Original Article

Physiological Correlation of Airway Pressure and Transpulmonary Pressure Stress Index on Respiratory Mechanics in Acute Respiratory Failure

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Abstract

Background: Stress index at post-recruitment maneuvers could be a method of positive end-expiratory pressure (PEEP) titration in acute respiratory distress syndrome (ARDS) patients. However, airway pressure (P_{aw}) stress index may not reflect lung mechanics in the patients with high chest wall elastance. This study was to evaluate the P_{aw} stress index on lung mechanics and the correlation between P_{aw} stress index and transpulmonary pressure (P_L) stress index in acute respiratory failure (ARF) patients.

Methods: Twenty-four ARF patients with mechanical ventilation (MV) were consecutively recruited from July 2011 to April 2013 in Zhongda Hospital, Nanjing, China and Ospedale S. Giovanni Battista-Molinette Hospital, Turin, Italy. All patients underwent MV with volume control (tidal volume 6 ml/kg) for 20 min. PEEP was set according to the ARDSnet study protocol. The patients were divided into two groups according to the chest wall elastance/respiratory system elastance ratio. The high elastance group (H group, $n = 14$) had a ratio ≥30%, and the low elastance group (L group, $n = 10$) had a ratio <30%. Respiratory elastance, gas-exchange, P_{aw} stress index, and P_L stress index were measured. Student's *t*-test, regression analysis, and Bland–Altman analysis were used for statistical analysis.

Results: Pneumonia was the major cause of respiratory failure (71.0%). Compared with the L group, PEEP was lower in the H group (5.7 ± 1.7 cmH_2O vs. 9.0 ± 2.3 cmH_2O, $P < 0.01$). Compared with the H group, lung elastance was higher (20.0 ± 7.8 cmH_2O/L vs. 11.6 ± 3.6 cmH_2O/L, $P < 0.01$), and stress was higher in the L group (7.0 ± 1.9 vs. 4.9 ± 1.9, $P = 0.02$). A linear relationship was observed between the P_{aw} stress index and the P_L stress index in H group ($R^2 = 0.56$, $P < 0.01$) and L group ($R^2 = 0.85$, $P < 0.01$).

Conclusion: In the ARF patients with MV, P_{aw} stress index can substitute for P_L to guide ventilator settings.

Trial Registration: ClinicalTrials.gov NCT02196870 (https://clinicaltrials.gov/ct2/show/NCT02196870).

Key words: Airway Pressure; Lung Compliance; Pulmonary; Respiratory Failure; Stress

Introduction

Mechanical ventilation (MV) is an important treatment for acute respiratory failure (ARF) in that it can improve hypoxemia, maintain lung volumes, and recruit alveoli collapse.[1] However, because of barotrauma, volutrauma, and biotrauma, MV could cause or aggravate acute lung injury not only in acute respiratory distress syndrome (ARDS) patients but also in patients with normal lung function.[2,3]

The stress index, which traces the slope of the pressure-time curve during constant flow ventilation, could qualitatively detect alveolar tidal hyperinflation and tidal recruitment compared with static pressure-volume curves and computed tomography (CT) scan; therefore, titrated ventilator settings are preferred.[4,5] Grasso *et al*.[6] found that the stress index had the same accurate prediction of lung tidal hypertension and tidal recruitment in animals compared to CT scan. Huang *et al*.[7] indicated that the stress index at post-recruitment

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.185855

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Received: 22-01-2016 **Edited by:** Ning-Ning Wang
How to cite this article: Pan C, Chen L, Zhang YH, Liu W, Urbino R, Ranieri VM, Qiu HB, Yang Y. Physiological Correlation of Airway Pressure and Transpulmonary Pressure Stress Index on Respiratory Mechanics in Acute Respiratory Failure. Chin Med J 2016;129:1652-7.

maneuvers could be an excellent method of positive end-expiratory pressure (PEEP) titration in ARDS patients.

Nevertheless, the changes in respiratory system compliance do not reflect the lung compliance accurately, especially in patients with high chest wall elastance. Although transpulmonary pressure (P_L) could reflect the lung mechanics, the P_L stress index would require an esophageal catheter and a more complex calculation whereas the airway pressure (P_{aw}) stress index is measured noninvasively. The present study was designed to examine the effects of high chest wall elastance on changes of lung mechanics and the correlation between P_{aw} stress index and P_L stress index.

Methods

Patients

This study was a prospective physiological study. The protocol was approved by the Research Ethics Board of Zhongda Hospital (Southeast University, Jiangsu, China) and Ospedale S. Giovanni Battista-Molinette Hospital (Turin, Italy). Patients were consecutively recruited from July 2011 to April 2013 in Zhongda Hospital and Ospedale S. Giovanni Battista-Molinette Hospital, Turin. Written informed consent was obtained from substitute decision makers. The study was registered in http://www.ClinicalTrials.gov (No. NCT02196870).

Inclusion criteria were as follows: (1) minimum age of 18 years and <85 years of age, (2) duration of controlled MV for at least 36 h, (3) PaO_2/FiO_2 <300 mmHg (1 mmHg = 0.133 kPa), and (4) implementation of an esophageal catheter. Exclusion criteria were as follows: refusal of consent, hemodynamic instability (i.e., need for vasopressin, epinephrine at any dosage, or norepinephrine >5 μg/min, or dopamine or dobutamine >5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ to maintain systolic arterial blood pressure >90 mmHg), acute brain injury, upper gastrointestinal bleeding, pneumothorax, pneumomediastinum, chest tube with persistent air leak, severe vomiting, and contraindication to insertion of a gastric tube.

Experimental protocol

All patients meeting inclusion criteria were measured in a 30–45° semi-recumbent position under volume control MV. Patients were divided into two groups according to the ratio of chest wall elastance/respiratory system elastance. The high elastance group had a ratio ≥30%, and the low elastance group had a ratio <30%.[8]

Patients' preparation

Patients were administered a continuous infusion of morphine, fentanyl or remifentanil and propofol or midazolam for analgesia and sedation, and Richmond Agitation and Sedation Scales (RASSs) were 0–1. The patients were intubated and mechanically ventilated (Servo *i*, Maquet, Sweden) in the supine position, and ventilator settings were chosen by the physicians. An invasive artery line and an intravenous line were placed to monitor the arterial blood pressure and central venous pressure. An esophageal catheter was placed in an adequate position to measure esophageal pressure (P_{es}).[9]

Study protocol

At the initiation of the study, the patients were deeply sedated (RASS scales were −4–−5) without spontaneous breathing and ventilated in the control mode with a tidal volume (VT) of 6 ml/kg, respiratory rate of 15 breaths/min, inspiratory/expiratory ratio of 1:2, and a fraction of inspired oxygen and PEEP that were set according to the ARDSnet protocol.[10] A set of parameters was obtained 20 min later.

If patients experienced hypotension during sedation or high VT ventilation, fluid resuscitation was administered, and vasopressors was administered if necessary. If hypotension persisted after treatment, measurements had to be stopped, and the patient was withdrawn from the study.

Measurements

Respiratory elastance measurements

Flow was measured with a heated pneumotachograph (Ventrak 1550, Novametrix Company, USA) connected to a differential pressure transducer inserted between the Y-piece of the ventilator circuit and the endotracheal tube. The pneumotachograph was linear over the experimental range of flow. P_{aw} was measured proximal to the endotracheal tube with a pressure transducer. Changes in intrathoracic pressure were evaluated by assessment of P_{es}. The correct position of the esophageal balloon was verified by the occlusion test as previously described.[9] P_L was calculated by P_{aw} minus P_{es}. The pressure required to distend the respiratory system, named plateau pressure ($Pplat_{RS}$), and the pressure required to distend the lung, named end inspiratory P_L ($Pplat_L$). Total PEEP ($PEEP_{tot}$ = applied PEEP + intrinsic PEEP) of the respiratory system ($PEEP_{tot, RS}$) and of the chest wall ($PEEP_{tot, CW}$) were measured as the $Pplat_{RS}$ in P_{aw} and P_{es} during an end-expiratory occlusion, referenced to their values at the elastic equilibrium point of the respiratory system. All the variables described above were displayed and collected on a personal computer.

Static elastance of the respiratory system (Est_{RS}) was calculated with the following formula: $(Pplat_{RS} - PEEP_{tot, RS})/VT$. Static elastance of the chest wall (Est_{CW}) was calculated as $(Pplat_{CW} - PEEP_{tot, CW})/VT$. Static elastance of the lung (Est_L) was calculated as $Est_{RS} - Est_{CW}$.[11]

Stress index measurements

P_{aw} stress index and P_L stress index were measured as follows: flow, P_{aw}, and P_L signals were collected for a duration of 3 min every 5 min. The beginning and the end of each recorded breath by means of a threshold value (0.1 L/s) on the flow signal were identified. Individual flow and P_{aw} and P_L signals were hence averaged and smoothed by a filter that averaged the signal over a 120-millisecond time window. The beginning and the end of such a constant portion were marked by cursors onto the flow trace. To eliminate on and off flow transient, the constant flow portion was further narrowed by adding 50-millisecond offsets after the beginning (time 0) and before the end (time 1) of

the constant flow portion. The portions of mean P_{aw}-time and P_L-time curves encompassed in the time interval (time 0 – time 1) were fitted to the following equation using the Levenberg–Marquardt algorithm.[12] The R^2 value of the fitting was computed and displayed. The fitting algorithm provided the coefficients *a*, *b*, and *c* that best described the P_{aw}-time and P_L-time curve in such a time interval. The coefficient a represents the slope of the P_{aw}-time and P_L-time relationship in the time 0 – time 1 interval, and the coefficient *c* is the value of P_{aw} and P_L at time 0. The coefficient *b* (stress index) is a dimensionless number that describes the shape of the P_{aw}-time and P_L-time curves. The values of coefficient $b < 1$ indicate that compliance increases with time, whereas compliance decreases with time for the values of coefficient $b > 1$. Finally, $b = 1$ indicates a constant compliance during tidal inflation.[13] Calculations were aborted if one of the following conditions occurred: (1) the constant portion in the flow signal could not be found because of noise, artifacts, or air leakage; (2) the duration of the time 0 – time 1 interval was shorter than one-third of the inspiratory time; (3) the R^2 values of the fitting were 0.95; and/or (4) the values of coefficient b calculated on the first and second half of the time 0 – time 1 interval were either both lower than, higher than, or equal to 0.9–1.1.[13]

Stress measurements

Stress was calculated according to the formula: $\text{Stress} = (\text{Pplat}_{RS} - \text{PEEP}) \times \text{Est}_L/\text{Est}_{RS}$.[14]

Gas-exchanges

Arterial blood gasses, included pH, PCO_2, PO_2, PO_2/FiO_2, were measured.

Statistical analysis

According to former study, Albaiceta *et al*.[15] recruited ten ARDS patients to assess the differences in lung mechanics between ARDS from pulmonary (ARDSp) and extrapulmonary (ARDSe) origin, the results found there is differences between ARDSp and ARDSe lung mechanics are present in the P_{es}-volume curve, but also in the P_L-volume curve, therefore, in our physiological study, the sample size was 10 in each group. Sample size calculation showed that seven patients per group would provide 80% power at a two-sided α level of 0.05 to detect a 0.15 difference in P_{aw} stress index and P_L stress index.

Data are presented as the mean ± standard deviation (SD). Comparisons between the two groups were performed followed by a Student's *t*-test for the samples. A $P < 0.05$ indicated significant differences. Regression analysis was performed with the least-squares method. The consistency of the P_{aw} stress index and P_L stress index was evaluated by Bland–Altman analysis. Statistical analysis was performed using the software SPSS 20.0 (IBM, USA).

Results

There were 24 patients enrolled in the study, and all patients completed the study protocol. The Acute Physiology, Age, and Chronic Health Evaluation II (APACHE II) score was 16.7 ± 4.4, and pneumonia (71%) was the major condition that induced respiratory failure in the patients. PO_2/FiO_2 was 215.5 ± 49.5 mmHg. The P_{aw} stress index was 0.96 ± 0.11, and the P_L stress index was 0.98 ± 0.15 [Table 1].

Effects of chest wall elastance on respiratory elastance and oxygenation

The patients were divided into two groups according to the former study:[8] a high chest wall elastance group (H group) whose chest wall/respiratory system elastance was higher than 30% and a low chest wall elastance group (L group) whose chest wall/respiratory system elastance was lower than 30%. Compared with the L group, the PEEP setting was low in the H group (5.7 ± 1.7 cmH_2O vs. 9.0 ± 2.3 cmH_2O, $P < 0.01$). However, no significant difference was observed in oxygenation (219.5 ± 66.0 mmHg vs. 212.6 ± 36.0 mmHg, $P = 0.74$) and respiratory system elastance (24.9 ± 8.6 cmH_2O/L vs. 21.0 ± 6.0 cmH_2O/L, $P = 0.21$) between L and H groups [Table 2]. Compared with the H group, lung elastance was higher (20.0 ± 7.8 cmH_2O/L vs. 11.6 ± 3.6 cmH_2O/L, $P < 0.01$), and stress was higher (7.0 ± 1.9 cmH_2O vs. 4.9 ± 1.9 cmH_2O, $P = 0.02$) in the L group. The results showed that lung injury was more severe in the L group than in the H group [Table 2].

Correlation of stress index in airway pressure and transpulmonary pressure in the H group

No difference was observed between the stress index in P_{aw} and P_L (0.94 ± 0.11 vs. 0.99 ± 0.11, $P = 0.24$). A highly significant correlation was found between

Table 1: Clinical baseline characteristics of the acute respiratory failure patients ($n = 24$)

Parameters	Value
Age (years), mean ± SD	73.83 ± 11.17
Sex (male/female)	12/12
Surgical patients, *n* (%)	5 (21)
Medical patients, *n* (%)	19 (80)
Cause of ARF, *n* (%)	
Pneumonia	17 (71)
Intestinal obstruction	3 (13)
Hepatapostema	1 (4)
Pancreatitis	1 (4)
Transfusion-related acute lung injury	1 (4)
Inspiration	1 (4)
APACHE II, mean ± SD	16.7 ± 4.4
PEEP (cmH_2O), mean ± SD	7.0 ± 2.5
PaO_2/FiO_2 (mmHg), mean ± SD	215.5 ± 49.5
Est_{RS} (cmH_2O/L), mean ± SD	22.6 ± 7.3
Est_L (cmH_2O/L), mean ± SD	15.1 ± 7.0
Est_{CW} (cmH_2O/L), mean ± SD	7.5 ± 3.7
P_{aw} stress index, mean ± SD	0.96 ± 0.11
P_L stress index, mean ± SD	0.98 ± 0.15

APACHE II: Acute Physiology, Age, and Chronic Health Evaluation II; Est_{RS}: Respiratory system elastance; Est_L: Lung elastance; Est_{CW}: Chest wall elastance; P_{aw} stress index: Airway pressure stress index; P_L stress index: Transpulmonary pressure stress index; PEEP: Positive end-expiratory pressure; ARF: Acute respiratory failure; SD: Standard deviation.

Table 2: Comparison of lung mechanics and oxygenation between high and low chest wall elastance groups (mean ± SD)

Parameters	H group (n = 14)	L group (n = 10)	t	P
Age (years)	75.9 ± 9.7	71.0 ± 13.0	1.1	0.30
APACHE II	14.1 ± 3.9	16.7 ± 2.4	−1.9	0.07
PaO_2/FiO_2 (mmHg)	212.6 ± 36.0	219.5 ± 66.0	−0.3	0.74
PEEP (cmH_2O)	5.7 ± 1.7	9.0 ± 2.3	−4.1	0.00
Est_{RS} (cmH_2O/L)	21.0 ± 6.0	24.9 ± 8.6	−1.3	0.21
Est_L (cmH_2O/L)	11.6 ± 3.6	20.0 ± 7.8	−3.6	0.00
Est_{CW} (cmH_2O/L)	9.4 ± 3.5	4.9 ± 1.9	3.7	0.00
Est_{CW}/Est_{RS}	0.45 ± 0.09	0.20 ± 0.08	7.0	0.00
Stress	4.9 ± 1.9	7.0 ± 1.9	−2.7	0.02
P_{aw} stress index	0.94 ± 0.11	0.99 ± 0.11	−1.1	0.24
P_L stress index	0.98 ± 0.16	1.02 ± 0.20	−5.4	0.59

H group: High chest wall elastance group; L group: Low chest wall elastance group; APACHE II: Acute Physiology, Age and Chronic Health Evaluation II; Est_{RS}: Respiratory system elastance; Est_L: Lung elastance; Est_{CW}: Chest wall elastance; P_{aw} stress index: Airway pressure stress index; P_L stress index: Transpulmonary pressure stress index; SD: Standard deviation.

P_{aw} and P_L in the H group. In the linear regression analysis, the correlation coefficient R^2 of the stress index in P_{aw} and P_L is 0.56 ($P < 0.01$) [Figure 1]. According to the Bland–Altman analysis, all data were distributed on a mean ± 2SD scale (Bias: −0.04 ± 0.11, 95% limits of agreement: −0.25–0.17) [Figure 2]. The results suggested that for the patients with high chest wall elastance did not act on the P_{aw} stress index, and the P_{aw} stress index and P_L stress index were consistent in evaluating lung mechanics.

Correlation of stress index in airway pressure and transpulmonary pressure in the L group

No difference between the P_{aw} stress index and the P_L stress index was observed in the L group (0.98 ± 0.16 vs. 1.02 ± 0.20, $P = 0.49$). A correlation was found between P_{aw} and P_L, and the correlation coefficient R^2 of the stress index in P_{aw} and P_L was 0.85 ($P < 0.01$) [Figure 3]. According to the Bland–Altman analysis, all were distributed on a mean ± 2SD scale (Bias: −0.03 ± 0.11, 95% limits of agreement: −0.25–0.18) [Figure 4]. The results showed that for the patients with chest wall elastance/respiratory system elastance lower than 30%, the P_{aw} stress index was similar to the P_L stress index in evaluating lung mechanics.

Discussion

High chest wall elastance plays a role in lung mechanics and it could influence stress index sometimes; however, high chest wall elastance did not work on P_{aw} stress index in respiratory failure patients in this study. The main finding of the present study was that the P_{aw} stress index can substitute for P_L in MV for patients with ARF.

The respiratory system consists of the lungs and the chest wall. P_{aw} acts on the respiratory system and can be divided into P_L and transchest wall pressure. Therefore, at the

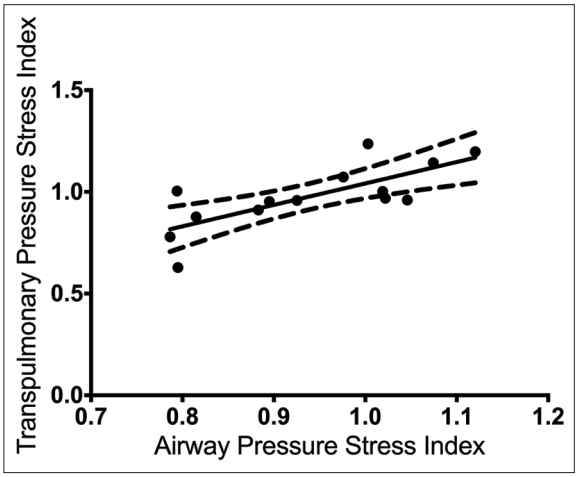

Figure 1: Correlation between P_{aw} stress index and P_L stress index in H group ($n = 14$). Regression equation of the line: $Y = 1.054x \times -0.01249$, $R^2 = 0.56$, $P < 0.01$. P_{aw}: Airway pressure; P_L: Transpulmonary pressure; H group, high chest wall elastance group.

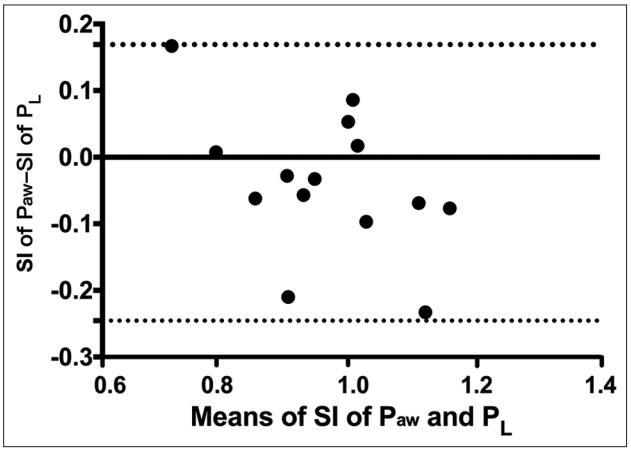

Figure 2: Bland–Altman analysis of P_{aw} stress index and P_L stress index in H group ($n = 14$). Bias: −0.04 ± 0.11, 95% limits of agreement: −0.25–0.17. P_{aw}: Airway pressure; P_L: Transpulmonary pressure; SI: Stress index; H group: High chest wall elastance group.

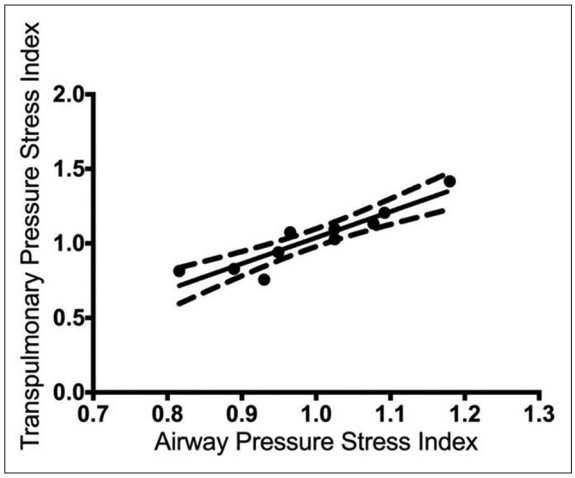

Figure 3: Correlation between P_{aw} stress index and P_L stress index in L group ($n = 10$). Regression equation of the line: $Y = 1.749x \times -0.7106$, $R^2 = 0.85$, $P < 0.01$. P_{aw}: Airway pressure; P_L: Transpulmonary pressure; L group: Low chest wall elastance group.

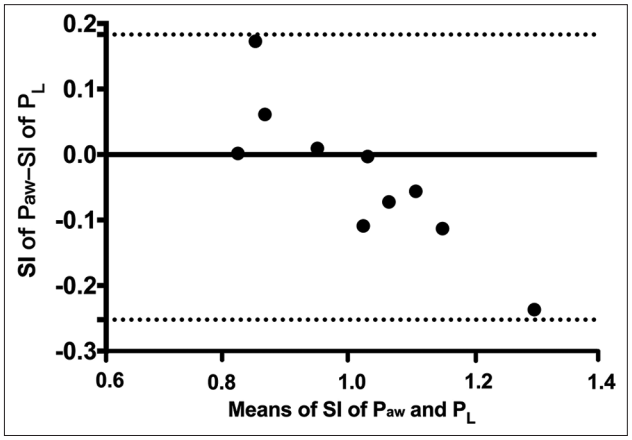

Figure 4: Bland–Altman analysis of P_{aw} stress index and P_L stress index in L group (n = 10). Bias: −0.03 ± 0.11, 95% limits of agreement: −0.25–0.18. P_{aw}: Airway pressure; P_L: Transpulmonary pressure; SI: Stress index; L group: Low chest wall elastance group.

same airway $Pplat_{RS}$, if the chest wall elastance increases, transchest wall pressure increases and P_L decreases accordingly. If the effects of high chest wall elastance are ignored, a misunderstanding of the changes in lung elastances could occur.[11] In our study, no difference in oxygenation and respiratory system elastance was observed between the two groups; however, compared with the L group, lung injury was less severe in the H group. Therefore, lung elastance and lung stress were lower in the H group. The results mean that for the patients with high chest wall elastance on MV settings, respiratory mechanics could be influenced.

The stress index traces the shape of the dynamic pressure-time profile during constant flow inflation, which can be useful in predicting the mechanical stress needed to minimize ventilator-induced lung injury (VILI).[16] Ranieri *et al*.[16] proved that stress index is the index of P_L changes with time during constant flow, when lung elastances are constant, P_L changes linearly with time (stress index is between 0.9 and 1.1), and the lung injury, inflammatory factors releasing are less than the conditions of P_L changes nonlinearly with time (stress index is <0.9 and more than 1.1) in isolated lung model of acute lung injury. However, it is not easy to measure P_L in the clinical setting. Many experimental and clinical studies have shown that the P_{aw} stress index allows prediction of an optimal ventilatory strategy that could minimize the occurrence of VILI.[4,6,17] In a clinical study, the P_{aw} stress index was used to titrate PEEP in ARDS patients and it could improve lung compliance, alveolar overinflation, and end-expiratory lung volume and decrease the release of inflammatory factors.[7] However, a clinical study found that only 66% of the P_{aw} stress index was equal to the P_L stress index.[8] In a later animal study involving a large pleural effusion, when the P_{aw} stress index >1, the CT scan showed significant amounts of alveolar collapse in the dependent lung area and no obvious overdistention in the nondependent lung area.[18] This finding suggests that when the chest wall elastance increases, the P_{aw} stress index may not reflect lung mechanics.

The P_{aw} stress index could be used to reflect lung mechanics in the patients with pulmonary ARF. Owens monitored 22 pneumonia-induced ARF patients and found that the P-V curve of the respiratory system could reflect the changes in lung elastance.[19] Pereira found that changes in chest wall elastance only influenced the lower inflection point of the respiratory system P-V curve, and the effects of the chest wall on respiratory mechanics could be compensated by PEEP.[20] Therefore, Grasso *et al*. and Terragni *et al*.[4,21] showed that the P_{aw} stress index and the P_L stress index have a good correlation in ARDS patients. The results were similar in our study. Twenty-four ARF patients were involved in this study, and the P_{aw} stress index and the P_L stress index showed a linear correlation. The P_{aw} stress index could be substituted for the P_L stress index, which reflects changes in lung mechanics.

Our study showed that the P_{aw} stress index was equal to the P_L stress index when chest wall elastance/respiratory system elastance >30%, this result suggests that chest wall elastance changes had no effects on respiratory system elastance in the high chest wall elastance group. This result was the same in Mergoni's study, in which Mergoni *et al*.[22] found that chest wall elastance did not change with the increase in P_{aw} in patients with ARF. However, when the P_L stress index was too low, the P_{aw} stress index may not be equal to the P_L stress index. The reason could be related to the impact of the lower inflection point of the chest wall P-V curve on the respiratory system P-V curve. This reason could explain why the P_{aw} stress index was not equal to the P_L stress index in the high chest wall elastance group in Chiumello's study.[8]

Limitations in our study are as follows: (1) respiratory P-V curves are not monitored in our study. (2) Patients involved were not administered lung-recruited and PEEP titration. The purpose of the study was to observe the physiological effects of the chest wall on MV patients and the relationship between the stress index of P_L and P_{aw}. The effects of lung recruitment and PEEP on the results were not observed. (3) Patients with suspected high intra-abdominal pressure were not involved in our study. Therefore, the results could not explain the relationship between the stress index of P_L and P_{aw} in high intra-abdominal-pressure patients with a stiff chest wall.

In conclusion, high chest wall elastance plays a role in lung mechanics; however, high chest wall elastance did not work on P_{aw} stress index in respiratory failure patients in this study. It is worth remarking, however, that this physiological study was performed on a limited number of patients and that further studies on the stress index of P_L and P_{aw} in patients with a stiff chest wall are clearly necessary to ascertain whether the advantage suggested by our data is reliable.

Financial support and sponsorship

This study was supported by the grants from the National Natural Science Foundation of China (No. 81300043, No. 81370180, and No. 81501705), and the Natural Science Foundation of Jiangsu Province (No. H201434).

Conflicts of interest

There are no conflicts of interest.

References

1. Xie J, Qiu H. Mechanical ventilation in acute respiratory distress syndrome: Past, present and future. Chin Med J 2014;127:1801-3. doi: 10.3760/cma.j.issn.0366-6999.20140560.
2. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med 2013;369:2126-36. doi: 10.1056/NEJMra1208707.
3. dos Santos CC. The role of the inflammasome in ventilator-induced lung injury. Am J Respir Crit Care Med 2012;185:1141-4. doi: 10.1164/rccm.201204-0649ED.
4. Grasso S, Stripoli T, De Michele M, Bruno F, Moschetta M, Angelelli G, *et al.* ARDSnet ventilatory protocol and alveolar hyperinflation: Role of positive end-expiratory pressure. Am J Respir Crit Care Med 2007;176:761-7. doi: 10.1164/rccm.200702-193OC.
5. Ferrando C, Suárez-Sipmann F, Gutierrez A, Tusman G, Carbonell J, Garcia M, *et al.* Adjusting tidal volume to stress index in an open lung condition optimizes ventilation and prevents overdistension in an experimental model of lung injury and reduced chest wall compliance. Crit Care 2015;19:9. doi: 10.1186/s13054-014-0726-3.
6. Grasso S, Terragni P, Mascia L, Fanelli V, Quintel M, Herrmann P, *et al.* Airway pressure-time curve profile (stress index) detects tidal recruitment/hyperinflation in experimental acute lung injury. Crit Care Med 2004;32:1018-27. doi: 10.1097/01.CCM.0000120059.94009.AD.
7. Huang Y, Yang Y, Chen Q, Liu S, Liu L, Pan C, *et al.* Pulmonary acute respiratory distress syndrome: Positive end-expiratory pressure titration needs stress index. J Surg Res 2013;185:347-52. doi: 10.1016/j.jss.2013.05.012.
8. Chiumello D, Mietto C, Protti A, Berto V, Marino A, Gallazzi E, *et al*. Stress index: Is the airway pressure a good surrogate of the transpulmonary pressure? Am J Respir Crit Care Med 2010;181:1. doi: 10.1164/ajrccmconference.2010.181.1_MeetingAbstracts.A4076.
9. Chiumello D, Guérin C. Understanding the setting of PEEP from esophageal pressure in patients with ARDS. Intensive Care Med 2015;41:1465-7. doi: 10.1007/s00134-015-3776-3.
10. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342:1301-8. doi: 10.1056/NEJM200005043421801.
11. Gattinoni L, Chiumello D, Carlesso E, Valenza F. Bench-to-bedside review: Chest wall elastance in acute lung injury/acute respiratory distress syndrome patients. Crit Care 2004;8:350-5. doi: 10.1186/cc2854.
12. Kermani BG, Schiffman SS, Nagle HT. Using neural networks and genetic algorithms to enhance performance in an electronic nose. IEEE Trans Biomed Eng 1999;46:429-39. doi: 10.1109/10.752940.
13. Ranieri VM, Zhang H, Mascia L, Aubin M, Lin CY, Mullen JB, *et al.* Pressure-time curve predicts minimally injurious ventilatory strategy in an isolated rat lung model. Anesthesiology 2000;93:1320-8. doi: 10.1097/00000542-200011000-00027.
14. Protti A, Andreis DT, Monti M, Santini A, Sparacino CC, Langer T, *et al.* Lung stress and strain during mechanical ventilation: Any difference between statics and dynamics? Crit Care Med 2013;41:1046-55. doi: 10.1097/CCM.0b013e31827417a6.
15. Albaiceta GM, Taboada F, Parra D, Blanco A, Escudero D, Otero J. Differences in the deflation limb of the pressure-volume curves in acute respiratory distress syndrome from pulmonary and extrapulmonary origin. Intensive Care Med 2003;29:1943-9. doi: 10.1007/s00134-003-1965-y.
16. Ranieri VM, Vitale N, Grasso S, Puntillo F, Mascia L, Paparella D, *et al.* Time-course of impairment of respiratory mechanics after cardiac surgery and cardiopulmonary bypass. Crit Care Med 1999;27:1454-60. doi: 00003246-199908000-00008.
17. Fanelli V, Mascia L, Puntorieri V, Assenzio B, Elia V, Fornaro G, *et al.* Pulmonary atelectasis during low stretch ventilation: "Open lung" versus "lung rest" strategy. Crit Care Med 2009;37:1046-53. doi: 10.1097/CCM.0b013e3181968e7e.
18. Formenti P, Graf J, Santos A, Gard KE, Faltesek K, Adams AB, *et al.* Non-pulmonary factors strongly influence the stress index. Intensive Care Med 2011;37:594-600. doi: 10.1007/s00134-011-2133-4.
19. Owens RL, Hess DR, Malhotra A, Venegas JG, Harris RS. Effect of the chest wall on pressure-volume curve analysis of acute respiratory distress syndrome lungs. Crit Care Med 2008;36:2980-5. doi: 10.1097/CCM.0b013e318186afcb.
20. Pereira C, Bohé J, Rosselli S, Combourieu E, Pommier C, Perdrix JP, *et al.* Sigmoidal equation for lung and chest wall volume-pressure curves in acute respiratory failure. J Appl Physiol (1985) 2003;95:2064-71. doi: 10.1152/japplphysiol.00385.2003.
21. Terragni PP, Filippini C, Slutsky AS, Birocco A, Tenaglia T, Grasso S, *et al.* Accuracy of plateau pressure and stress index to identify injurious ventilation in patients with acute respiratory distress syndrome. Anesthesiology 2013;119:880-9. doi: 10.1097/ALN.0b013e3182a05bb8.
22. Mergoni M, Martelli A, Volpi A, Primavera S, Zuccoli P, Rossi A. Impact of positive end-expiratory pressure on chest wall and lung pressure-volume curve in acute respiratory failure. Am J Respir Crit Care Med 1997;156(3 Pt 1):846-54. doi: 10.1164/ajrccm.156.3.9607040