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Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients

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Abstract *Objective:* To determine the incidence, risk factors, and outcome of barotrauma in a cohort of mechanically ventilated patients where limited tidal volumes and airway pressures were used. *Design and setting:* Prospective cohort of 361 intensive care units from 20 countries. *Patients and participants:* A total of 5183 patients mechanically ventilated for more than 12 h. *Measurements and results:* Baseline demographic data, primary indication for mechanical ventilation, daily ventilator settings, multiple-organ failure over the course of mechanical ventilation and outcome were collected. Barotrauma was present in 154 patients (2.9%). The incidence varied according to the reason for mechanical ventilation: 2.9% of patients with chronic obstructive pulmonary disease; 6.3% of patients with asthma; 10.0% of patients with chronic interstitial lung disease (ILD); 6.5% of patients with acute respiratory distress syndrome (ARDS); and 4.2% of patients with pneumonia. Patients with and without barotrauma did not differ in any ventilator parameter. Logistic regression analysis identified as factors independently associated with barotrauma: asthma [RR 2.58 (1.05–6.50)], ILD [RR 4.23 (95%CI 1.78–10.03)]; ARDS as primary reason for

mechanical ventilation [RR 2.70 (95%CI 1.55–4.70)]; and ARDS as a complication during the course of mechanical ventilation [RR 2.53 (95%CI 1.40–4.57)]. Case-control analysis showed increased mortality in patients with barotrauma (51.4 vs 39.2%; $p=0.04$) and prolonged ICU stay. *Conclusions:* In a cohort of

patients in whom airway pressures and tidal volume are limited, barotrauma is more likely in patients ventilated due to underlying lung disease (acute or chronic). Barotrauma was also associated with a significant increase in the ICU length of stay and mortality.

Keywords Barotrauma · Pneumothorax · Mechanical ventilation · Tidal volume · PEEP · ARDS

Introduction

Barotrauma is a feared complication of mechanical ventilation and is associated with increased morbidity and mortality [1, 2, 3]. Variations in the reported incidence of ventilator-associated barotrauma [4, 5, 6, 7] may relate to differences in the patients' underlying disease. Barotrauma is increased in patients with severe underlying lung disease, especially in patients with ARDS [1, 2, 4, 8, 9, 10, 11], aspiration pneumonia [7], *Pneumocystis carinii* pneumonia [14], and pre-existing chronic obstructive lung disease [2, 15, 16].

Considerable controversy surrounds the roles of airway pressure, positive end-expiratory pressure (PEEP) and tidal volume in the development of barotrauma [8, 9]. Several investigators have found an association between PEEP and the development of barotrauma [12, 17, 18, 19], but other investigators have detected no such relationship [8, 10, 11, 20]. Amato et al. [9] reported that the use of tidal volumes of 12 ml/kg and high plateau pressures resulted in 42% rate of pneumothorax and 71% mortality rate compared with 7% rate of pneumothorax and 38% mortality rate in patients in whom tidal volume and plateau pressure were limited. These investigators concluded that in order to reduce the frequency of barotrauma, we have to use small tidal volumes, adjust PEEP based on lung mechanics and monitor lung compliance [9]. Weg et al. [8], however, observed no relationship with either high airway pressures or high tidal volumes and the development of barotrauma in a prospective trial of patients with ARDS. It is important to point out that this study was not methodologically designed to assess the relation between pneumothorax and mortality, and that it was a retrospective analysis. The controversy that exists between these studies may reside in the fact that different pressures are used as variables, and the way in which they are measured. In particular, it should be recalled that peak inspiratory pressure does not accurately reflect the true alveolar distention, thus partly explaining why it has been difficult to correlate the incidence of barotrauma with peak inspiratory pressure. Overall, the trend over the years in ventilator settings has been to reduce tidal volume and airway pressures, but limited prospective data related to barotrauma are available. Furthermore, whether the de-

velopment of barotrauma increases mortality is also controversial [1, 3, 7].

Clinicians have become aware of the dangers associated with excessive tidal volumes and ventilator pressures; thus, the occurrence of barotrauma and the factors associated with it are not known. We studied the incidence of barotrauma and the risk factors for its development in a large, heterogeneous, population of mechanically ventilated patients. We determined the morbidity and mortality associated with barotrauma by comparing patients with barotrauma with a matched case-control cohort without barotrauma.

Patients and methods

We used the database of a prospective, multicentre, international cohort of 5183 adult patients who received mechanical ventilation for more than 12 h from 1 to 31 March 1998 at 361 intensive care units. The general physiological and clinical characteristics of the patients were previously described and reported [21]. The institutional review board at each centre approved the study protocol.

The following information was collected on each patient receiving mechanical ventilation: demographic data (sex, age, weight, date of admission to the ICU, SAPS II score at the time of ICU admission [22]); type of problem (medical or surgical); day of initiating mechanical ventilation; primary indication for mechanical ventilation (chronic obstructive pulmonary disease (COPD); asthma; coma; neuromuscular disease; chronic pulmonary disease non-COPD); causes of acute respiratory failure acute respiratory distress syndrome (ARDS); postoperative status; congestive heart failure; aspiration; pneumonia; sepsis; trauma; cardiac arrest; variables related to management (mode of ventilation, respiratory rate, tidal volume, applied PEEP, need for vasoactive drugs and need for neuromuscular blockers, and arterial blood gas analysis). Development of the following events was assessed daily during the course of mechanical ventilation for a maximum of 28 days: ARDS; barotrauma; pneumonia; sepsis; renal failure; hepatic failure; and coagulopathy. Sepsis, pneumonia and ARDS were considered as events only if they appeared more than 48 h after mechanical ventilation was started. A patient was considered to have any of the above conditions if it was present for at least two consecutive days. Each of these conditions has been previously defined [21]. The arterial blood gases correspond to the values obtained once daily at approximately 8:00 a.m. The ventilator variables corresponded to the time that the arterial blood gases were obtained. The use of neuromuscular blockers, sedatives and vasoactive drugs (given for at least 3 h in a 24-h period) was recorded daily for a maximum of 28 days. Weaning refers to the discontinuation of mechanical ventilation. The onset was the time that the physician in charge considered patient likely to be able to resume spontaneous breathing. The patients were prospectively followed for a maxi-

mum of 28 days of mechanical ventilation and/or until discharge from the hospital and/or death.

The most frequently used mode of ventilation, and the highest airway pressures and tidal volumes at any time during the course of mechanical ventilation, were compared in patients with and without barotrauma. In patients who developed barotrauma, we compared the airway pressures and tidal volumes of the day before the detection of barotrauma with the highest pressures and tidal volumes at any time during the duration of mechanical ventilation in patients without barotrauma. We also compared the highest pressures and tidal volumes at any time before the detection of barotrauma and the average ventilator pressures and tidal volumes in patients with and without barotrauma during the first week of mechanical ventilation.

Barotrauma was defined as the development of air outside the tracheobronchial tree resulting from presumptive alveolar rupture and manifested by at least one of the following: interstitial emphysema; pneumothorax; pneumomediastinum; pneumoperitoneum; or subcutaneous emphysema [8]. All cases of extra-pulmonary air that the investigators thought were related to chest trauma or secondary to placement of a central line were excluded ($n=55$).

To determine the morbidity (ICU and hospital length of stay) and mortality of barotrauma, we did two case-control analyses. We matched patients with barotrauma to those without barotrauma in our database. The matched variables were the following: variables present at the initiation of mechanical ventilation (age, SAPS II score, limited activity as previous functional status); primary indication for mechanical ventilation (coma, ARDS, pneumonia, sepsis); variables related to patient management (need for vasoactive drugs, need for neuromuscular blockers, tidal volume less than

5 ml/kg, PEEP equal to 0 cmH₂O, peak airway pressure higher than 50 cmH₂O, plateau airway pressure higher than 35 cmH₂O); variables occurring over the course of the mechanical ventilation (development of ARDS, sepsis, shock, acute renal failure, hepatic failure, metabolic acidosis, and various values of PaO₂ to FiO₂ ratio). The variability range for matching age was ± 10 years and for SAPS II was ± 10 points.

Statistical analysis

Results are expressed as means and standard deviation, median with the interquartile range, and proportions as appropriate. We used the Student's *t* test to compare continuous variables and the chi-square test to compare proportions.

To evaluate the potential risk factors for barotraumatas, with all patients, we performed a multivariate analysis using a conditional logistic-regression model and a forward stepwise selection method to correct for co-linearity. The independent variables recorded at baseline included age, SAPS II score, sex, primary reason for mechanical ventilation, mode of mechanical ventilation, tidal volume (in millilitres per kilogram), peak airway pressure, plateau airway pressure, PEEP, and complications during the period of mechanical ventilation that were related to the development of barotrauma (ARDS, pneumonia, sepsis). The variables age, SAPS II score, mode of mechanical ventilation, tidal volume and PEEP were coded "dummy" variables and compared between patients with and without barotrauma. Peak airway pressure and plateau airway pressure were dichotomized using cut-off points that were consistent with clinical relevance or with previously published threshold values (peak airway pressure higher than 50 cm H₂O and

Table 1 Comparison of demographic data of those patients without and those with barotrauma. *SAPS* Simplified Acute Physiology Score, *COPD* chronic obstructive pulmonary disease, *ARDS* acute respiratory distress syndrome

	Patients without barotrauma ($n=5029$)	Patients with barotrauma ($n=154$)	<i>p</i> value
Mean age \pm SD (years)	59 \pm 17	56 \pm 20	0.05
Mean SAPS II score \pm SD	44 \pm 17	44 \pm 17	0.60
Gender (<i>n</i>)			0.29
Male	3046 (60.6)	99 (64.3)	
Female	1932 (38.4)	53 (34.4)	
Principal reason for mechanical ventilation (<i>n</i>)			0.001
COPD	507 (10.1)	15 (9.7)	
Asthma	74 (1.5)	5 (3.2)	
Coma	849 (16.9)	15 (9.7)	
Neuromuscular disease	89 (1.8)	5 (3.2)	
Chronic interstitial lung disease	54 (1.1)	6 (3.9)	
Acute respiratory failure			0.63
ARDS	216 (4.3)	15 (9.7)	
Postoperative	1053 (20.9)	27 (17.5)	
Congestive heart failure	531 (10.6)	8 (5.2)	
Aspiration	123 (2.4)	6 (3.9)	
Sepsis	449 (8.9)	9 (5.8)	
Pneumonia	691 (13.7)	30 (19.5)	
Trauma	393 (7.8)	14 (9.1)	
Cardiac arrest	98 (1.9)	2 (1.3)	
Complications developed over the course of mechanical ventilation (<i>n</i>)			<0.001
ARDS	196 (3.9)	13 (8.4)	
Ventilator-associated pneumonia	414 (8.2)	11 (7.1)	
Sepsis	427 (8.5)	14 (9.1)	

Numbers in parentheses are percentages

plateau airway pressure higher than 35 cm H₂O). Variables associated with barotrauma in the univariate analysis and having a *p* value less than 0.10 were entered into the multivariate regression analysis. Factors were considered significant if the *p* value was less than 0.05 in the multivariate analysis. We calculated odds ratios and 95% confidence intervals for all significant predictors of barotrauma.

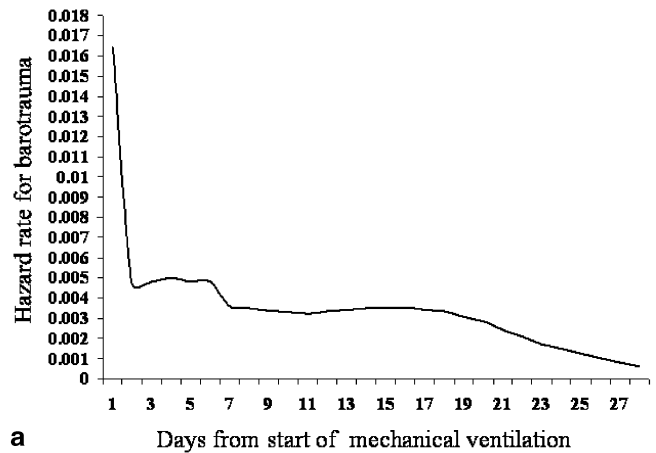
Results

Incidence and risk factors of barotrauma

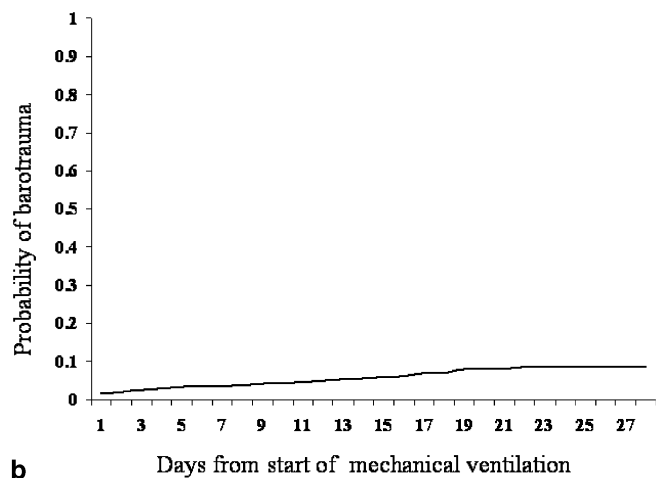
A total of 154 patients developed barotrauma (2.9%) while receiving mechanical ventilation. Barotrauma was diagnosed at a mean time of 3.4±4.2 days, and it was more frequent in younger patients (mean age 56±20 vs 59±17 years in patients who did not develop barotrauma; *p*=0.05). Barotrauma was also more common in patients with underlying lung disease as the principal reason for mechanical ventilation (pneumonia, chronic interstitial lung disease, ARDS); and in patients that developed the following complications during the course of mechanical ventilation: ARDS, VAP and sepsis (Table 1).

The hazard rate for barotrauma from the start of mechanical ventilation and the probability for developing barotrauma over the days of mechanical ventilation are shown in Fig 1. The overall incidence of barotrauma was 0.52 cases per 1000 ventilator days. Barotrauma was more likely to be present during the first 3 days with a fall in the hazard rate over the remaining time of mechanical ventilation.

The ventilator parameters, including tidal volume, pressures (peak and plateau), and PEEP are summarized in Table 2. There were no differences in the barotrauma group between the pressures the day before the diagnoses of barotrauma and the highest values during the course of mechanical ventilation. The analyses presented are the former values. There were no differences between the highest mean, peak, plateau or PEEP pressures recorded in patients who did not develop barotrauma, as compared with the airway pressures the day before the diagnoses of barotrauma in the barotrauma group. There were no differences in tidal volume or ventilator modes (data not shown) between study groups. A subgroup analysis of patients with ARDS, COPD and asthma did not show any significant difference between patients with and without barotrauma. The univariate and multivariate analyses identified chronic interstitial lung disease, ARDS (before and after mechanical ventilation) and pneumonia as the factors associated with the development of barotrauma (Table 3).



a



b

Fig. 1 **A** Hazard rate for barotrauma from the start of mechanical ventilation. **B** Probability of developing barotrauma over the time of mechanical ventilation

Association between barotrauma and morbidity and mortality

With our matching procedure, we were able to identify in the control group 142 of the 154 (92%) cases of barotrauma in the morbidity analysis (Table 4) and 148 of the 154 (96%) cases in the mortality analysis (Table 5). The analyses of the attributable morbidity show differences in both the days of mechanical ventilation (8.6±9.5 days in patients with barotrauma vs 5.8±5.4 days in the matched control cases; *p*<0.001); and in the length of ICU stay (14±13.6 days in patients with barotrauma vs 10.9±11.4 days in the patients without barotrauma; *p*=0.04).

The crude mortality rates for patients developing barotrauma and match control cohort were 76 of 148 (51.4%) and 58 of 148 (39.2%; *p*=0.04), respectively [absolute attributable mortality 12.2% (95% CI: 0.9–

Table 2 Comparison of ventilatory parameters of the patients without and those with barotrauma. PEEP positive end-expiratory pressure

	Patients without barotrauma (n=5029)	Patients with barotrauma (n=154)	p value
Mean Pressures±SD (cmH ₂ O)			
Peak	33.1±8.5	31.9±8.8	0.07
>50 cmH ₂ O (n)	257 (5.1)	7 (4.5)	0.75
Plateau	24.2±4.2	23.9±4.4	0.45
>35 cmH ₂ O (n)	158 (3.1)	7 (4.5)	0.32
PEEP	4.9±3.8	4.6±4.0	0.22
<5 cmH ₂ O (n)	3813 (75.8)	110 (71.4)	0.07
6–10 cmH ₂ O (n)	984 (19.6)	32 (20.8)	
11–15 cmH ₂ O (n)	204 (4.0)	10 (6.5)	
>15 cm H ₂ O (n)	28 (0.5)	2 (1.3)	
Mean tidal volume±SD (ml/kg; n)	9.6±2.3	9.5±1.9	0.53
<5	52 (1.0)	1 (0.6)	0.83
6–8	729 (14.5)	23 (14.9)	
9–12	3979 (79.1)	124 (80.5)	
>12	269 (5.3)	6 (3.9)	

Numbers in parentheses are percentages

In the patients without barotrauma, the pressures and volumes are the highest values at any time during the course of mechanical ventilation. In patients with barotrauma the data presented are pressures and volumes of the day before the detection of barotrauma

Table 3 Risk factors for barotrauma

	Univariate analysis		Multivariate analysis	
	Relative risk (95% CI)	p value	Relative risk (95% CI)	p value
Asthma	2.17 (0.91–5.13)	0.07	2.58 (1.02–6.51)	0.04
Chronic interstitial lung disease	3.46 (1.6–7.52)	0.001	4.23 (1.78–10.03)	0.001
Previous ARDS	2.31 (1.38–3.88)	<0.001	2.70 (1.55–4.70)	<0.001
Pneumonia	1.50 (1.01–2.21)	0.04	–	–
ARDS that developed during mechanical ventilation	2.19 (1.26–3.80)	0.005	2.53 (1.40–4.57)	0.002

Previous ARDS denotes ARDS as a cause of mechanical ventilation

Numbers in parentheses denote range

23.4)]. The relative risk of increased (RRI) mortality attributable to barotrauma was 31.1% (95% CI 2.3–59.8).

Discussion

The main findings in this study are that in mechanically ventilated patients, barotrauma is more likely to be present in patients with underlying lung diseases (ARDS, interstitial lung disease or asthma) and in patients that developed ARDS and/or ventilator-associated pneumonia as complications of mechanical ventilation. Barotrauma had no correlation with the mode of ventilation or ventilator settings, but it was associated with an increased duration of mechanical ventilation, ICU and hospital length of stay, and increased ICU mortality.

In this cohort of mechanically ventilated patients, the incidence of barotrauma was 2.9%. Investigators have reported the incidence of barotrauma to be as low as 0.5% in postoperative patients [5] and as high as 87% in patients with ARDS [1]. Our study confirms that the major risk factor for barotrauma is the underlying reason

for mechanical ventilation. In agreement with previous reports [1, 2, 3, 4] patients with chronic interstitial lung disease and ARDS were more likely to develop barotrauma.

Investigators have reported a variable time from the start of mechanical ventilation to the presentation of barotrauma. In this study, 80% of the patients with barotrauma developed it within the first 3 days of mechanical ventilation (Fig. 1A). Six patients, five with ARDS diagnosed during the course of mechanical ventilation, developed barotrauma after 2 weeks of ventilatory support. These results are similar to the reports by Schnapp et al. [3] in patients with multiple underlying medical conditions and in patients with ARDS [8, 13]. Gattinoni et al. [1] reported that barotrauma was more common in patients with late ARDS (>2 weeks; 87%) than in patients with intermediate ARDS (1–2 weeks; 46%) or early ARDS (<1 week; 30%). Recently, Eisner et al. [12], in a large cohort study of 718 patients with ARDS, reported that 93 patients (13%) developed barotrauma. [8, 13]. The cumulative incidence of barotrauma more than doubled during the first four study days of

Table 4 Analysis of the morbidity (days of mechanical ventilation and length of stay in the ICU) due to barotrauma

	Patients without barotrauma (n=142)	Patients with barotrauma (n=142)	<i>p</i> value
Mean age±SD (years)	58±18	58±19	0.27
Mean SAPS II score±SD (points)	46±17	45±16	0.57
Prior functional status: limited activity (<i>n</i>)	47 (33.1)	56 (39.4)	0.27
Primary reason of mechanical ventilation			
Coma (<i>n</i>)	20 (14.1)	13 (9.2)	0.19
ARDS (<i>n</i>)	9 (6.3)	14 (9.9)	0.28
Sepsis (<i>n</i>)	13 (9.2)	8 (5.6)	0.26
Need for vasoactive drugs (<i>n</i>)	67 (47.2)	75 (52.8)	0.34
Need of neuromuscular blockers (<i>n</i>)	21 (14.8)	27 (19.0)	0.34
Peak pressure >50 cmH ₂ O (<i>n</i>)	3 (2.1)	6 (4.2)	0.50
Plateau pressure >35 cmH ₂ O (<i>n</i>)	8 (5.6)	10 (7.0)	0.63
ARDS (<i>n</i>)	14 (9.9)	19 (13.4)	0.35
Sepsis (<i>n</i>)	22 (15.5)	25 (17.6)	0.63
Shock (<i>n</i>)	37 (26.1)	36 (25.4)	0.89
Acute renal failure (<i>n</i>)	31 (21.8)	33 (23.2)	0.78
Hepatic failure (<i>n</i>)	11 (7.7)	10 (7.0)	0.82
Coagulopathy (<i>n</i>)	15 (10.6)	16 (11.3)	0.85
Metabolic acidosis (<i>n</i>)	14 (9.9)	9 (6.3)	0.28
PaO ₂ /FiO ₂ (<i>n</i>)			0.89
>300	32 (22.5)	26 (18.3)	
200–300	20 (14.9)	24 (16.9)	
150–200	42 (29.6)	42 (29.6)	
100–150	20 (14.1)	24 (16.9)	
<100	13 (9.2)	15 (10.6)	
Outcomes			
Median days of mechanical ventilation (IQR)	4 (2.7)	6 (2.12)	<0.001
Median length of stay in the ICU (IQR)	7 (4.14)	9 (5.18)	0.01

Numbers in parentheses are percentages

Table 5 Analysis of the mortality of barotrauma

	Patients without barotrauma (n=148)	Patients with barotrauma (n=148)	<i>p</i> value
Mean Age±SD (years)	59±18	57±19	0.28
Mean SAPS II score±SD (points)	46±17	45±16	0.34
Prior functional status: limited activity (<i>n</i>)	61 (41.2)	60 (44.5)	0.90
Primary reason of mechanical ventilation			
Coma (<i>n</i>)	13 (8.8)	13 (8.8)	1.00
ARDS (<i>n</i>)	10 (6.8)	15 (10.1)	0.30
Sepsis (<i>n</i>)	15 (10.1)	9 (6.1)	0.20
Need of vasoactive drugs (<i>n</i>)	73 (49.3)	83 (56.1)	0.24
Need of neuromuscular blockers (<i>n</i>)	23 (15.5)	30 (20.3)	0.29
Peak pressure >50 cmH ₂ O, n (%)	8 (5.4)	7 (4.7)	0.79
Plateau pressure >35 cmH ₂ O, n (%)	9 (6.1)	11 (7.4)	0.64
ARDS during mechanical ventilation (<i>n</i>)	16 (10.8)	21 (14.2)	0.38
Sepsis during mechanical ventilation (<i>n</i>)	25 (16.9)	29 (19.6)	0.54
Shock	44 (29.7)	45 (30.4)	0.90
Acute renal failure (<i>n</i>)	33 (22.3)	36 (24.3)	0.68
Hepatic failure (<i>n</i>)	11 (7.4)	11 (7.4)	1.00
Coagulopathy (<i>n</i>)	22 (14.9)	22 (14.9)	1.00
Metabolic acidosis (<i>n</i>)	17 (11.5)	10 (6.8)	0.16
PaO ₂ /FiO ₂ (<i>n</i>)			0.31
>300	28 (18.9)	26 (17.6)	
200–300	38 (24.3)	36 (25.7)	
150–200	54 (36.5)	43 (29.1)	
100–150	16 (10.8)	27 (18.2)	
<100	12 (8.1)	16 (10.8)	
Outcome			
Mean ICU mortality±SD	58 (39.2)	76 (51.4)	0.04

Numbers in parentheses are percentages

ventilatory support, from 5.8% (95% CI 4.3–7.8%) on day one to 13% (95% CI 10.6–15.6) on day 4.

The development of barotrauma has been associated with the ventilator settings, including mode [23], lung compliance below 30 ml/cm H₂O, higher airway pressures [6], plateau pressures above 35 cm H₂O [13], higher PEEP [12, 16] and higher tidal volume [9]; however, there are controversial data available from the two largest studies in patients with ARDS. In the report by Weg et al. [8], the development of barotrauma was not related to the ventilator airway pressures or tidal volumes, but it is important to point out that plateau pressures were not measured and peak and mean airway pressures were not elevated; however, Eisner et al. [12] found that after controlling for covariants [age, ventilator group (6 vs 12 ml/kg)], baseline PEEP, plateau pressure and tidal volume, and co-morbidities), higher PEEP was related to an increased risk of barotrauma [relative hazard (RH) 1.5; 95% CI 0.98–2.3]. In the study by Eisner et al. [12] both PEEP and FiO₂ were adjusted by protocol rules to achieve adequate levels of oxygenation. Higher requirements for PEEP and FiO₂ correlated with worse lung injury. In our study there was a trend towards higher PEEP in patients who experienced barotrauma. Recently, Bousarsar et al. [13], in a retrospective study and extensive literature review, identified a threshold in ventilator pressures above which barotrauma occurs. These investigators found a strong correlation with plateau pressure rather than peak inspiratory pressure, and described that plateau pressures below of 35 cmH₂O was not associated with barotrauma; thus, in these studies and in our report the low incidence of barotrauma could be related to the low plateau pressures, and patients that experience barotrauma are more likely to have worse lung condition, which required higher PEEP for oxygenation.

Barotrauma in mechanically ventilated patients has been associated with increased risk of mortality [1, 3, 7, 9]. We recently reported that barotrauma was an independent predictor of mortality during mechanical ventilation (RH 1.92; CI 95% 1.28–2.88) [21]. In a study of 100 patients with acute lung injury, barotrauma was an independent marker of mortality after adjusting for other factors [3]. Nevertheless, the authors considered that less than 2% of the deaths were attributable to pneumothorax

[3]. In patients with ARDS, Gattinoni et al. [1] reported that barotrauma was associated with a significant mortality (66 vs 46%; $p < 0.01$) and Amato et al. [9] found that the barotrauma and mortality were higher in patients ventilated with high tidal volumes and airway pressures. To determine if barotrauma itself contributes to morbidity and mortality, we used a matched-control analysis. Patients with similar clinical characteristics, with or without barotrauma were compared. We found significant differences between the cases and controls, including increased ICU and hospital length of stay and higher ICU mortality in the patients with barotrauma; thus, in a clinical setting where the plateau pressures and tidal volume are lower than the ones used in the control group by Amato et al. [9], barotrauma is associated with higher morbidity and mortality not related to the patients' disease severity and may be an independent marker of severity of illness.

Conclusion

In conclusion, our study confirms that in a cohort of mechanically ventilated patients where limited tidal volumes and airway pressures were used, barotrauma is present in a small number of patients, and is more closely related to the patient's underlying medical condition than to the ventilator parameters. Because clinicians have become aware of the dangers of excessive tidal volume and airway pressures, the incidence of barotrauma has drastically diminished; thus, when relative high tidal volumes and plateau pressures are avoided the ventilator pressures (peak pressure, plateau pressure and PEEP) and tidal volumes are not longer associated with increased risk of barotrauma. Finally, our data demonstrates that barotrauma is associated with increased morbidity or mortality.

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References

- Gattinoni L, Bombino M, Pelosi P, Lissoni A, Pesenti A, Fumagalli R, Tagliabue M (1994) Lung structure and function in different stages of severe adult respiratory distress syndrome. *J Am Med Assoc* 271:1772–1779
- Gammon RB, Shin MS, Buchalter SE (1992) Pulmonary barotrauma in mechanical ventilation. Patterns and risk factors. *Chest* 102:568–572
- Schnapp LM, Chin DP, Szaflarski N, Matthay MA (1995) Frequency and importance of barotrauma in 100 patients with acute lung injury. *Crit Care Med* 23:272–278
- Gammon RB, Shin MS, Groves RH, Hardin JM, Hsu C, Buchalter SE (1995) Clinical risk factors for pulmonary barotrauma: a multivariate analysis. *Am J Respir Crit Care Med* 152:1235–1240
- Cullen DJ, Caldera DL (1979) The incidence of ventilator-induced pulmonary barotrauma in critically ill patients. *Anesthesiology* 50:187–190

6. Petersen GW, Baier H (1983) Incidence of pulmonary barotrauma in a medical ICU. *Crit Care Med* 11:67–69
7. de Latorre FJ, Tomasa A, Klamburg J, Leon C, Soler M, Rius J (1977) Incidence of pneumothorax and pneumomediastinum in patients with aspiration pneumonia requiring ventilatory support. *Chest* 72:141–144
8. Weg JG, Anzueto A, Balk RA, Wiedemann HP, Pattishall EN, Schork MA, Wagner LA (1998) The relation of pneumothorax and other air leaks to mortality in the acute respiratory distress syndrome. *N Engl J Med* 338:341–346
9. Amato MBP, Barbas CSV, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CRRF (1998) Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med* 338:347–354
10. Stewart TE, Meade MO, Cook DJ, Granton JT, Hodder RV, Lapinsky SE, Mazer CD, McLean RF, Rogovein TS, Schouten BD, Todd TRJ, Slutsky AS (1998) Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. *N Engl J Med* 338:355–361
11. Brochard L, Roudot-Thoraval F, Roupie E, Delclaux C, Chastre J, Fernandez-Mondejar E, Clementi E, Mancebo J, Factor P, Matamis D, Ranieri M, Blanch L, Rodi G, Mentec H, Dreyfuss D, Ferrer M, Brun-Buisson C, Tobin M, Lemaire F (1998) Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 158:1831–1838
12. Eisner MD, Thompson T, Hayden D, Anzueto A, Matthay MA (2002) Airway pressures and early barotrauma in patients with acute lung injury and the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 165:978–982
13. Bousarsar M, Thierry G, Jaber S, Roudot-Thoraval F, Lemaire F, Brochard L (2002) Relationship between ventilatory settings and barotrauma in the acute respiratory distress syndrome. *Intensive Care Medicine* 28:406–413
14. Sepkowitz KA, Telzak EE, Jonathan W, Gold JW, Bernard EM, Blum S, Carrow M, Dickmeyer M, Armstrong D (1991) Pneumothorax in AIDS. *Ann Intern Med* 114:458–459
15. Kumar A, Pontoppidam H, Falke KJ, Wilson RS, Laver MD (1973) Pulmonary barotrauma during mechanical ventilation. *Crit Care Med* 4:181–186
16. Zwillich CW, Pierson DJ, Creagh CE, Sutton FD, Schatz E, Petty TL (1974) Complications of assisted ventilation: a prospective study of 354 consecutive patients. *Am J Med* 57:161–170
17. Argiras EP, Blakeler CR, Dunnill MS, Otremski S, Sykes MK (1987) High PEEP decreases hyaline membrane formation in surfactant deficient lung. *Br J Anaesth* 59:1278–1285
18. Woodring JH (1985) Pulmonary interstitial emphysema in the adult respiratory distress syndrome. *Crit Care Med* 13:786–791
19. Zimmerman JE, Dunbar BS, Klingensmaier CH (1975) Management of subcutaneous emphysema, pneumomediastinum, and pneumothorax during respiratory therapy. *Crit Care Med* 3:69–73
20. The Acute Respiratory Distress Syndrome Network (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 342:1301–1308
21. Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, Benito S, Epstein SK, Apezteguia C, Nightingale P, Arroliga AC, Tobin MJ, Mechanical Ventilation International Study Group (2002) A 28-day international study of the characteristics and outcomes in patients receiving mechanical ventilation. *J Am Med Assoc* 287:345–355
22. Le Gall JR, Lemeshow S, Saulnier FR (1993) A new simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *J Am Med Assoc* 270:2957–2963
23. Mathru M, Rao TLK, Venus B (1983) Ventilator-induced barotrauma in controlled mechanical ventilation versus intermittent mandatory ventilation. *Crit Care Med* 11:359–361
24. Williams TJ, Tuxen DJ, Scheindestel CD (1992) Risk factors for morbidity in mechanically ventilated patients with severe asthma. *Am Rev Respir Dis* 146:607–615