The transpulmonary pressure as an indicator of lung stress in the disorder of chest wall mechanics in pediatric acute lung injury: Study in pig model

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Abstract

Objectives: To determine the role of the end-inspiratory transpulmonary pressure as an indicator of the lung stress in the disorder of chest wall mechanics, in pig model.

Design: Experimental study.

Setting: Department of Surgery and Radiology, Veterinary Medicine, Bogor Agricultural Institute.

Subjects: Nine healthy mixed breed domestic piglets were divided into 2 groups: intervention/splinted chest wall (n=5) and control (n=4).

Intervention: This study had approval from Animal Care and Use Committee. The care and handling animal were accorded with National Institute of Health guideline. All of animals were anesthetized, muscle paralyzed and bronchial lavage with warm saline, in supine position. Both group were mechanically ventilated and underwent lung recruitment using incremental-decremental technique. Chest wall splinting was conducted in intervention group while the control group did not.

Measurement and Main Results: Transpulmonary pressures calculated after measure the esophageal pressure using esophageal catheters. The transpulmonary pressure in intervention group prior to (1.80±2.28 cmH2O) and after (11.00±5.83 cmH2O) recruitment maneuver, increased significantly compared with control group prior to (1.25±3.68 cmH2O) and after (3.25±1.18 cmH2O), with p value 0.04. The difference of mean end-inspiratory transpulmonary pressure (Ptp plateau) between intervention and control group was significant (p=0.05). ∆Ptp plateau values have strong correlation with the increasing of chest wall elastance (Ecw) in the intervention group (p=0.001, R^2=0.8) and control group (p=0.007, r=0.7), as well as the correlation of ∆Ptp plateau with decreasing the lung compliance (Cl) (p=0.05, r=0.8). The strong correlation between ∆Ptp plateau and ∆Paw (p=0.001, r=0.7) in the intervention group showed the potency of the transpulmonary pressure to reflect the real lung distending pressure and the lung stress.

Conclusions: The measurement of end-inspiratory transpulmonary pressure is reliable as an indicator of lung stress in disorder of chest wall mechanics.

Key words: Disorder of chest wall mechanics, the end-inspiratory transpulmonary pressure, lung stress.

Introduction

Acute respiratory failure that cause by acute lung injury (ALI) remains a serious problem in critically ill children. (1) It was about 2.2 to 12 per 100,000 children per year suffered ALI, with 18-60% mortality. (2-4) Multi organ failure (45.8%) and refractory hypoxemia (19.3%) are the highest cause of death, even though the improvement of ventilator machine technology and lung protective strategic protocol had applied. (5-7) Mechanical ventilation in ALI is an essential component in fulfilling the supply oxygen to various organs and is the only treatment that has been proven to reduce the mortality of ALI/ARDS significantly. (8) The inappropriate use of mechanical ventilation may worsen lung damage that has occurred because it could increase cytokines activity and induced a series of inflammatory cells cascade that aggravate structure of the lung damage. (9)

For many decades, pressure-based respiratory mechanics have serve to the judgment of clinician monitoring mechanical ventilation based on airway pressure (Paw) alone. (10,11) Currently the essence of giving respiratory support with a conventional ventilator is titration of pressure at the airway opening (Pao), which is based on the assump-
ation of that this pressure is equal to transpulmonary pressure (PL). (10,11) In the disorder of chest wall mechanics, optimization of plateau pressure at the end of inspiration is more suitable as a final expression of distension pressure inspiration. (12) Recruitment maneuver is useful to prevent collapse of the alveoli by increasing transpulmonary pressure. (13) Frequently, recruitment maneuver performed based on the lung compliance (Cl) but does not consider the chest wall elastance (Ecw), which is alternation by the surrounding environment. (14-17) The esophageal pressure measurement and the transpulmonary pressure calculation can directly be used as a guide in PEEP changes. (16,18,19) More evidences are needed on the accuracy of esophageal pressure measurements in patients with disorder of chest wall mechanics to reflect as the real intra-thoracic pressure. (12,18) Therefore, we try to achieve and determine the role of the end-inspiratory transpulmonary pressure as an indicator of lung stress in the disorder of chest wall mechanics, in pig model.

Material and Methods
This study is an experimental study which was conducted in Faculty of Veterinary Medicine, Bogor Agricultural Institute, Eijkman Institute and Faculty of Medicine, University of Indonesia in November 2011-March 2013. We used Sus scrofa, 1.5 to 3-month-old, 5-10 kg body weight as an animal model to mimic 9-month- to 2-year-old pediatric patients. We included the healthy piglet, with 5-10 kg, and underwent isolation phase for 2 weeks. Exclusion criteria were piglets confirmed have anatomic shunt in the heart by echocardiography and the laboratory results were incomplete. Total minimal sample needed for this study was 10 piglets, 5 piglets for each group.

All the animal model underwent adaptation and isolate period, pre-research screening included physical examination, blood test and gas analysis, radiologic and echocardiography. Then all the animal experienced sedation and anesthesia intubation, ventilation, warm saline installation for bronchoalveolar lavage (BAL), recruitment maneuver (RM) with incremental-decremental PEEP technique and euthanasia. The piglets were anesthetized by combination of ketamine, xylazine intra muscular (IM) (20 mg/kgBW, 2 mg/kBW, respectively), followed by atropine (0.04 mg/kgBW), propofol (4 mg/kgBW/hour), midazolam (0.5 mg/kgBW/hour) and fentanyl (0.005 mg/kgBW/hour). One mg/kgBW/dose vecuronium (IV) every 30 minutes was given to maintain deep sedation. Before and after recruitment maneuver, respiration and hemodynamic data were documented. In intervention group, the animal experienced chest wall splinting at the 60-mmHg splinting pressure in purposed to disturb the chest wall. The transpulmonary pressure was calculated by measuring the esophageal pressure using the esophageal catheter. Measurement of esophageal pressure used in this study refers to the measurement technique developed by Milic-Emili et al. and Baydur et al. in their experimental studies.

Data was displayed in charts, tables, and manuscripts. Data was analyzed include the descriptive and comparative analysis. Normality of each data was tested with Shapiro-Wilk test. All values were reported as means±SD unless otherwise some parameters used median. The comparison before and after intervention within each group was analyzed by pair t test, while the comparison between intervention group and control group was analyzed using t independent test. Difference were considered to be statistically significant if p value<0.05 and 95% confidence intervals. The correlation between two data was also analyzed by Pearson’s test for normal distribution data, and Spearman test for not normal distributed data.

Results
Characteristic of the animal model
The mean value of body weight was 5.680±1.362 kg (intervention group) and 6.250±1.121 kg (control group). The difference of mean body weight between intervention and control group were not statistically significant (p>0.05). All the animal models were 1.5-month-old and dominate by male gender (Table 1).

Respiratory pressure before and after recruitment maneuver
The mean value of airway pressure (∆Paw) which were needed to expand the collapse lung before recruitment maneuver was 7 (6-7) cmH2O and 19 (14-24) cmH2O after recruitment maneuver in intervention group. In this group, the differences in mean value of airway pressure was significant (p=0.043). It was contrary to the control group which was the mean value of airway pressure before recruitment maneuver 6.50 (5.00-8.00) cmH2O compare to after recruitment maneuver 11.50 (11.00-37.00) cmH2O (p=0.05).

In intervention group, the mean value of end inspiratory transpulmonary pressure (Ptp plateau) was 8.60±2.30 cmH2O before and 30.00±6.89 cmH2O after recruitment maneuver (p=0.002). Significant difference was also showed in the mean
value of Ptp plateau in the control group. Before recruitment maneuver it was 5.20±3.40 cmH2O and after it was 14.50±4.50 cmH2O (p=0.007).

In this study, the lung stress value was equal to the value of ∆PL=∆Ptp plateau, which is the driving force of lung inflation, influenced by the difference of airway pressure and the pressure in the surrounding of the lungs. The value of ∆Ptp plateau obtained in this study in the intervention group prior to (1.80±2.28 cmH2O) and after (11.00±5.83 cmH2O) the recruitment maneuver increased significantly compared to this control group prior to (1.25±3.68 cmH2O) and after (3.25±1.18 cmH2O) the maneuver. The difference of ∆Ptp plateau value between the two groups was statistically significant (p=0.049) (Table 2).

Correlation between the pressure of respiratory system with the elastance and compliance
In this study the value of end inspiratory transpulmonary pressure (Ptp plateau) had strong correlation with chest wall elastance (p=0.001, r=0.8, R²=0.8) and lung compliance (p=0.007, r= -0.7, R²=0.6). It can be seen in Figure 1, the elastance increased proportionally to the value of Ptp plateau. On the contrary, Figure 2 reveals that lung compliance decrease consistently with Ptp plateau value. The mean value of Ptp plateau in this study was increased constantly, higher than the mean value of airway pressure. The strong correlation between ∆Ptp plateau and ∆Paw (p=0.050, R²=0.4) in the intervention group and (p=0.000, R²=0.9) in the control group, showed that the value of transpulmonary pressure reflected intra-thoracic pressure in the mechanical disorder of chest wall (Figure 3).

Discussion
In the intervention group, the mean value of airway pressure (∆Paw) before and after recruitment maneuver was 7 (6-7) cmH2O and 19 (14-24) cmH2O respectively. These differences were statistically significant (p=0.043), differed with ∆Paw in control group (p>0.05).

Monitoring of airway pressure in this study reveals general appearance of ALI. Mean value of airway pressure (∆Paw) needed to inflate collapsed lung in splinted animal model before recruitment maneuver was 7 (6-7) cmH2O and after recruitment maneuver was 19 (14-24) cmH2O. In splinted group, the difference of airway pressure value was significant (p=0.043), but not in the control group (p>0.05). The mean value of airway pressure was 6.50 (5-8) cmH2O before recruitment maneuver and was 11.50 (11-37) cmH2O after recruitment maneuver. There was a wide interval of airway pressure value after recruitment maneuver in both groups. This might be caused by the peak inspiratory pressure (PIP), it highly increased from 9 cmH2O to 28 cmH2O in splinted group and 10 cmH2O to 18 cmH2O in control group.

Very high increase in airway pressure is needed to open airway against chest wall (splinting) pressure to enable lung expansion. The ratio PaO2/FiO2 was decrease obviously in splinted group. It is assumed the collapsed lung was more severe in the splinted group, and therefore required higher pressure to open lungs and suffice gas exchange.

In splinted group, mean value of Ptp plateau was 8.60±2.30 cmH2O before recruitment maneuver and 30.00±6.89 cmH2O after recruitment maneuver (p=0.002). Significant difference also was in the mean value of Ptp plateau in the control group. Before recruitment maneuver it was 5.20±3.40 cmH2O and after it was 14.50±4.50 cmH2O with p value of 0.007 (Table 2).

The mean airway and transpulmonary pressure data showed the transpulmonary pressure consistently changes and increases both in intervention and control groups. The mean of end-inspiratory transpulmonary pressure was much higher in the splinted than control group might be caused by increasing of the intrapulmonary pressure while esophageal pressure remains constant. Splinted chest wall using constant pressure created esophageal pressure, which was measured to represent pleural pressure that did not change in the stiff chest wall.

Transpulmonary pressure measurement and its correlation with chest wall mechanic
In daily clinical practice, airway pressure in proximal end of airway is one of the indicator in monitoring lung inflation. This method is considered have many disadvantages, especially incapacity to demonstrate the real pressure inside the lung. Moreover, this limitation causes inadequate oxygenation and ventilation, albeit maximum pressure is given. Along with mechanical properties laid on the normal chest wall, the airway pressure still useful and accurate. But when it comes to unsynchronize movement between lung and breathing muscle, the value is no longer accurate.

In other condition, the diaphragmatic wall fails to swing freely due to the pressure given by the abdominal wall, resulting in the increase of pressure in the chest cavity. This clinical condition is seen in children with increased intra abdominal pressure due to mechanical cause or inflammation (for example abdominal distention in sepsis and necrotiz-
necrotizing enterocolitis). Pediatric patients with phrenic nerve paralysis, which plays important role in the movement of respiratory muscles, would face the same difficulties due to failure in inflating their chest wall. In a condition of unsynchronized elastance and compliance between lung and the chest wall, a guideline providing more accurate information regarding the magnitude of gas pressure by the ventilator is necessary.

Gattinoni (19) presented a theory and paradigm to re-assess the mechanics of respiration, especially a more in-depth understanding of the elastance and compliance of the respiratory system. It is based on the fact that nearly 30% of cases treated with ventilator in ICU presented with increased intra-abdominal pressure secondary to various causes, which would result in increased chest wall elastance. The administration of airway pressure would increase the pleural pressure with the implication of decreased transpulmonary pressure, which is the pressure of lung movements; thus, increasing the need to maintain the pressure to keep the airway open. The results would be increased airway pressure with the risk of decreased venous return and hemodynamic disturbances. (18)

A study by Chiumello (12) using human subjects suggested that specific lung elastance has a constant value of approximately 13.5 cmH2O that unchanged with the change of ventilator setting. In this study, lung elastance was reported to be 3 times (intervention group/high elastance) to 4 times higher (control group/low elastance) than the study by Chiumello et al. (12) This may be because the bronchial lavage procedure performed here caused severe damages in lung function.

In this study, the stress value documented was equal to the value of ∆Ptp ≈ ∆Ptp plateau, which is the driving force of lung inflation, influenced by the difference of airway pressure and the pressure in the surrounding of the lungs. The value of ∆Ptp plateau obtained in this study in animals in the intervention group prior to (1.80±2.28 cmH2O) and after (11.00±5.83 cmH2O) the recruitment maneuver increased significantly compared to the animal in control group prior to (1.25±3.68 cmH2O) and after (3.25±1.18 cmH2O) the maneuver. The difference of ∆Ptp plateau value between the two groups of animal models was statistically significant, with p value of 0.049.

∆Ptp plateau represents inspiratory transpulmonary pressure, which was the driving force of lung expansion. The value of ∆Ptp plateau (= ∆PL) was assumed from the amount of stress given to lungs. ∆V represents lung volume that was inflatable by applying pressure. Value of ∆V describes distention of the lungs.

From the tabulation of airway pressure parameters and their correlation with pressure and elastance and compliance, we can derive this respiratory mechanics equation:

1. $E_{cw}=\Delta PL/\Delta V$
2. $E_{rs}=\Delta Paw/\Delta V$
3. $EL=\Delta Paw-\Delta PL/\Delta V$
4. $Value of E_{cw}$ increases, while $\Delta V$ is kept constant, and therefore $\Delta PL$ increases.

$EL=\text{constant}, \Delta V$ is constant. In control group, $\Delta PL$ was found to be significantly higher than that of splinted group. Hence, it required higher $\Delta Paw$ to achieve the same $\Delta V$. Lung stress and its correlation with lung injury may be judged by stress manifestation and consequences within respiratory system function or to lungs as the organ target. The driving pressure needed to inflate lungs as the manifestation of lung stress was the $P_{tp}$ plateau. (12,20)

Strain and stress of the lungs are major determinants of VILI and not measured in daily practice, therefore some studies aim to find surrogate parameters, such as clinical criteria, plateau airway pressure and tidal volume according to ideal body weight. (21)

**Conclusion**

1. The mean value of transpulmonary pressure in this study increased constantly, higher than the mean value of airway pressure ($\Delta Paw$).
2. The end-inspiratory transpulmonary pressure ($\Delta P_{tp}$ plateau) was associated with the increasing of chest wall elastance and decreasing lung compliance, before and after recruitment maneuver.
3. Strong correlation between $\Delta P_{tp}$ plateau and $\Delta Paw$ in both groups, showed that transpulmonary pressure could reflect the intra-thoracic pressure. So that it could indicate lung stress in the disorder of chest wall mechanic in pig model.

**Recommendation**
The incremental-decremental technique of recruitment maneuver had proved able to treat hypoxemia in ALI. Measurement of the transpulmonary pressure using esophageal catheter might be applied in monitoring intra-thoracic pressure in infants and children. Further study is needed to evaluate the use of transpulmonary pressure as a guide during recruitment maneuver in infants and children in attempts to reduce lung stress due to over distention.
### Table 1. Characteristics of animal model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention group (n=5)</th>
<th>Control group (n=4)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>1.5</td>
<td>1.5</td>
<td>-</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>5.680±1.362</td>
<td>6.250±1.121</td>
<td>0.523</td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>3</td>
<td>-</td>
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</table>

### Table 2. Respiratory pressure parameters in intervention group compared to control group, pre and post RM

<table>
<thead>
<tr>
<th>Parameter (cmH2O)</th>
<th>Intervention group</th>
<th>Control group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Median (min-max)</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Pes</td>
<td>Pre</td>
<td>1.20±0.84</td>
<td>1.00±0.82</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>1.20±0.84</td>
<td>1.25±0.96</td>
</tr>
<tr>
<td>PIP</td>
<td>Pre</td>
<td>9 (9-11)</td>
<td>10 (8-11)</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>28 (18-42)</td>
<td>18 (14-42)</td>
</tr>
<tr>
<td>PEEP</td>
<td>Pre</td>
<td>3 (2-4)</td>
<td>3 (3-4)</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>10 (4-18)</td>
<td>4.5 (3-9)</td>
</tr>
<tr>
<td>ΔPaw</td>
<td>Pre</td>
<td>7 (6-7)</td>
<td>6.50 (5-8)</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>19 (14-24)</td>
<td>11.50 (11-37)</td>
</tr>
<tr>
<td>Ptp plateau</td>
<td>Pre</td>
<td>8.60±2.30</td>
<td>5.25±3.40</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>30.00±6.89</td>
<td>14.50±4.51</td>
</tr>
<tr>
<td>Ptp PEEP</td>
<td>Pre</td>
<td>2.80±2.77</td>
<td>1.75±2.87</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>10.60±7.33</td>
<td>6.00±5.48</td>
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<tr>
<td>ΔPtp plateau</td>
<td>Pre</td>
<td>1.80±2.28</td>
<td>-1.25±3.68</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>11.00±5.83</td>
<td>-3.25±1.18</td>
</tr>
<tr>
<td>ΔPtp PEEP</td>
<td>Pre</td>
<td>-3.00</td>
<td>-9.00 -2.00</td>
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<tr>
<td></td>
<td>Post</td>
<td>-8.400±4.393</td>
<td>-11.75±1.32</td>
</tr>
</tbody>
</table>

Legend: Pes=esophageal pressure; PIP=peak inspiratory pressure; PEEP=positive end-expiratory pressure; ΔPaw=gradient PIP-PEEP; Ptp plateau=end-inspiratory transpulmonary pressure; Ptp PEEP=end-expiratory transpulmonary pressure; ΔPtp plateau=gradient end-inspiratory transpulmonary pressure; ΔPtp PEEP=gradient end-expiratory transpulmonary pressure
**Figure 1.** Correlation between ΔPtp plateau and Ecw

**Figure 2.** Correlation between ΔPtp plateau and Cl
Figure 3. Correlation between ΔPtp plateau and Paw

![Graph showing correlation between ΔPtp plateau and Paw]
References