, and obesity class III, were aggregated into 1 group (obese) for data analysis.

Physicians in the Department of Internal Medicine at Texas Tech University Health Sciences Center manage patients admitted to the medical intensive care unit at University Medical Center who require mechanical ventilation. This management involves either direct care or consultative care. The Department of Internal Medicine has a pulmonary and critical care fellowship, and these trainees are involved in the management of these patients. University Medical Center has a code sepsis protocol designed to identify patients with possible sepsis as early as possible and to complete critical management steps, including cultures, the initiation of antibiotic therapy, and fluid administration, as soon as possible. Patients identified by the code sepsis protocol are routinely reviewed at 6 hours to make certain the sepsis bundle has been completed. Indications for mechanical ventilation included acute respiratory failure, altered mental status with inability to protect the airway, and refractory shock.

We hypothesized that intrathoracic pressures measured during mechanical ventilation measured in the morning on the first full day of admission would have an association with outcomes, including mortality. In effect, pressures were recorded at approximately 8 AM on the second day of hospitalization. These pressures included plateau pressure, peak pressure, PEEP level, and calculated driving pressure (plateau pressure—PEEP). Therefore, the primary outcome in this study was in-hospital mortality; secondary outcomes were the duration of mechanical ventilation, ICU LOS, and hospital LOS. We also assumed that increased BMIs would have an effect on intrathoracic pressures.

Descriptive statistics were used to describe the characteristics of the study cohort. Categorical variables were summarized as frequencies, and continuous variables were summarized using means and standard deviations or medians and ranges, as appropriate. Multiple variable logistic regression was used to test associations between intrathoracic pressures and outcomes while adjusting for other risk factors, including age, gender, APACHE II scores, the number of comorbid conditions, and PaO_2/FiO_2 ratio. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated to evaluate these associations. Poisson regression was used to assess the association between BMI and ICU and hospital LOS, while adjusting for all risk factors. The reference group for these analyses was the patients with a normal BMI (18.5-24.9 kg/m^2). Statistical significant level was set at 0.05. Multiple testing adjustment was not performed. Analyses were performed using SAS software (Windows version 9.3; SAS Institute, Cary, NC).

This study had approval by the Texas Tech University Health Science Center Institutional Review Board in Lubbock, Texas.

Results

This study included 312 patients. The mean age was 59.1 ± 16.3 years; 57.4% were men. The mean BMI was 29.3 ± 10.7 kg/m^2 (Table 1). The underweight group had 26 patients (8.3%), the normal BMI group had 88 patients (28.2%), the overweight group had 91 patients (29.2%), the obese class I group had 36 patients (11.5%), the obese class II group had 32 patients (10.3%), and the obese class III group had 39 patients (12.5%). The 3 obese groups were aggregated into 1 group for data analysis. The median APACHE 2 score was 14. Overall 20.8% of patients required dialysis; 65.4% of patients required vasopressor support. The duration of mechanical ventilation ranged from 5.5 days in underweight patients to 10.2 days in overweight patients. The overall mortality rate was 42.6% (133/312). Other details about this study cohort have been reported in another publication.[5]

Gas exchange parameters and ventilator parameters were recorded on the second full day of hospitalization, after the patients had stabilized and clinicians had time to adjust ventilator settings (Table 1). The mean PaO_2/FiO_2 ratio was 202 mmHg and was slightly lower in the obese BMI group (186 mmHg). The mean PEEP level was 6.5 cm H_2O and was similar in all BMI groups (Table 1). Mean peak airway pressure was 23.5 cm H_2O; the lowest values were in the underweight

Table 1. Clinical information in cohorts characterized by body mass index.

PARAMETER	ALL SUBJECTS	UNDERWEIGHT	NORMAL	OVERWEIGHT	OBESE	*P* VALUE
Number	312	26	88	91	107	
Age, mean ± SD	59.1 ± 16.3	57.5 ± 18.9	59.8 ± 17.8	59.2 ± 17.0	58.7 ± 13.7	.938
Gender (M), N (%)	179 (57.4%)	14 (53.9%)	56 (63.6%)	56 (61.5%)	53 (49.5%)	.181
BMI, mean ± SD*	29.3 ± 10.7	16.7 ± 1.6	21.9 ± 1.8	27.3 ± 1.5	40.3 ± 11.1	<.001
Infection site						
Pulmonary, N (%)	144 (46.2%)	15 (57.7%)	40 (45.5%)	42 (46.2%)	47 (43.9%)	.654
Extra pulm, N (%)	109 (34.9%)	7 (26.9)	33 (37.5%)	29 (31.9%)	40 (37.4%)	.649
Mixed, N (%)	59 (18.9%)	4 (15.4%)	15 (17.1%)	20 (22.0%)	20 (18.7%)	.808
Clinical status						
# comorbidities**, median (min, max)	1 (0, 4)	1 (0, 3)	1 (0, 3)	1 (0, 4)	2 (0, 4)	.004
Lactate, mean ± SD	3.3 ± 3.3	3.0 ± 3.4	4.0 ± 3.9	3.0 ± 2.9	3.0 ± 2.9	.322
APACHE II, median (min, max)	14 (3, 33)	14 (4, 25)	16 (3, 33)	15 (3, 26)	14 (3, 33)	.359
Vasopressor, Yes N (%)	204 (65.4%)	14 (53.9%)	62 (70.5%)	53 (58.2%)	75 (70.1%)	.173
Dialysis, Yes N (%)	65 (20.8%)	2 (7.7%)	20 (22.7%)	12 (13.2%)	31 (29.0%)	.015
PaO_2/FiO_2, mean ± SD***	2.0 ± 1.7	2.1 ± 1.4	2.2 ± 2.6	2.1 ± 1.2	1.9 ± 1.1	.775
Ventilator pressures						
PEEP, mean ± SD****	6.5 ± 2.7	5.6 ± 1.3	6.6 ± 2.8	6.3 ± 2.2	6.8 ± 3.2	.487
Peak P, mean ± SD	23.5 ± 7.1	20.8 ± 6.3	22.2 ± 6.9	23.4 ± 7.1	25.4 ± 7.2	<.001
Plateau P, mean ± SD	19.6 ± 6.1	17.2 ± 4.5	18.5 ± 6.4	19.7 ± 6.0	21.0 ± 5.9	.005
Driving P, mean ± SD	13.1 ± 5.7	11.8 ± 4.2	11.8 ± 5.7	13.4 ± 6.1	14.2 ± 5.5	.010
Outcome						
Mortality, Y N (%)	133 (42.6%)	10 (38.5%)	45 (51.1%)	35 (38.5%)	43 (40.2%)	.296

*BMI-kg/m^2 ; **Comorbidities include AKI, DM, ESRD, OHS, CHF, and liver disease; ***PaO_2/FiO_2 ratio is divided by 100 for the table; ****all pressures are in cm H_2O.

group (20.7 cm H_2O) and highest values in the overweight and obese BMI groups (23.4 and 25.4 cm H_2O, respectively, $P < .001$). The mean plateau pressure was 19.6 cm H_2O; the lowest values were in the underweight group (17.2 cm H_2O), and highest in the overweight and obese BMI groups (19.6 and 21.0 cm H_2O, respectively, $P = 0.005$). The mean driving pressure was 13.1 cm H_2O in all patients; the lowest values were in the underweight group (11.7 cm H_2O), and highest in the overweight and obese groups (13.4 and 14.2 cm H_2O, respectively, $P = 0.010$).

Patients were classified into groups based on driving pressure (<15 cm H_2O, ⩾15 cmH_2O), plateau pressure (<30 cm H_2O, ⩾30 cm H_2O), PaO_2/FiO_2 ratios (<150 mmHg, ⩾150 mmHg), and PEEP (<8 cm H_2O, ⩾8 cm H_2O) levels (see Tables 2 and 3). The multi-variable model for mortality included age, gender, BMI, number of comorbidities, APACHE II scores, and PaO_2/FiO_2 ratios. The ventilator pressure measurements were entered into the model separately, and these calculations indicated that increased levels of PEEP, driving pressure, plateau pressure, and peak pressure predicted increased mortality (Table 4). Patients with BMIs below normal (<18.5 kg/m^2) required shorter periods of mechanical ventilation and ICU stays (Table 5). Patients with overweight BMIs (>25 kg/m^2, ⩽30 kg/m^2) had longer ICU stays. Patients with high PEEP levels (⩾8 cm H_2O) had longer periods of mechanical ventilation.

There were strong positive correlations between plateau pressure and driving pressure (Spearman correlation = 0.858, $P < .001$), between plateau pressure and peak pressure (Spearman correlation = 0.672, $P < .001$), between plateau pressure and PEEP (Spearman correlation = 0.327, $P < .001$), between driving pressure and peak pressure (Spearman correlation = 0.589, $P < .001$), and between peak pressure and PEEP (Spearman correlation = 0.197, $P < .001$) and a negative

Table 2. Relationship between plateau pressures and driving pressures and outcomes (mortality and LOS).

PARAMETER	DRIVING PRESSURE < 15	DRIVING PRESSURE ⩾ 15	*P* VALUE	PLATEAU PRESSURE < 30	PLATEAU PRESSURE ⩾30	*P* VALUE
Number	179	103		266	20	
Age, mean ± SD	60.2 ± 16.8	57.4 ± 15.1	.113	59.7 ± 16.1	53.6 ± 15.4	.094
Gender (M), N (%)	114 (63.7%)	49 (47.6%)	.012	153 (57.5%)	11 (55.0%)	1.000
BMI, mean ± SD*	28.4 ± 10.73	31.41 ± 10.44	.005	29.29 ± 10.82	31.06 ± 8.18	.183
Infection site						
Pulmonary, N (%)	86 (48.0%)	43 (41.8%)	.097	117 (44.0%)	14 (70.0%)	.038
Extra pulm, N (%)	65 (36.3%)	33 (32.0%)		97 (36.5%)	2 (10.0%)	
Mixed, N (%)	28 (15.6%)	27 (26.2%)		52 (19.6%)	4 (20.0%)	
Clinical status						
# comorbidities**, median (min, max)	1 (0, 4)	2 (0, 4)	.197	1 (0, 4)	1 (0, 4)	.890
Lactate, mean ± SD	3.2 ± 2.9	3.5 ± 3.8	.573	3.3 ± 3.2	3.4 ± 4.0	.579
APACHE II, median (min, max)	14 (3, 33)	15 (4, 33)	.106	15 (3, 33)	11.5 (5, 22)	.088
PaO_2/FiO_2, mean ± SD	211 ± 202	190 ± 116	.414	208 ± 179	135 ± 104	.007
Vasopressor, Yes N (%)	114 (63.7%)	75 (72.8%)	.245	173 (65.0%)	19 (95.0%)	<.001
Dialysis, Yes N (%)	30 (16.8%)	29 (28.2%)	.144	55 (20.7%)	4 (20.0%)	.949
Ventilator pressures						
PEEP, mean ± SD***	6.6 ± 2.8	6.4 ± 2.6	.857	6.4 ± 2.6	8.9 ± 4.0	<.001
Peak P, mean ± SD	21.0 ± 6.1	28.3 ± 6.0	<.001	22.8 ± 6.7	32.7 ± 6.3	<.001
Plateau P, mean ± SD	16.6 ± 3.7	25.5 ± 4.6	<.001	18.6 ± 5.0	32.9 ± 2.6	<.001
Driving P, mean ± SD	10.1 ± 3.0	19.0 ± 3.9	<.001	12.3 ± 4.9	23.9 ± 4.5	<.001
Outcomes						
Ventilator time, days, mean ± SD	8.4 ± 5.7	9.7 ± 10.3	.342	8.9 ± 7.9	7.9 ± 4.0	.953
LOS, ICU days, mean ± SD	11.3 ± 9.0	12.1 ± 13.5	.978	11.8 ± 11.1	9.5 ± 7.4	.356
LOS, hospital days, mean ± SD	17.0 ± 14.5	17.3 ± 15.7	.676	17.3 ± 15.1	12.6 ± 10.2	.105
Mortality, Yes N (%)	76 (42.5%)	46 (44.7%)	.815	109 (41.0%)	14 (70.0%)	.022

*BMI-kg/m^2; **Comorbidities include AKI, DM, ESRD, OHS, CHF, and liver disease; ***all pressures are in cm H_2O.

correlation between driving pressure and PEEP (Spearman correlation = −0.12, *P* = .052) (Figure 1). Plateau pressure, driving pressure, and peak pressure increased across BMI categories (underweight, normal, overweight, and obese) with *P* values of .005, .010, and .001, respectively (Figure 2). There was no relationship between PEEP and BMI category.

Discussion

This study demonstrates that increased ventilator pressures are associated with increased mortality in patients with sepsis requiring mechanical ventilation. There was a statistically significant increase in the odds ratio for mortality with increases in PEEP, driving pressure, plateau pressure, and peak pressure. There was a 5% increase in mortality for every cm H_2O increase in driving pressure and a 7% increase in mortality for every cmH_2O increase in plateau pressure. There was a significant correlation between the plateau pressure and driving pressure, and there was a trend towards a decrease in driving pressure with increases in PEEP levels. Finally, there were increases in peak pressure, driving pressure, and plateau pressure across BMI categories, namely underweight, normal weight, overweight, and obese.

Table 3. Relationship between gas exchange parameters and outcomes.

PARAMETER	$PAO_2/FIO_2 < 150$	$PAO_2/FIO_2 \geq 150$	*P* VALUE	PEEP < 8	PEEP ⩾ 8	*P* VALUE
Number	134	178		222	88	
Age, mean ± SD	60.3 ± 15.5	58.2 ± 16.7	.361	59.6 ± 16.6	57.8 ± 15.6	.495
Gender (M), N (%)	80 (59.7%)	99 (55.6%)	.544	123 (55.4%)	55 (62.5%)	.312
BMI, mean ± SD*	29.3 ± 11.5	29.4 ± 10.2	.847	28.7 ± 9.5	30.8 ± 13.3	.452
Site of infection						
Pulmonary, N (%)	82 (61.2%)	62 (34.8%)	<.001	90 (40.5%)	53 (60.2%)	.007
Extra pulm, N (%)	29 (21.6%)	80 (44.9%)		85 (38.3%)	24 (27.3%)	
Mixed, N (%)	23 (17.2%)	36 (20.2%)		47 (21.2%)	11 (12.5%)	
Clinical status						
# comorbidities**, median (min, max)	1 (0, 4)	2 (0, 4)	.294	1 (0, 4)	1 (0, 4)	.383
Lactate, mean ± SD	3.1 ± 2.7	3.4 ± 3.6	.981	2.9 ± 2.9	4.1 ± 3.8	.024
APACHE II, median (min, max)	15.5 (3, 33)	14 (3, 33)	.089	14 (3, 33)	16 (3, 33)	.268
PaO_2/FiO_2, mean ± SD	89 ± 29	287 ± 184	<.001	227 ± 188	140 ± 94	<.001
Vasopressor, Yes N (%)	94 (70.2%)	110 (61.8%)	.384	131 (59.0%)	73 (82.9%)	<.001
Dialysis, Yes N (%)	26 (19.4%)	39 (21.9%)	.774	44 (19.8%)	21 (23.9%)	.365
Ventilator pressures						
PEEP, mean ± SD***	7.6 ± 3.3	5.7 ± 1.8	<.001	5.0 ± 0.4	10.3 ± 2.4	<.001
Peak P, mean ± SD	24.2 ± 7.4	23.0 ± 6.9	.117	22.8 ± 6.9	25.5 ± 7.4	.002
Plateau P, mean ± SD	20.9 ± 6.6	18.6 ± 5.5	.003	18.5 ± 5.4	22.4 ± 6.6	<.001
Driving P, mean ± SD	13.3 ± 6.4	12.9 ± 5.2	.599	13.5 ± 5.3	12.14 ± 6.4	.080
Outcomes						
Ventilator time, days, mean ± SD	9.5 ± 9.5	8.0 ± 5.5	.164	8.4 ± 8.1	9.3 ± 5.6	.011
LOS, ICU days, mean ± SD	11.7 ± 12.6	10.8 ± 8.8	.781	11.0 ± 11.0	11.7 ± 9.7	.428
LOS, hospital days, mean ± SD	16.4 ± 15.1	16.6 ± 14.2	.298	16.6 ± 14.4	16.4 ± 14.9	.390
Mortality, Yes N (%)	62 (46.3%)	71 (39.9%)	.311	83 (37.4%)	50 (56.8%)	.003

*BMI-kg/m^2; **Comorbidities include AKI, DM, ESRD, OHS, CHF, and liver disease; ***all pressures are in cm H_2O.

Amato and colleagues analyzed individual data from 3562 patients with ARDS enrolled in 9 randomized trials.[3] They analyzed the driving pressure as an independent variable and its association with survival. Using a statistical technique known as multilevel mediation analysis, they demonstrated that at a constant PEEP level an increase in driving pressure was associated with increased mortality, at a constant plateau pressure a decrease in driving pressure was associated with a reduced mortality, and at a constant driving pressure an increase in PEEP was not associated with an increase in mortality. Overall, the results indicated that a 1 standard deviation increase in driving pressure (approximately 7 cmH_2O) was associated with a 40% increase in the odds of mortality risk (odds ratio: 1.4; 95% confidence interval: 1.31–1.51), and driving pressures greater than 15 cmH_2O were associated with increased mortality. Our study suggests that a 7 cmH_2O increase in driving pressure would be associated with a 35% increased risk of mortality. Schmidt and coworkers retrospectively analyzed 622 mechanically ventilated adults without ARDS to determine the association between driving pressure and mortality.[6] In patients without ARDS, driving pressure was not independently associated with hospital mortality; it was associated with mortality in patients with a PaO_2/FiO_2 ratio of less than 300 mmHg. Villar et al. did a secondary

Table 4. Mortality analysis.

	ALIVE (N = 179)	EXPIRED (N = 133)	ODDS RATIO (RAW)	ODDS RATIO (ADJUSTED)
Age	57.0 (21.0,91.0)	65.0 (21.0,99.0)	1.02(1.01, 1.04)	1.02 (1.01, 1.05)
Gender				
Female	80 (44.7)	53 (39.9)		
Male	99 (55.3)	80 (60.2)	1.22 (0.77, 1.92)	1.27 (0.77, 2.12)
BMI*				
18.5-24.9	43 (24.0)	45 (33.8)		
<18.5	16 (8.9)	10 (7.5)	0.60 (0.24, 1.46)	0.53 (0.19, 1.49)
25-29.9	56 (31.3)	35 (26.3)	0.60 (0.33, 1.08)	0.60 (0.31, 1.17)
>30	64 (35.8)	43 (32.3)	0.64 (0.36, 1.13)	0.68 (0.35, 1.29)
# Comorbidity	1.0 (0.0,4.0)	2.0 (0.0,4.0)	1.11 (0.89, 1.39)	1.06 (0.83, 1.35)
APACHE II	14.0 (3.0,33.0)	15.0 (4.0,33.0)	1.04 (1.00, 1.08)	1.02 (0.97, 1.06)
PaO_2/FiO_2	1.8 (0.3,5.7)**	1.6 (0.3,5.7)	0.98 (0.86, 1.12)	0.98 (0.85, 1.12)
PEEP***	5.0 (2.0,20.0)	5.0 (2.0,15.0)	1.12 (1.03, 1.22)	1.12 (1.02, 1.23)
Driving pressure	12.0 (2.0,31.0)	13.0 (2.0,31.0)	1.02 (0.98, 1.07)	1.05 (1.00, 1.11)
Plateau pressure	18.0 (5.0,39.0)	20.0 (8.0,38.0)	1.05 (1.01, 1.09)	1.07 (1.02, 1.12)
Peak pressure	22.0 (9.0,41.0)	24.0 (5.0,46.0)	1.03 (1.00, 1.07)	1.05 (1.02, 1.09)

*BMI in kg/m^2; **PaO_2/FiO_2 divided by 100; ***all pressures in cm H_2O.

analysis of 778 patients with moderate to severe ARDS and measured the risk of hospital death based on quantiles of tidal volume, positive end-expiratory pressure, plateau pressure, and driving pressure.[7] They found that plateau pressures greater 29 cm H_2O and that driving pressures greater than 19 cmH_2O were associated with an increased risk of death. They also found that plateau pressures provided a slightly better prediction of outcome than driving pressure. These studies indicate the calculating driving pressure provides additional information about lung mechanics and can help identify pressures associated with poor outcomes. Our study involved a heterogeneous group of patients with sepsis and acute respiratory failure and demonstrated that all ventilator pressures were associated with increased risk for mortality.

More accurate interpretation of ongoing pathophysiological events requires measurement of intrapleural pressures that are usually approximated by esophageal pressures. However, esophageal pressures provide only a single reading and may not accurately reflect pressures on the dorsal surface of the lung or on the ventral surface of the lung. Beitler et al. compared PEEP adjustment using pleural pressure measurements versus an empiric high PEEP-FiO_2 table in the 200 patients with moderate to severe ARDS.[8] The primary outcome was a composite score of death and days free from mechanical ventilation through day 28. All patients had an esophageal balloon replaced, and in the esophageal pressure adjusted PEEP group, PEEP was adjusted to maintain an end expiratory transpulmonary pressure of 0 to 6 cmH_2O. Approximately 30% of patients in both groups died, and there were no significant differences in 60-day mortality, 1-year mortality, or the number of ventilator-free days. The transpulmonary pressure at end expiration was near 0 in both groups through day 7, and the set PEEP levels were very similar in both groups. The esophageal pressure was approximately 15 cmH_2O at end expiration, the airway driving pressure was approximately 12 cmH_2O, and the plateau pressure was less than 30 cmH_2O in both groups through 7 days. The PaO_2/FiO_2 ratio improved in both groups by day 1. This study would suggest that in patients with moderate to severe ARDS adjustments in PEEP using esophageal pressures do not result in significant differences in death or days free from mechanical ventilation through day 28.

Increased body mass indices can have important effects on respiratory system mechanics. These effects depend on the degree of obesity and the distribution of fatty tissue.[2,9] Obese patients in the supine position often have cephalad movement of the diaphragm and have reduced lung volumes. In addition, they have increased intrapleural pressures and atelectasis in dependent lung zones of the lung. This usually results in

Table 5. Mechanical ventilation, ICU length of stay, and hospital length of stay.

		MV DAYS		LOS, ICU		LOS HOSPITAL	
		MEAN ± SD	*P* VALUE	MEAN ± SD	*P* VALUE	MEAN ± SD	*P* VALUE
BMI*	18.5-24.9 (n = 88)	8.08 ± 4.97	reference	10.30 ± 8.02	reference	14.98 ± 10.95	reference
	<18.5 (n = 26)	5.48 ± 3.25	.022	6.08 ± 4.09	.003	13.81 ± 11.08	.633
	25-29.9 (n = 91)	10.22 ± 10.99	.100	13.30 ± 13.09	.025	18.63 ± 15.40	.054
	>30 (n= 107)	8.55 ± 5.89	.727	11.31 ± 10.78	.394	16.55 ± 16.85	.360
Driving pressure**	⩾15	9.69 ± 10.30	.302	12.61 ± 13.50	.811	17.32 ± 15.71	.819
	<15	8.37 ± 5.63		11.10 ± 9.00		16.74 ± 14.38	
Plateau pressure	⩾30	7.95 ± 4.04	.953	9.50 ± 7.36	.356	12.55 ± 10.23	.106
	<30	8.91 ± 7.86		11.82 ± 11.06		17.32 ± 15.11	
PEEP	⩾8	9.28 ± 5.57	.011	11.74 ± 9.67	.428	16.44 ± 14.96	.390
	<8	8.40 ± 8.12		11.00 ± 10.97		16.61 ± 14.43	
PaO_2/FiO_2	⩾150	8.04 ± 5.51	.164	10.78 ± 8.84	.781	16.56 ± 14.16	.298
	<150	9.47 ± 9.45		11.69 ± 12.57		16.38 ± 15.09	

P values in this table are unadjusted; bold numbers are statistically significant at the .05 level.
*BMI-kg/m^2; **all pressures are in cm H_2O.

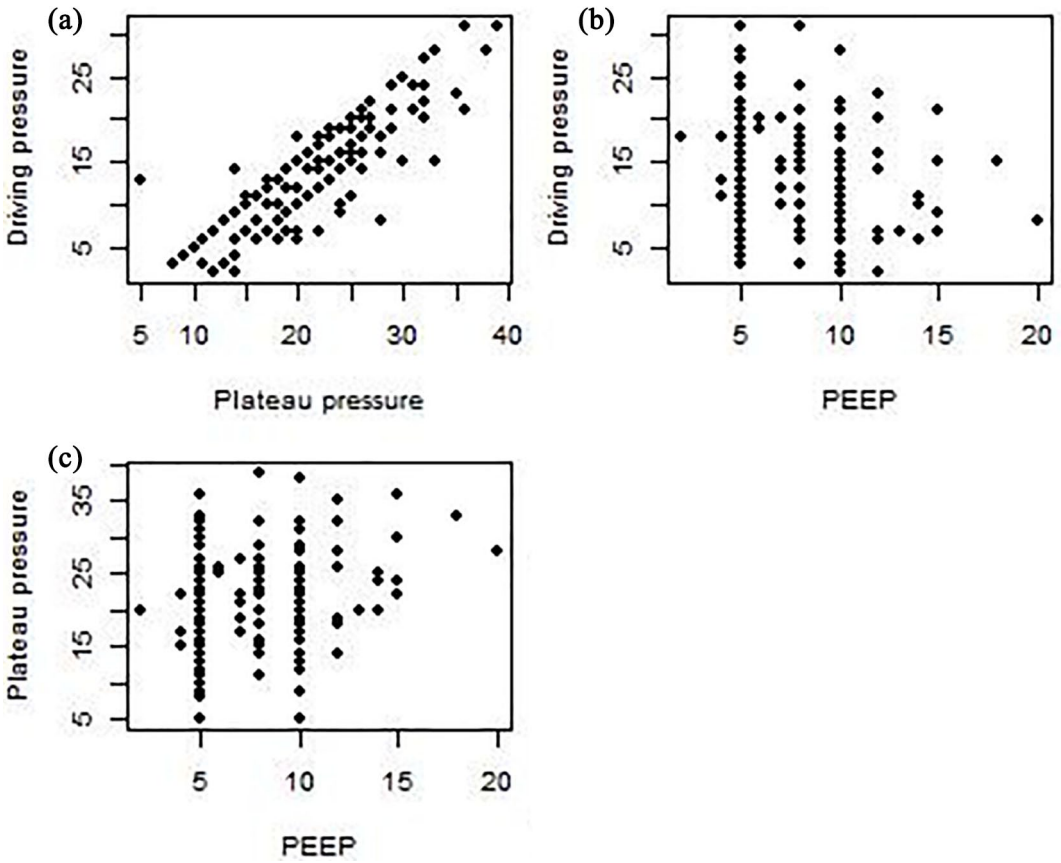

Figure 1. Pressure relationships during mechanical ventilation. This figure shows the relationships between. (A) Plateau pressure and driving pressure. (B) PEEP and driving pressure. (C) PEEP and plateau pressure.

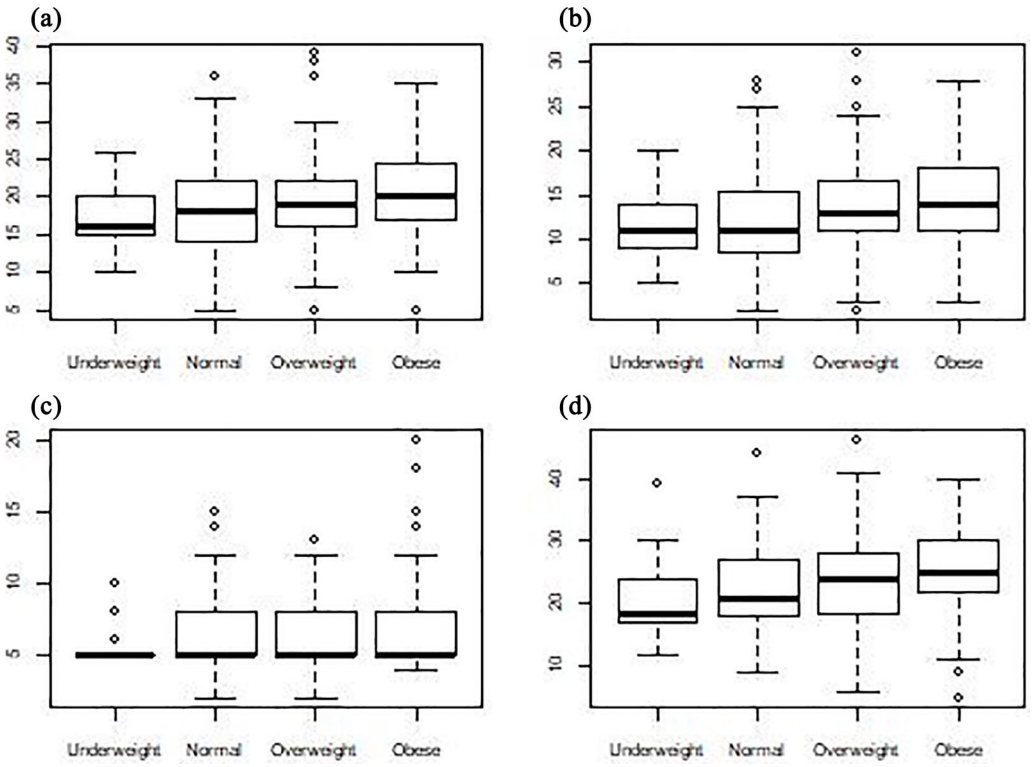

Figure 2. Pressure relationships and body mass index category. This figure shows the relationships between BMI category and Plateau pressure (A). Driving pressure (B). PEEP (C). and Peak pressure (D).

ventilation/perfusion mismatch and hypoxemia. In addition, during tidal breathing on the mechanical ventilator, there would be cyclical opening and closing of atelectatic regions which can induce lung trauma (atelectatic trauma). This potentially contributes to the overall lung injury and contributes to biotrauma. Increased PEEP levels could reduce atelectasis in dependent lung zones and reduce the trauma associated with cyclical opening and closing of these regions. The main problem involves determining the optimal PEEP level. Our results indicate that an increased BMI is associated with increased ventilator pressure. However, the underlying pathophysiologic basis for this association likely varies from patient to patient and will depend on the extent and distribution of parenchymal disease, pleural disease and/or fluid, chest wall mechanics, and intra-abdominal processes. These concerns significantly increase the complexity of the clinical evaluation of these patients. These difficulties are briefly discussed in the next paragraph.

De Jong reported a retrospective analysis of data prospectively collected on patients with ARDS.[10] They analyzed the plateau pressure, the compliance of the respiratory system, and the driving pressure of the respiratory system within 24 hours of ARDS diagnosis and compared these results in survivors and non-survivors at 90 days. These 3 measurements predicted mortality in a multi-variable analysis in nonobese patients but not in obese patients. This result would suggest that monitoring driving pressure in obese patients has less value than in nonobese patients. Bime et al. retrospectively analyzed the data collected in the ALVEOLI trial which included 505 patients (335 nonobese and 150 obese).[11] The overall mortality was 28%. This study compared the effect of either a high or low PEEP ventilatory strategy in patients being managed with low tidal volume ventilation who had acute respiratory distress syndrome. Through the first 7 days of mechanical ventilation, the low PEEP group had a mean PEEP level of approximately 9 cmH_2O, and the high PEEP group had a level which ranged from 12 to 14 cmH_2O. Obese patients defined by a BMI $> 30\ kg/m^2$ had improved survival at 60 days compared to nonobese patients. There was no difference in the proportion of patients who were weaned and extubated by 28 days or in the frequency of barotrauma in obese patients who were assigned to a higher PEEP level in comparison to a lower PEEP level. Fumagalli et al. compared 3 methods to determine optimal PEEP levels and lung recruitment in obese patients with acute respiratory distress syndrome.[12] They found that setting PEEP according to a PEEP decremental trial after a recruitment maneuver reduced lung elastance and increased oxygenation. These 3 studies suggest that the best method to manage oxygenation in obese patients with acute respiratory failure is unclear. A randomized trial comparing driving pressure, optimal transpulmonary pressures using esophageal balloons, and recruitment maneuvers with higher levels of PEEP in obese patients would require substantial effort and expertise.

The studies reviewed in this discussion demonstrate the complex considerations involved in the development of optimal (safer) mechanical ventilation which avoids ventilator-induced

lung injury. Ventilator pressures provide important information regarding the severity of the respiratory disease in all patients with acute respiratory failure.[13] However, multiple factors influence these pressures during episodes of acute respiratory failure. For example, diffuse infiltrative processes decrease lung compliance and increase pressure requirements to deliver tidal volumes. The chest wall also influences respiratory system mechanics. Pleural fluid, chest wall edema, and various intra-abdominal disorders, such as ileus, ascites, and surgical procedures, decrease chest wall compliance and increase pressure requirements to deliver tidal volumes. Measurement of static pressures, such as the driving pressure and plateau pressure, provides an incomplete description of respiratory system mechanics.[13] However, these pressure measurements do provide readily available information about outcomes and complications.[14-16]

Routine ICU care can improve respiratory mechanics and potentially improve outcomes. These measures should include consistent elevation of the head of the bed and prevention of excessively positive fluid balances. In some patients the abdominal compartment syndrome develops and changes respiratory system mechanics, and this problem can be identified with bladder pressure measurements. Finally, bedside ultrasonography can identify patients with areas of consolidation and atelectasis at the lung bases.[17] PEEP adjustments can reduce these areas in many patients.

Limitations

This study was a retrospective single center study with a diverse patient population. Information was collected from electronic medical records and may have been incomplete. For example, the number of comorbidities could influence outcomes, and it is difficult to adjust the analysis based on the severity of any particular comorbidity in a given patient. Outcomes may reflect different management strategies by the teams involved in patient care. However, our study included only patients with sepsis requiring mechanical ventilation who represent a somewhat uniform but complex patient population frequently managed in ICUs.

Conclusion

This study demonstrates that ventilator pressure measurements made early during the in the management of patients with acute respiratory failure requiring mechanical ventilation provide prognostic information about outcomes, including mortality. All readily available pressure measurements predicted outcomes. These pressures provide a global index of underlying pathophysiology and, of course, are not disease or pathology specific. In this study the driving pressure did not provide any better information than the plateau pressure. In this patient cohort, peak pressure, driving pressure, and plateau pressure all increased with BMI classified into categories. Obese patients likely require higher levels of PEEP to maintain optimal oxygenation. In addition, obese patients need more bedside assessment to determine pathophysiologic changes associated with increases in ventilator pressures.

Authors' Contributions

All authors participated in the drafting, editing, and approval of the manuscript.

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