Measurement of Functional Residual Capacity and Pulmonary Carbon Monoxide Diffusing Capacity during Mechanical Ventilation with PEEP

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First, our new simplified method to measure FRC and $D_{LCO}$ simultaneously during mechanical ventilation was described in detail. Secondly, we applied the method to ARDS patients and observed the effects of PEEP on arterial blood gases (ABGs), FRC and $D_{LCO}$ of these patients. As reported hitherto, FRC was consistently increased by PEEP, whereas ABGs in some cases were not necessarily improved with increase in FRC. $D_{LCO}$/FRC remained unchanged, although $D_{LCO}$ increased with PEEP.

We concluded that the dissociation of FRC and ABG data in a group of patients could be caused by wasted ventilation which might be attributed to $V_A/Q$ uneveness.

(Key Words: Functional Residual Capacity, Pulmonary Diffusing Capacity, PEEP, ARDS)

INTRODUCTION

One of the recent advances in respiratory care for adult respiratory distress syndrome (ARDS) is in employing positive end-expiratory pressure (PEEP) with mechanical ventilation.

Such a sophisticated method of respiratory care, however, resulted in some difficulty in assessing ventilatory functions in the course of treatment. Conventionally, arterial blood gas analysis and chest radiography have been used to evaluate the pathophysiological status of patients. However, many cases have been seen in which results of such diagnostic procedures showed some discrepancy from the patient's actual clinical status. Therefore, measurements of pulmonary functions during mechanical ventilation becomes very important and necessary for respiratory care.

We have developed a simplified system for determining functional residual capacity (FRC) and pulmonary carbon monoxide diffusing capacity ($D_{LCO}$) simultaneously during mechanical ventilation with PEEP in the intensive respiratory care unit or in the regular ward. In the present study, we describe the method and rationale of the measuring system as well as the results of clinical applications to patients of ARDS, focusing on the effects of PEEP on arterial blood gas, FRC and $D_{LCO}$.

MATERIALS AND METHODS

The apparatus is illustrated in Fig. 1. A compartment for FRC meas-
Measurement was originally designed by Heldt and his coworkers (6). They measured helium concentration as a tracer gas with a mass spectrometer. The mass spectrometer was, however, not compact enough for our purpose and it also required high electric power. Therefore, a katharometer was employed for measuring helium concentration in the present system.

The present system consists of a 2 L syringe, a 2 L bag-in-box device, a katharometer (helium meter, Anima Corporation, Tokyo), a carbon monoxide analyzer (Beckman LB-2), oxygen analyzer (Beckman OM-11) and a hot-wire flow meter (Minato Ikagaku Inc., Osaka). A series of solenoid valves assures an unidirectional flow of a gas mixture through the following circuit. The first step is to calibrate the gas analyzers and then to fill the syringe with the gas mixture. The filled gas mixture enters the bag-in-box. After equilibrium of a gas mixture with dead space air, a patient's ventilation is switched from a ventilator to the bag-in-box through a four-ported pneumatic valve (V13') at his FRC level. The FRC level can be determined either manually monitoring the ventilatory flow pattern or automatically with a microcomputer system. After rebreathing a gas mixture for one minute, the patient is again connected up to a mechanical ventilator. During the rebreathing period, $D_{LCO}$ can be measured.

The following equation was to determine FRC

$$FRC = \frac{He_i \times 2.23}{He_f \times (1 - 0.05)} - 2.28$$

where $He_i$ stands for helium concentration at the initial condition and $He_f$ for that after rebreathing which was corrected for interference by oxygen.
The numerical number of 2.23, 2.28 and 0.05 in the equation indicate volume of the bag and the connecting circuit line, the total system volume which was equal to 2.23 plus mouth piece volume and the final carbon dioxide fraction in the bag, respectively. Our method of determining $D_{Lco}$ was done according to Lewis' method with some modification (9). Fig. 2 shows the actual process of determination. Fractional concentration of CO in the bag ($F_{co}$) is shown in the third panel. The bottom panel indicates semilogarithmic drawing of $F_{co}$. CO disappears exponentially for a time period of 15 seconds and more. The reason why the exponential change did not begin with first measurement point may be due to concurrent mixing of bag and lungs. A regression line to ln$F_{co}$ at the bottom panel was drawn by least square analysis, from which CO concentration at time zero and at one minute rebreathing were obtained.

The equation to calculate $D_{Lco}$ in the present study was as follows.

$$D_{Lco} = \frac{(FRC + 2.28) \times (\ln f_i - \ln f_f)}{(P_B - 47) \times 1.0}$$

Where $f_i$, $f_f$ and $P_B$ indicated CO concentrations at time zero and at one minute rebreathing, and barometric pressure, respectively. 2.28 equals the
volume of bag and the circuit.

Oxygen concentration in the bag decreased from the initial concentration of approximately 90% to 40% after one minute rebreathing. The change in oxygen and nitrogen concentrations in the gas mixture during FRC measurement will cause an error in the reading of helium concentration through katharometer (19). Therefore we have calibrated the katharometer for various background gases (Fig. 3) and made a correction for the actual reading.

![Graph showing relationship between helium meter reading and true concentration in pure oxygen, air, and pure nitrogen.](Fig. 3)

The present method of measuring FRC was applied to volunteers under mechanical ventilation. Initially the ventilator (Bennett MA-1) was set at a condition of intermittent positive pressure ventilation with a tidal volume 600ml and respiratory frequency of 20 per minutes while breathing air. During rebreathing period for one minute, the respiratory frequency was increased to 35 per minutes.

Table 1 shows a list of patients who received respiratory care in the intensive care unit or in the regular wards of Tokai University Hospital. ARDS was diagnosed referring to the criteria of National Heart, Lung and Blood Institute of the United States (12). (1) It is usually found in association with a serious illness that requires hospitalization but often does not involve the lungs initially. (2) There is usually a latent period after hospitalization of several hours to a few days during which respiratory involvement is minimal or absent. (3) After the latent period, acute respiratory failure develops that may progress relentlessly and cause the
patient's death. This study does not include patients with surgical post operative disorders as underlying disease of ARDS. All the patient showed diffuse and rapidly progressive infiltration on the chest X-ray.

Table 1  Clinical features of patients studied. S and D stand for survival and death, respectively.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Outcome</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. T.Y.</td>
<td>58</td>
<td>M</td>
<td>Lung cancer, COPD, Pulmonary fibrosis</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>2. E.M.</td>
<td>83</td>
<td>M</td>
<td>Near drawing, Sepsis</td>
<td>D</td>
<td>Arrhyshmia</td>
</tr>
<tr>
<td>3. Y.W.</td>
<td>30</td>
<td>F</td>
<td>SLE, Sepsis</td>
<td>D</td>
<td>DIC</td>
</tr>
<tr>
<td>4. R.A.</td>
<td>48</td>
<td>F</td>
<td>Dermatomyositis Pulmonary fibrosis</td>
<td>D</td>
<td>Resp. Failure</td>
</tr>
<tr>
<td>5. S.H.</td>
<td>74</td>
<td>M</td>
<td>Pemphyus vurgaris Viral pneumonia</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>6. K.K.</td>
<td>76</td>
<td>M</td>
<td>Pneumonia, Sepsis</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>7. T.E.</td>
<td>34</td>
<td>F</td>
<td>Paraquat intoxication</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>8. H.N.</td>
<td>80</td>
<td>M</td>
<td>Lung cancer Pulm. fibrosis</td>
<td>D</td>
<td>Rennal failure</td>
</tr>
<tr>
<td>9. Z.O.</td>
<td>77</td>
<td>M</td>
<td>Lung cancer, COPD Lymphangitis</td>
<td>D</td>
<td>Bleeding tendency</td>
</tr>
<tr>
<td>10. K.T.</td>
<td>37</td>
<td>M</td>
<td>Paraquat intoxication</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>11. S.Y.</td>
<td>72</td>
<td>F</td>
<td>Paraquat Intoxication</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>12. T.M.</td>
<td>57</td>
<td>M</td>
<td>Lung cancer</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
<tr>
<td>13. H.I.</td>
<td>58</td>
<td>F</td>
<td>Dermatomyositis Pulmonary fibrosis</td>
<td>D</td>
<td>Resp. failure</td>
</tr>
</tbody>
</table>

Arterial blood gas analysis and measurement of FRC and $D_{Lco}$ were performed at least 20 minutes after setting inspiratory oxygen concentration and pressure level of PEEP (8). FRC and $D_{Lco}$ under mechanical ventilation with PEEP were measured through the rebreathing method presented in the preceding part of this paper.

In most patients consciousness and spontaneous breathing were supressed by administration of morphine hydrochrolide, diazepam and pancronium bromide.

As it is difficult to compare values of arterial oxygen tensions ($PaO_2$) obtained under different inspiratory oxygen concentrations, a ratio of arterial/alveolar tension ($a/PAO_2$) was employed for evaluation according to Gilbert (5).

The alveolar oxygen tension ($PAO_2$) was calculated by a simplified alveolar air equation assuming the gas exchange ratio (R) to be 0.8.

$$PAO_2 = P_{O2} - \frac{Paco_2}{R}$$

Fig. 4 shows a comparison of FRCs measured on the same subject by two different methods at both sitting and supine position. Nitrogen washout method was performed through a conventional 7 minute open circuit apparatus (RIMCOS-11, Rikoh inc., Tokyo). FRC measured by the present
method is generally underestimated compared to that obtained by nitrogen washout method. The difference of FRC at two body position is consistent with those reported by Agostoni and Mead (1) as well as Blair and Hickam (3).

![Graph showing FRC measured by N2 washout method and He equilibrium method](image)

**Fig. 4** FRC measured by rebreathing (helium equilibrium) and nitrogen washout method.

Fig. 5 shows that FRC under mechanical ventilation were larger than those under spontaneous ventilation.

![Graph showing FRC during Spont. Vent and PPV](image)

**Fig. 5** FRC measured by rebreathing method under spontaneous breathing and under mechanical ventilation.
Most normal volunteers could not endure hyperventilation with PEEP, therefore FRC with PEEP for normal volunteers was not obtained.

Values of CO diffusing capacity measured by the present rebreathing method were compared with those determined single breath method (Fig. 6). CO diffusing capacity measured by rebreathing method is consistently less than that by single breath technique, although it should be compared with care because the former was determined under mechanical ventilation and because $D_{Lco}/FRC$ of the rebreathing method was somewhat different from $D_{Lco}/V_A$ of the latter.

Mean $D_{Lco}/FRC$ obtained by the present method under mechanical ventilation was 7.20 ml/mmHg-min.

Fig. 7 shows changes in $a/AP_{O_2}$ during the time course of treatment with PEEP. $a/AP_{O_2}$ on the first day was obtained under PEEP therapy when a physician set a certain PEEP level which was thought to be optimal for the patient. Therefore, the initial $a/AP_{O_2}$ may be said to be slightly higher than that generally expected from the patient of ARDS.

The sequential changes in $a/AP_{O_2}$ may be divided into two groups within four days as seen in Fig. 7. $a/AP_{O_2}$ in one group of patients did not exceed 0.2 and remained in spite of PEEP therapy, while those in the other group exceeded 0.2 and had the tendency to rise gradually during treatment. It can be said that the underlying disease or initial values of $a/AP_{O_2}$ do not contribute to the prognosis.

Effects of various PEEP levels on $a/AP_{O_2}$ were shown in Fig. 8. There was also no consistent relationship between the underlying disease and improvement of $a/AP_{O_2}$. It may be said that those who had fair prognosis in Fig. 7 (solid lines) showed good responses of $a/AP_{O_2}$ to an increase of PEEP level as seen in Fig. 8. It is noteworthy that some of the poor prognosis group (dotted lines) also showed good responses of $a/AP_{O_2}$ to increase in PEEP level.
Fig. 7  sequential changes of $a/\text{APo}_2$ during PEEP therapy.

Fig. 8  PEEP level and $a/\text{APo}_2$
Fig. 9 indicates the results of FRC measurements in some of the above cases and consistently shows that FRC increased with PEEP. The degree of improvement of FRC, however, had no relationship to the prognosis of the patients. And, the correlation between FRC and PEEP level was poor.

![Graph showing relationship between PEEP level and FRC.](image)

**Fig. 9** Relationship between PEEP level and FRC.

![Graph showing relationship between PEEP level and $a/A_P\text{O}_2$.](image)

**Fig. 10** Relationship between PEEP level and $a/A_P\text{O}_2$.
To see the effect of FRC on Arterial oxygen tension, a/AP_{O_2}s are plotted against FRCs in Fig. 10. A fairly linear relationship between FRC and a/AP_{O_2} was observed for good responders, while in poor responders a/AP_{O_2} did not increase with an increment of FRC.

D_{Lco} also improved with PEEP in all measured cases, but the absolute values of these ARDS patients were approximately a half or one third of the normal (Fig. 11). D_{Lco} divided by FRC remained essentially the same as the control values regardless of PEEP therapy as seen in the right column of Fig. 11.

![Graph showing changes of D_{Lco} and D_{Lco}/FRC with PEEP](image)

**DISCUSSION**

To evaluate the pathophysiological status of patients who fall into ARDS, it is important to assess lung function precisely, rather than perform conventional clinical tests such as chest radiography or arterial blood gas analysis.

The present method may not necessarily offer physiologically accurate data, but it may estimate the patient's pathophysiological status simply and quickly, even under mechanical ventilation. The total apparatus is small in
size and suitable for simultaneous measurements of FRC and D_{Lco} at the bedside.

There are a few different methods for measuring FRC such as gas dilution method either closed or open circuit (13, 14, 19), body plethysmography, and so on (2). The method by Heldt et al (6) was found suitable and advantageous for our purpose to estimate FRC and D_{Lco} simultaneously under mechanical ventilation with PEEP. Some modifications were made. A katharometer was used instead of mass spectrometer because it is handy and does not require any special power line. A four-ported pneumatic valve can separate the bag-in-box securely from patient-ventilator during gas equilibration period. Bag exhaustion may be completed by compression which enabled us to repeat measurements quickly. The advantage of this system was to measure CO diffusing capacity simultaneously with FRC measurement by adding a small amount of carbon monoxide into the oxygen-helium mixture.

As shown in Fig. 4, the present method measures a smaller FRC than that by the nitrogen washout method. This may in part be due to imperfect equilibration of the gas mixture during a rather short period of rebreathing (11, 20). The present method, therefore, may not be suitable for measurement of cases with moderate to severe airway obstruction.

FRC under mechanical ventilation measured by the present method was larger than that under spontaneous ventilation. It is not clear whether hyperventilation will raise FRC level or increase lung volume. We may assume that this is due to mechanical ventilation itself since hyperventilated animals do not relax their respiratory muscles.

Measurement of D_{Lco} was carried out by Lewis' rebreathing method (9) modified as follows. Lewis suggested that a bag volume had some influence on the measurement, but a bag of fixed volume was employed here which enabled both FRC and D_{Lco} to be measured simultaneously but less accurately. This method is satisfactory for our purpose which aims at respiratory care of seriously ill patients whose lung function is poor and unstable.

Since each solenoid valve may be controlled on pannel of display, the system can be manipulated by an attendant. When a microcomputer (MZ-80B, Sharp Inc., Tokyo) is used, the manipulation and calculation can be done automatically (Fig. 5).

We may summarize the advantages of the present system as follows. Simultaneous measurements of FRC and D_{Lco} may be repeat within a short time and the possibility of accidents such as barotrauma caused by fighting against the ventilator are reduced. The apparatus is compact and does not need high electric power, thereby enabling its use by the patient's bedside. Measurement can be satisfactorily run even when a patient requires high oxygen concentration. Since FRC and D_{Lco} are measured simultaneously under the same conditions, much more useful information can be obtained about the pathological status of patients during the course of treatment.

The method for measuring FRC and D_{Lco} was applied to patients with adult respiratory distress syndrome (ARDS) under mechanical ventilation with positive end-expiratory pressure (PEEP). The effectiveness of PEEP in
relation to arterial blood gases, FRC and $D_{Lco}$ was studied.

In their early report in 1971, Petty and his colleagues (16) showed a 34 years old patient whose respiratory distress was refractory to PEEP therapy. They did not explain clearly why the patient's clinical course was so progressive. Many of the patients in the present study were suffering from different pulmonary disease such as lung cancer, cryptogenic pulmonary fibrosis and so on. It is not clear why many patients with lung cancer who were treated with anti-neoplastic agents were included in this category of ARDS. A speculation is that this may be due to some adverse effects of alkylating agents on the structure and functions of the lungs (15). And, it was mandatory for us to know whether those patients would response to or refract to PEEP therapy.

We could divide our patients studied into two groups by sequential analysis of arterial/alveolar oxygen tension ratio. The definition line between the effective and ineffective group was tentatively drawn at a/ $AP_{O_2}$ of 0.2. If arterial carbon dioxide tension is assumed to be 40 torr, a/ $AP_{O_2}$ of 0.2 yields arterial oxygen tension of 47 torr under $F_{I_{O_2}}$ of 0.4. It is interesting to note that fractional inspired oxygen concentration of 0.4 corresponds to a limiting value for preventing oxygen intoxication and $P_{A_{O_2}}$ around 50 torr is indispensable for keeping normal tissue metabolism.

The results shown in Fig. 7 suggest that efficacy of PEEP therapy, that is, prognosis of the patient can be judged within four days after the commencement of the therapy. It may be said that, if any improvement was not seen after that period, another therapeutic plan should be considered (7, 18).

It has been reported that the efficacy of PEEP can be achieved mainly through the increment of FRC (10, 17) and the increment of FRC is linearly related to the PEEP level. In the present study, the increment of FRC did not have any definite relationship with the PEEP level, although FRC itself increased invariably with PEEP. Moreover, there was no difference in the degree of FRC increment between good and poor responders. This suggests that the PEEP was not too weak to expand the consolidated lungs in the ineffective cases (poor responders). It may be concluded from the results of $a/ AP_{O_2}$ and FRC that the increased FRC in the ineffective cases could contribute only to an increase in wasted ventilation which was caused by ventilation-perfusion inequality.

To the best our knowledge, the present study is the first to report $D_{Lco}$ measured during PEEP therapy on ARDS patients. As it is known that $D_{Lco}$ is an indicator of $V_A/Q$ uneveness as well as diffusive conductance (4), the results of $D_{Lco}$ should be interpreted with care. And it is believed that the most important pathophysiological aspects of ARDS is a serious increase in shunted blood flow which caused intractable hypoxemia. We defined poor responder as a group of patients who showed little improvement in $a/ AP_{O_2}$ despite of slight increase in FRC and in $D_{Lco}$ with PEEP. We may conclude that, in poor responders, as increase in FRC only contributes to wasted ventilation which might be caused by $V_A/Q$ uneveness and the shunt remains almost unchanged.
ACKNOWLEDGEMENTS

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