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Potential effect of pulmonary fluid viscosity on positive end-expiratory pressure and regional distribution of lung ventilation in acute respiratory distress syndrome

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ABSTRACT

Background: Computational fluid dynamic simulations have showed that the elevated viscosity of pulmonary fluids may increase the likelihood of airway closure, thus exacerbating inhomogeneity of regional lung ventilation. Unfortunately, there have been few studies directed toward measurements of viscosity of pulmonary fluids and its effect on airway opening pressure and regional distribution of lung ventilation in acute respiratory distress syndrome.

Methods: In this study, pulmonary fluids from 8 ARDS patients were measured using a cone and plate rheometer on days 1, 3, 7 and 14 in the treatment of the disorder. Ventilator settings were simultaneously recorded, including tidal volume, positive end-expiratory pressure, fraction of inspired oxygen (FiO\textsubscript{2}), and so on. The regional distribution of lung ventilation was monitored by a bedside electrical impedance tomography system.

Findings: The results showed that rheological properties of pulmonary fluids behaved as either Newtonian or non-Newtonian across all patients studied. Significant intersubject and intrasubject variations in measured viscosities were observed, spanning ranges from approximately 1 cP to 7 \times 10^4 cP at shear rates between 0.075 – 750 s\textsuperscript{-1}.

The product of the positive end-expiratory airway pressure and fraction of inspired oxygen was well correlated with fluid viscosity in patients with high viscosity pulmonary fluids. Furthermore, lung ventilation in these patients was highly inhomogeneous and influenced by rheology of pulmonary fluids.

Interpretation: The current findings provided the direct clinical data for theoretical models of airway reopening and may have important clinical implications in explaining inhomogeneity of lung ventilation and selecting initial levels of positive end-expiratory pressure in mechanically ventilated patients.

1. Introduction

Acute respiratory distress syndrome (ARDS) constitutes a syndrome of acute hypoxemic respiratory failure that arises from disruption of the alveolar-capillary membrane and influx of protein-rich edema fluid into the air spaces, a hallmark of this condition (Laffey and Matthay, 2017). It accounts for more than 10% of intensive care unit admissions and has a morality rate of approximately 30% to 40% (Thompson et al., 2017).

Risk factors for ARDS include direct lung-injury factors (e.g., pneumonia and aspiration of gastric content) or indirect injury (e.g., sepsis and pancreatitis).

In the management of ARDS, the protective lung ventilation strategy has utilized moderate to high levels of positive end-expiratory pressure (PEEP) to mitigate the repeated recruitment/derecruitment (atelectrauma) and to improve oxygenation (Meade et al., 2008). The optimal level of PEEP, however, remains debated. From a mechanical point of
view, the levels of the pressure (P) needed to open a small airway or an
alveolus are determined by the tissue tethering force (P_t), hydrostatic
pressure (P_{hydro}), the surface tension at the air-liquid interface (P_s)
and viscous pressure from pulmonary fluids (P_v) (Chen et al., 2015; Whang
et al., 2017), as stated in the following equation:

\[ P = P_t + P_{hydro} + P_s + P_v \]  

(1)

For a single patient, the elastic stress term P_t can be taken as constant
in the acute phase of ARDS because the properties of the connective
tissue of the lung do not change. Therefore, variations in P are mainly
calculated by P_{hydro}, P_s and P_v, which are further dependent on changes of
physical properties of the pulmonary edema fluid in the course of the
disorder. Gaver III and coworkers (Gaver et al., 1990; Gaver et al., 2006)
experimentally obtained a set of regression formula Eq. 2 and Eq. 3 used
to calculate P_s and P_v, respectively.

\[ P_s = \frac{8 \gamma}{R} \]  

(2)

\[ P_v = 7.7 \mu \rho \Gamma \]  

(3)

where capillary number is defined as Ca \(= \frac{\mu U}{\gamma}\), \(\mu\) is viscosity, \(U\) is the
velocity of airway opening, \(\gamma\) represents surface tension, and \(R\) repre-
sents the radius of airway.

Eq. 2 and Eq. 3 clearly show that an increase in surface tension or
viscosity of pulmonary fluids can result in an increase in P_s or P_v, thus a
higher PEEP needed to keep small airways or alveoli open at end expi-
ration. Recently, Chen and Colleagues found that approximately one-
quarter to one-third of patients with ARDS who were mechanically
ventilated at low PEEP exhibited airway closure (Chen et al., 2017; Sun
et al., 2017). Airway closure exacerbates inhomogeneity of regional lung
ventilation that is likely associated with ventilator-induced lung injury
(VILI) (Bellani et al., 2016). Yamaguchi et al. demonstrated that the
distribution and dynamic surface tension of pulmonary surfactant were
important for enhancing the recruitment uniformity in an asymmetric
airway bifurcation (Yamaguchi et al., 2014; Yamaguchi et al., 2017).
Unfortunately, there have been few studies directed toward measure-
ments of viscosity and surface tension of pulmonary fluids and its effect
on PEEP and regional distribution of lung ventilation in ARDS.

Motivated by theoretical calculations and clinical studies reviewed
above, we want to know about a rough range of viscosity of pulmonary
fluids in patients with ARDS of different origins. Therefore, in this study
we used a plugged telescopic catheter to obtain pulmonary fluids in 8
patients with ARDS and measured fluid apparent viscosity in a cone and
plate rheometer. Based on measurements of viscosity, we further
addressed the following two objectives: (1) to describe the macro-
roheology of pulmonary fluids; and (2) to investigate the potential effect
of pulmonary fluids viscosity on the level of PEEP and the regional
distribution of lung ventilation.

2. Methods

2.1. Patients and study design

We enrolled 8 ARDS patients from March 2018 to December 2019 in
the surgical intensive care unit (SICU) of Zhongshan Hospital Fudan
University. The study was granted by the institutional review board of
the hospital, and written informed consent was obtained from the pa-
tients or their surrogates. The baseline characteristics of the patients
were recorded immediately after the diagnosis of ARDS was made.
Thereafter, all patients were managed throughout the entire study by
the Acute Respiratory Distress Syndrome Network’s low-tidal volume
ventilation protocol (Acute Respiratory Distress Syndrome, N, et al.,
2000). The pulmonary fluids were collected using a bronchoalveolar
lavage catheter (cat. No. CF12; XiangSheng Medical Products, Shanghai,
China) on days 1, 3, 7 and 14. The viscosity of the fluids was determined
by a cone and plate rheometer (Model DV3TLV; Brookfield Engineering
Laboratories, Inc., Middleboro, MA, USA). To assess the regional lung
ventilation distribution at a specific level of PEEP, we attached a 16-elec-
 trode belt to each patient’s thorax. The belt was connected to a bedside
electrical impedance tomography (EIT) continuous recording system
(PulmoVista 500, Dräger Medical GmbH, Lübeck, Germany). On each
observation day, we measured status images of three thoracic cross-
sectional planes along a cephalocaudal axis in the supine position,
which correspond to the lung apex, middle lung and lung base,
respectively.

2.2. Collection of pulmonary fluids

In the first place, the telescoping catheter was inserted into the
endotracheal tube via an access port adapter, with the curved tip of the
catheter directed toward the desired lung. The catheter was then
advanced until gentle resistance was met, after which the inner catheter
was advanced further along the tracheobronchial tree until resistance
confirmed a “wedged” position in a subsegmental bronchus (up to the 5th
generation bronchus) to avoid contamination with proximal large
airway secretions (Leong et al., 2013). Finally, the fluids were aspirated
using a syringe connected to the end of catheter and collected in air tight
plastic containers. Physiological saline was not allowed to instill into the
lung to avoid dilution of pulmonary fluids during the operation of the
catheter. We took 1 ml of fluids for the immediate measurement of
viscosity and the rest of specimens was stored at ~80 °C in the frigo-
zer compartment of refrigerators for other microbiological analysis. When
thawing frozen specimens caution must be taken not to allow the fluids
to expose at room temperature for a long time because changes in the
fluid composition and its viscosity will occur.

2.3. Measurements of viscosity

A Wells-Brookfield DV3T cone/plate rheometer was adopted for
measuring viscosity of pulmonary fluids. Depending on the cone in use,
the DV3T cone/plate rheometer can determine viscosity of as small as
0.5–2.0 ml samples, particularly suitable to applications where sample
availability is limited such as biological fluids. An external water bath
was connected to the sample cup to maintain the temperature of the
sample under test at 37 °C (body temperature). Prior to each set of
viscosity measurements, the spindle and sample cup were rinsed with
95% ethanol and dried with gauze. The spindle position was adjusted to
a gap height of 0.0005 in. (0.0013 mm) above the surface of the plate.

One milliliter of pulmonary fluids at room temperature was placed in
the center of the sample cup. The sample cup was then attached to the
rheometer. After one- to two-minute interval for thermal equilibrium,
the rotational speed of the spindle was gradually increased to the
maximum of 250 revolutions per minute (rpm), corresponding to shear
rate 1875 s⁻¹, followed by a deceleration over the same range. Note that
the shear rate equals the shear rate constant multiplying by the rota-
tional speed in rpm for the spindle used. Each specimen was then sub-
jected to all rotational speeds of the instrument even though the %
Torque reading may not be in the recommended range of 10–100%. At
any given shear rate, the end condition of the test was configured as the
elapsed time greater than 20 s for a steady viscosity state. Rheograms
were obtained indicating how viscosity can change as a function of both
rotational speed (shear rate) and time.

3. Results

The main demographic and clinical characteristics and pulmonary
fluid viscosity, as well as outcomes, are summarized in Table 1. Signif-
icant intersubject and intrasubject variations in measured values of
viscosity were observed, spanning viscosity ranges as high as 7×10⁴
centipoise (cP) and as low as approximately 1 cP (viscosity of water at
room temperature). Of note, the examined eight ARDS patients could be
divided into two groups according to the measured viscosity values. The
Table 1
Patients characteristics, outcomes and pulmonary fluid viscosity.

| Patient No. | PaO2 (mm Hg) | Respiratory Rate (breaths/min) | Tidal Volume (ml/kg PBW) | PEEP (cm H2O) | FiO2 | Respiratory-System Complianceb (ml/cmH2O) |
|-------------|---------------|-------------------------------|--------------------------|---------------|------|------------------------------------------|
| 1           | 72.8          | 125                           | 25                       | 18            | 4.9  | 4.9                                      |
| 2           | 53.3          | 74.2                          | 16                       | 20            | 5.0  | 5.0                                      |
| 3           | 95.9          | 110                           | 17                       | 17            | 6.0  | 6.0                                      |
| 4           | 104           | 128                           | 18                       | 18            | 6.5  | 6.5                                      |
| 5           | 44.7          | 56.1                          | 18                       | 18            | 9.0  | 9.0                                      |
| 6           | 57            | 80.6                          | 36                       | 8             | 8.0  | 8.0                                      |
| 7           | 71.8          | 95                            | 18                       | 20            | 8.1  | 8.1                                      |
| 8           | 55            | 126                           | 22                       | 20            | 8.0  | 8.0                                      |
| Mean        | 69.3          | ±21.2                         |                           |               | ±6.9 | ±6.9                                      |

Definition of abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation score (the score can range from 0 to 71, higher scores correspond to more severe disease and a higher risk of death); cP = centipoise; D = died; NA = Not available; Pack yr = 20 cigarettes/day for one year; S = survived.

*For patients who died or were discharged while breathing without assistance during the first 14 days data are not available on some days.*

Fig. 1. Representative rheograms of pulmonary fluids from two ARDS patients. Panels a and b represent relationship between viscosity (cP) and shear rate (rpm) on pulmonary fluids from patient 1 and 8, respectively. Panels c and d represent viscosity as a function of shear time (s) for pulmonary fluids from patient 1 and 8, respectively. cP = centipoise, rpm = revolutions per minute, and the shear rate equals the shear rate constant (SRC) multiplying by the rotational speed in rpm for the rheometer used. The SRC is 7.5 and 2 in panels a and b, respectively.
first group (gray rows in Table 1) included patients 1, 2 and 3 whose pulmonary fluids had relatively low viscosities (approximately less than 100 cP). Consistent with naked-eye observation, this type of fluid had good fluidity. The second group included patients 4 to 8 whose pulmonary fluids exhibited strikingly high viscosity. Visually, this type of fluid resembled semi-solids. It did not flow easily and often tightly adhered to the wall of container.

Furthermore, representative rheograms of pulmonary fluids from two groups are shown in Fig. 1. Samples of whole blood from healthy humans (square) and 0.9% NaCl solution (triangle) were used as reference standards of known Newtonian viscosity. The pulmonary fluids from patient 1 (Fig. 1a and c) behaved as a Newtonian fluid, that is, when the shear rate was varied, the viscosity almost remained constant (Fig. 1a). Moreover, the fluids' viscosity did not change with time when subjected to a constant shear speed of 50 rpm (Fig. 1c). In contrast, the pulmonary fluids from patient 8 (Fig. 1b and d) exhibited the behavior of a non-Newtonian fluid: firstly, the fluids displayed a decreasing viscosity with an increasing shear rate called shear-thinning, a typical characteristic of pseudoplastic fluid. Secondly, the fluids showed a progressive decrease in viscosity with shearing action time when exposed to a constant shear speed of 5 rpm (Fig. 1d). This effect is termed “thixotropy”. Note that non-Newtonian properties like shear-thinning or thixotropy were only observed in ARDS patients with high-viscosity pulmonary fluids.

The viscosity of pulmonary fluids and the corresponding PEEP as well as FiO2 in four ARDS patients with high viscosity pulmonary fluids are shown in Fig. 2. We found that data points on days 1, 3 and 7 in patients 4 and 6 fall nearly on a straight line. We therefore additionally measured viscosity and recorded respiratory values on days 5 and 10 in patients 7 and 8 (not shown in Table 1) for statistically significant results. As was expected, the correlation between the viscosity and product of applied PEEP and FiO2 was highly significant and almost close to identity (R^2 = 0.9837, p = 0.0082 and R^2 = 0.9955, p = 0.0023 in patients 7 and 8, respectively).

Functional EIT images of two representative ARDS patients (patients 1 and 7) are reported in Fig. 3. Regions of interest (RoIs) within a status image are defined as four adjacent quadrants positioned in an upper left/right and lower left/right arrangement. Numerical values in the RoIs represent regional minute impedance changes that occur in each of regions as a percentage of the whole electrode plane, i.e., regional distribution of ventilation over the last minute. In patient 1, most of ventilation was delivered to the ventral lung regions (RoI 1 and RoI 2), and visually there are no significant changes in the regional distribution of ventilation between days 1 and 3. In contrast in patient 7, the lung ventilation tended to be more and more homogenous over time, with ventilation mostly occurring in RoI 1 on day 1, afterwards was delivered to the whole ventral lung regions (RoI 1 and RoI 2) on day 3, and finally distributed to both ventral and dorsal lung regions on day 7. We further invoked the global inhomogeneity index (GI) suggested by Zhao et al. (Zhao et al., 2009) to quantitatively evaluate the degree of inhomogeneity of the intrapulmonary air distribution.

It is interesting to note that the viscosity of pulmonary fluids in patient 7 paralleled a tendency for gradual decrease from day 1 to day 3 and then to day 7; while the viscosity of pulmonary fluids in patient 1 did not show similar changes on days 1 and 3. The relation between the viscosity and the GI index is shown in Fig. 4. In patient 7, as the pulmonary fluid viscosity reduced from day 1 to day 7, the GI indices also decreased accordingly. Considering both patients ventilated at the same PEEP levels (8 cmH₂O), we speculated that variation in viscosity of pulmonary fluids from patient to patient and also day to day was an important factor that resulted in imbalances of regional lung ventilation.

4. Discussion

The computational fluid dynamic simulation and in vitro experimental models of airway reopening have demonstrated that a marked rise in pulmonary fluid viscosity could render mechanical stresses associated with airway reopening to increase, probably inflicting injury to the pulmonary epithelium (Bilek et al., 2003; Gaver et al., 2006; Chen et al., 2015; Stewart and Jensen, 2015). In this clinical study, we therefore measured the changes of viscosity of pulmonary fluids in eight ARDS patients in the course of the syndrome. Furthermore, we investigated the possible associations between viscosity and respiratory parameters as well as regional distribution of lung ventilation. The main findings of this study were that: (1) the viscosity of pulmonary fluids was in a wide range of from ~1 cP to more than 10^4 cP at shear rates between 0.075–750 s⁻¹. Rheological properties of pulmonary fluids were complex, behaving as either Newtonian or non-Newtonian fluid across the whole ARDS patients; (2) our data supported the theoretical prediction that for ARDS patients with high pulmonary fluid viscosity the product of therapeutic PEEP and FiO2 was well correlated with fluid viscosity (Gaver et al., 1990; Gaver et al., 2006; Low et al., 1997), suggesting the viscous forces were the predominant factor for airway opening; whereas for ARDS patients with low pulmonary fluid viscosity such correlation was not observed; and (3) continuous bedside monitoring of mechanical ventilation using EIT showed that the regional distribution of lung ventilation in ARDS patients was highly inhomogeneous and influenced by physical properties of pulmonary fluids such as the amount of edema, surface tension and viscosity.

The cone and plate rheometer is the most commonly used device in the literature for measurement of pulmonary fluid viscosity (Chen et al., 2019; Lai et al., 2009). The current measurement is agreement with literature data on properties of pulmonary fluid macro rheology (Table 2). As compared with other pulmonary disorders, for instance cystic fibrosis (CF), COPD, chronic bronchitis or bronchiectasis, the rheological behavior of pulmonary fluids in ARDS is more complicated. It transitions deep in the lung from a non-Newtonian, two-layered fluid in the proximal airways to a single layer of Newtonian fluid that is primarily saltwater, yet with significant concentrations of surfactant and plasma proteins. In addition, the layer of Newtonian fluid is likely to convert into non-Newtonian fluid due to a variety of causes of lung injury or in different phases of the syndrome (Fan et al., 2018; Laffey and Matthay, 2017).

The current measurements of pulmonary fluid viscosity provided the direct clinical data for theoretical models of airway reopening proposed by Gaver III and coworkers (Gaver et al., 1990; Gaver et al., 2006) and Stewart and Jensen (Stewart and Jensen, 2015). Computational models showed that there existed good correlation between airway opening pressures and viscosities in a fraction of patients whose pulmonary fluid viscosity was relatively high. However, this preliminary study only
indicated the correlation between the fluid viscosity and the product of PEEP × \(\text{FiO}_2\) instead of PEEP alone. It can be further seen from Fig. 3 that in patient 7 the viscosity on days 1 and 3 are clearly different in spite of the same PEEP settings (8 cmH\(_2\)O) on these days. One possible reason is that we set the value of PEEP according to \(\text{FiO}_2/\text{PEEP}\) combinations as recommended by the ARDSnet ventilation protocol. Theoretically, the viscosity will exhibit a good correlation with the level of PEEP only if the latter is set based on the maximum static lung compliance while simultaneously keeping constant \(\text{FiO}_2\). But this is usually unacceptable in clinical treatment for a minimal intervention in patients with ARDS.

**Table 2**

| Reference | Viscosity(cP) | Technique          |
|-----------|--------------|--------------------|
| Human (recurrent bronchitis) (Puchelle, 1981) | \(2.48 \times 10^4\) | Concentric cylinder rheometer |
| Human (mild chronic bronchitis) (Puchelle, 1981) | \(1.14 \times 10^4\) | Concentric cylinder rheometer |
| Human (severe chronic bronchitis) (Puchelle, 1981) | \(1.25 \times 10^4\) | Concentric cylinder rheometer |
| Human (Bacconais et al., 1999) | 200 | Cone and plate rheometer |
| Human (CF) (Bacconais et al., 1999) | 600 | Cone and plate rheometer |
| Human (Jeanneret-Grosjean et al., 1988) | \((1.2-1.5) \times 10^5\) | Magnetic microrheometer |
| Human (CF) (Dawson et al., 2003) | \(-7 \times 10^4\) | Cone and plate rheometer |
| Calf lung surfactant dispersions (King et al., 2001) | 38 | Cone and plate rheometer |
| Human (CF) (Feather and Russell, 1970) | 21–134 | Cone and plate rheometer |
| Human (chronic bronchitis) (Feather and Russell, 1970) | 117–144 | Cone and plate rheometer |
| Human (bronchiectasis) (Feather and Russell, 1970) | 58 | Cone and plate rheometer |
| Human (ARDS) (the current study) | \(0.97-7.76 \times 10^4\) | Cone and plate rheometer |

cP = centipoise; CF = cystic fibrosis.

Fig. 3. EIT images of ARDS patients 1 (top row) and 7 (bottom row) showing different regional distribution of ventilation. The image of a cross-sectional plane of the chest is divided into 4 regions of interest (ROIs) and arranged as quadrants. Numerical values in the ROIs represent regional minute impedance changes that occur in each of regions as a percentage of the whole electrode plane, i.e., regional distribution of ventilation over the last minute. The left, middle, and right panels show images at the same thoracic plane on days 1, 3 and 7 respectively. cP: centipoise; \(\mu\): viscosity; NA: data are Not Available because of the death of the patient.

Fig. 4. Relationship between the logarithmic viscosity of pulmonary fluids and the global inhomogeneity index in two ARDS patients.
Quantitative measurements of pulmonary fluid viscosity and surface tension may therefore have important clinical implications. First, the quantitative measurements of surface tension and viscosity make it possible to roughly estimate the initial levels of PEEP required in performing a recruitment maneuver. Second, lung volume recruitment maneuvers may be an important component of a lung protective ventilation strategy. Similarly, knowing the values of viscosity and surface tension of pulmonary fluids help clinicians determine the individualized inflation pressure and PEEP required in performing a recruitment maneuver (Fan et al., 2008;Gattinoni et al., 2006). Third, a number of in-vitro experimental studies (Silek et al., 2003; Huh et al., 2007; Kay et al., 2004) have demonstrated that lung epithelial cells may be subjected to severe damage when mechanical stresses generated during airway reopening exceed the safe thresholds. The determination of viscosity and surface tension enables us to make an approximate estimation of mechanical stresses by computational models, thereby adjusting the ventilation settings or therapeutic strategy in time so as to avoid VILI as much as possible. Finally, measurements of pulmonary fluids provide an objective means for evaluating mucolytic aerosol therapy in ARDS patients.

An interesting finding was that for a fraction of patients with highly viscous pulmonary fluids the regional distribution of ventilation became more homogeneous as viscosity decreased during the treatment course. It is possible that the decrease in fluid viscosity was caused by the resolution of the inflammatory cells and the reduction of mucus production as the lung recovered. More even distribution of ventilation suggested more patent airways or lung units. Of note, the settings of PEEP in patient 7 (Fig. 3) did not show an increasing trend over time, and therefore we speculated that the opening of more airways or lung units may be attributed to a decrease of critical airway or alveolar opening pressure, which in turn depends on viscosity and surface tension of pulmonary fluids (Chen et al., 2015; Gaver et al., 1990; Gaver et al., 2006). In addition, future studies should consider the effects of other factors such as the intra-abdominal pressure or amount of pulmonary fluid on regional lung ventilation.

In spite of only a small number of patients enrolled in our study, we found that the emerging EIT in combination with rheological measurements of pulmonary fluids is a promising technique in monitoring the regional distribution of ventilation and titrating PEEP at bedside in mechanically ventilated ARDS patients (Frerichs et al., 2017; Kobylanski et al., 2016; Muders et al., 2010). The current study confirmed an inhomogeneous regional distribution of gas in ARDS, as previously observed byGattinoni, Puybasset and coworkers on CT scan (Gattinoni et al., 2001; Puybasset et al., 2000) and by Victorino and coworkers using EIT (Victorino et al., 2004). It is morphological alterations and differences in physical properties of pulmonary fluids together, we believe, that result in lung ventilation inhomogeneity in ARDS patients.

It is important to address the potential limitations of the present study. Firstly, the purified pulmonary fluids from small airways down to alveoli are not readily available due to difficulty in collection. Samples obtained may be contaminated with purulent secretions originated from the large airways if the tip of the catheter was not advanced into the desired bronchial subsegment. Secondly, the underlying diseases of ARDS may be inhomogeneous; therefore, pulmonary fluids may differ from various parts of the lung. In the future study, we will take multiple fluid samples from different lung subsegments and analyze the test samples in the laboratory to confirm that the fluid under examination is from the lower respiratory tract or the alveolar space (Du Rand et al., 2013). Thirdly, it is difficult to recover sufficient volumes of intra-alveoli fluid if small airways are occluded with large amount of purulent sputum. Finally, our finding in only a few patients must be interpreted with caution when extrapolated to the whole ARDS patients, especially when trying to analyze the relationship between fluid viscosity and regional distribution of lung ventilation. Further measurements in more ARDS patients will be required to examine this hypothesis.

5. Conclusions

To our knowledge, this is the first study to introduce the measurements of pulmonary fluid viscosity into the monitoring of ARDS patients. These preliminary results showed a large degree of variation in viscosity of pulmonary fluids between patients, and some subjects showed Newtonian fluid properties while others were non-Newtonian. By using EIT technique, we observed that in the course of ARDS the regional distribution of lung ventilation changed as viscosity of pulmonary fluids did, and therefore, this difference in rheological properties of pulmonary fluids may provide a possible explanation for inhomogeneity of lung mechanics in ARDS. Furthermore, we found that the viscosity of pulmonary fluids and the product of PEEP × FiO2 had a good correlation in a fraction of ARDS patients who had highly viscous pulmonary fluids. Future studies are needed to prove that in another fraction of patients who had relatively low viscosity pulmonary fluids, surface tension was the primary contribution to airway opening pressures.

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Author statement

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Declaration of Competing Interest

No conflicts of interest, financial or otherwise, are declared by the author(s).

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