Special Article*

Cardiopulmonary Function Tests and Its Clinical Application

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I. Introduction

The cardiopulmonary function tests should be aimed to detect 1) impairment of pulmonary function in lung diseases, 2) impairment of the right heart due to disorders of the lung, 3) impairment of the lung and the right heart due to disorders of the left heart. From this viewpoint this paper will be presented.

II. Cardiopulmonary functional tests and its clinical interpretation

In the past two decades, a large number of physiologic tests have been developed for the evaluation of cardiopulmonary function. Not all of these tests are required in the management of each patient. First of these is the spirographic analysis by which we can determine the patterns of altered function such as restrictive or obstructive ventilatory impairment. The second should be the examination of the arterial blood for its O₂, CO₂ and pH that briefly tells the extent of pulmonary insufficiency.

When the obstructive impairment is suspected, the measurement of lung volume, ventilation-perfusion relationships, pulmonary compliance and resistance, and when the restrictive impairment is suspected, the measurement of pulmonary compliance and diffusing capacity should be performed. And if necessary, the studies of pulmonary circulation should be required further.

III. Functional determination of the non-uniform distribution of pathological changes in the diseased lung and its clinical significance

Most tests of pulmonary function are to measure the overall function of the lung, although it is generally admitted that the diseases within the lung are non-

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uniformly distributed. The following studies were aimed to explain the non-uniform distribution of the disease in the lung using some mathematical methods.

Suppose, now, that the lung is a single model consisting of one elastic balloon and a conducting tube (Fig. 1). The balloon and the tubing are connected in series.

If one makes a forced expiration, the volume in the balloon \( V \) is expressed by equation (1) using exponential function, where \( V_0 = \text{original volume of the balloon} \), and \( T = \text{time-constant of the system} \). Next, the lung is considered to consist of a large number of mechanical units, the expired volume curve during maximum expiration is shown by equation (2). If the volume at time-constant \( T_K \) is defined as \( F(T_K) \), equation (3) is derived from equation (2). Generally speaking, the time-constant of those units should be continuously and widely distributed. Finally, the expiratory volume curve is expressed as equation (4), and the total volume of the \( V_L \) is defined as \( \int_0^\infty F(T) \, dt \), where \( F(T) \) is distribution function of the time-constant.

In the same way the clearance curve of the lung is expressed just same as equation (4) considering parameter \( T \) as clearance time-constant.

If the model lung with single air sac connected with a pathway in series is ventilated sinusoidally, the dynamic complex compliance is abruptly decreased at \( w = \frac{1}{T} \) with the increase of angular frequency. Thus, in generalized model, the dynamic complex compliance is presented as \( \int_0^\infty C(T) \frac{1}{1+jwT} \, dT \), and the distribution function is analyzed from the change of the dynamic complex compliance due to angular frequency.
Thus maximal expiratory volume curve, complex compliance curve, He-clearance curve, $K_{785}$-clearance curve, single breath curves of $N_2$, He and $CO_2$ and dye dilution curve are represented as integral transformation of distribution functions using individual parameter such as mechanical time-constant, clearance time-constant and dead time (Table 1).

Thus, the distribution of pathologic changes within the lung is assumed from these distribution functions. Fig. 2 shows the curves of distribution functions.

Table 1. Lung Function and Its Mathematical Analysis

<table>
<thead>
<tr>
<th>Type</th>
<th>Curve</th>
<th>Parameter</th>
<th>Equation</th>
<th>Analytical method</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tiffeneau curve</td>
<td>mechanical time constant</td>
<td>$\int_0^\infty V(T)e^{-\frac{T}{\tau}}dT$</td>
<td>inverse Laplace transformation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>complex compliance curve</td>
<td></td>
<td>$\int_0^\infty C(T)\frac{1}{1+j\omega T}dT$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>He-clearance curve</td>
<td>clearance time constant</td>
<td>$\int_0^\infty H(T)e^{-\frac{T}{\tau}}dT$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$K_{785}$-clearance curve</td>
<td></td>
<td>$\int_0^\infty K(T)e^{-\frac{T}{\tau}}dT$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>single breath curve of $N_2$, $CO_2$, He, etc.</td>
<td>dead time</td>
<td>$\int_0^\infty F(T)u(t-T)dT$</td>
<td>inverse transform</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dye dilution curve</td>
<td></td>
<td>$\int_0^\infty D(T)G(t-T)u(t-T)dT$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Distribution function obtained from analysis of the dynamic complex compliance in patients with pulmonary diseases.
calculated from complex compliance curves in normal subjects and the patients with chronic bronchitis, bronchial asthma and chronic pulmonary emphysema.

IV. Impairment of the cardiopulmonary function of the diseased lungs

A) Ventilatory impairment
1) Chronic bronchitis
   It should be pointed out that this disease includes the cases which have almost normal ventilatory function and those which have severe ventilatory defects such as pulmonary emphysema. This is the reason why the early diagnosis of this disease is so important. From this viewpoint, we proposed the $V \cdot AV$ diagrams which shows the relationships between functional residual capacity and the expired volume to the check valve point in forced expiratory volume curve. Using this diagram we can find out the slightly obstructive impairment which may not be detected by 1 second vital capacity or MMF test.

2) Bronchial asthma
   Spirometric studies in asthmatic state usually show both obstructive and restrictive impairment. Our studies show that obstructive impairment of this disease is due to the increase of both airway and lung tissue resistances. The restrictive impairment may be partially due to congestion of pulmonary capillaries, although we could not detect the increase of pulmonary capillary blood volume even in the moderately severe attacks of asthma.
   During the attacks of bronchial asthma, it was seen that the hysteresis loop of pressure-volume diagram and the stress relaxation curve are not proportionally changed to the changes of viscous resistance of the lung, and it was also observed that the distribution of time-constant is widely spread. From these observations I would like to conclude that the obstruction in asthmatic attacks occurs in upper airway rather than peripheral region of the airway. From our studies which showed the work in inspiration was always greater than the work in expiration, it is emphasized that dyspnea during attacks should be in inspiration rather than in expiration.
   Infective asthma (from Swineford's criteria) was most frequently seen in patients after the age of 40 years. This type of asthma shows severely obstructive impairment and increased static lung compliance.

3) Chronic pulmonary emphysema
   Based on our pathophysiological studies, it is said that aging and the repeated infection of the airway are greatly related to the development of emphysema. If there is a loss of lung elasticity due to destructive changes especially in the region of respiratory bronchioles or alveolar ducts, the intrapleural pressure may rise high enough to make compression of the airways. As the result, the resistance of airways increases which accelerates the destructive changes of the airways.
   The Emphysema Committee of Japan has made the classification and diagnostic
Table 2. Criteria of “Pulmonary Emphysema” by The Emphysema Committee of Japan

A. Generalized pulmonary emphysema

I. Chronic pulmonary emphysema

The following physiologic criteria are adopted. Besides them, the other manifestations may be shown in patient history, clinical & physical findings and roentgenologic findings.

a. Highly suspected

(1) Criteria I.

Function tests, i.e., spirography, determination of the residual volume, measurement of intrapulmonary gas distribution, etc. are necessary for diagnosis of this group.

(2) Criteria II.

Diminished forced expiratory flow rate (FEV1.0/VC 55%). MBC & MMF may be also used and reversibility of obstructive impairment by bronchodilators should be considered.

b. Suspected

Diminished forced expiratory flow rate (FEV1.0/VC=55-70%), or cases who do not satisfy the Criteria I.

c. Unclassified

Cases above-mentioned function tests are not preformed on, but pulmonary emphysema is clinically highly suspected.

II. Chronic pulmonary emphysema with pulmonary fibrosis

Criteria for this group are as same as those of I, but this group shows marked diffuse fibrotic change in the lung field radiographically.

III. Pulmonary emphysema which is combined with other pulmonary diseases such as pulmonary tuberculosis, pneumoconiosis, etc.

Chronic bronchitis, bronchial asthma and other senile conditions (combined emphysema) are excluded from this criteria.

B. Localized pulmonary emphysema

Bullae, bullous emphysema

Appendix:

Clinically diagnosed chronic pulmonary emphysema may indicate just syndrome. Relationships between the clinical emphysema and the morphologically detected emphysema are left as the future problem.

criteria of emphysema as Table 2. Spirographic analysis, especially the measurement of 1 second vital capacity is most useful to find out expiratory airway obstruction. The measurement of Check Valve Index \( \frac{FEV_{0.5}}{FIV_{0.5}} \) which we proposed is also useful to the diagnosis of emphysema.

It has been believed that the obstruction in expiration occurs in the region of peripheral airways. In morphometric studies, the resistance of airways lower than bronchioles are unbelievably small, and we could simply simulate the expiratory flow curve using two CR models in electrical circuit. From these facts it could be mentioned that the expiratory obstruction of emphysema occurs in large airways rather than in small airways.

Three types of emphysema were shown in Table 3, telling that the prognosis of the patient with pulmonary emphysema cannot be determined merely from the degree of ventilatory impairment. Prognosis is poor in patients with emphysema.
Table 3. Three Types in Patients with Chronic Pulmonary Emphysema

<table>
<thead>
<tr>
<th>Type</th>
<th>Bronchial asthma</th>
<th>Chronic bronchitis</th>
<th>Unclassified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>58ys</td>
<td>60ys</td>
<td>63ys</td>
</tr>
<tr>
<td>Symptoms at onset</td>
<td>asthmatic attack, dyspnea</td>
<td>cough, sputum and dyspnea</td>
<td>dyspnea</td>
</tr>
<tr>
<td>Cough and sputum</td>
<td>+</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>Asthma-like attack</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Râles</td>
<td>+</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>±</td>
<td>↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Static compliance</td>
<td>↑↑</td>
<td>↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Viscous resistance</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Treatment</td>
<td>very effective</td>
<td>effective</td>
<td>no change</td>
</tr>
</tbody>
</table>

combined with pulmonary fibrosis which usually has an decreased diffusing capacity.

4) Pulmonary tuberculosis

Recently functional impairment of the far advanced pulmonary tuberculosis has become more complicated. Cases with normal vital capacity with severely obstructive impairment and the others with considerably decreased diffusing capacity were discussed.

B) Impairment of diffusion

Fig. 3. The three types in patients with A-C block syndrome.
Now we can measure the diffusing capacity dividing into $D_M$ (diffusing capacity of the membrane) and $V_c$ (blood volume in the pulmonary capillaries exposed to alveolar gas). Based on the measurement of these two components we differentiated so-called A-C Block syndrome had reduced values of both $V_c$ and $D_M$. Measurement of $\%D_{co}$ versus vital capacity shows two patterns of diffusion impairment. One is the pattern of decreased surface area (this means reduced vital capacity) with normal $D_{co}$. The other is the pattern of longer diffusion pathway with normal vital capacity and reduced $D_{co}$ and $D_M$. The latter also showed decreased value of static lung compliance.

C) Impairment of pulmonary circulation

1) Impairment of pulmonary circulation due to pulmonary disorders

From the clinical standpoint, patients with primary pulmonary hypertension usually showed normal ventilatory function, although they demonstrate severe pulmonary hypertension, remarkable right ventricular hypertrophy and relatively rapid clinical course to death. In pulmonary diseases the role of anoxia in developing pulmonary hypertension was clinically and experimentally shown and the role of hypercapnea should also be noted. The relationships between the pulmonary vascular resistance and anoxia or hypercapnea are still obscure, because pulmonary vessels have poor vasoreactive action to these factors experimentally.

From our clinical studies, the role of bronchial artery blood flow in developing pulmonary hypertension could be neglected.

Fig. 4 shows the relationships between pulmonary hypertension and pulmonary function in special reference to causative disease. Pulmonary hypertension is often associated with pulmonary emphysema which has severely obstructive ventilatory defect and alveolar hypoventilation. Although the extent and the severity of pulmonary hypertension are generally related to the diminution of the vascular bed and the increased vascular resistance, its progress is not usually rapid except the cases of vascular origin.

The detection of right ventricular hypertrophy is the most important for diagnosis of chronic cor pulmonale. If the criteria of right ventricular hypertrophy are satisfied by electrocardiographic study and the pulmonary hypertension is detected by the right heart catheterization, the diagnosis of cor pulmonale can be easily made. Electrocardiographic evidence of right
ventricular hypertrophy and bulging of the pulmonary conus or enlargement of the right pulmonary artery on the chest X-ray films were related to pulmonary hypertension, and electrokymographic evidence in pulmonary artery wave was correlated to pulmonary artery pressure.

2) Impairment of pulmonary circulation due to heart diseases

Two processes can be thought for development of pulmonary circulatory impairment in heart diseases. One is the back pressure effect (in mitral valvular diseases) and the other is an increased blood flow to the pulmonary vascular bed. It should be noted that in both groups the resistance of pulmonary vessels abruptly increases when mean pulmonary artery pressure exceeds 40 mm.Hg. Persistent high pressure in the pulmonary artery will cause organic changes of the vascular system, which may further accelerate the increase of pressure.

The measurement of pulmonary blood volume using the dye dilution method showed the decrease of pulmonary blood volume and vascular compliance with the increase of pulmonary vascular resistance. Thus, the decreased ratio of the volume to the blood pressure is intimately related to the increase of pulmonary vascular resistance.

3) Pulmonary function in heart diseases

Slightly restrictive defect, decreased static lung compliance and decreased $D_v$.
are found in patients with pulmonary congestion due to mitral stenosis. In a patient of cardiac asthma, the pulmonary function tests show obstructive impairment, hyperinflation and impairment of gas distribution. Indeed these functional defects of cardiac asthma are quite similar to bronchial asthma. So differential diagnosis of the two types of asthma should be done carefully.

V. Disturbance of central nervous system in cardiopulmonary insufficiency

Pulmonary encephalopathy is the most important syndrome in cardiopulmonary insufficiency. Increased $P_{CO_2}$ in arterial blood should play a main role to the development of pulmonary encephalopathy. Anoxemia, decreased pH, congestion in venous system and disturbances of brain metabolism will also accelerate this impairment.

VI. Treatment for cardiopulmonary disorders

Before we start the treatment we should figure out the state of disability by measurement of arterial blood gas pressure on one hand, and on the other hand we should know the state of ventilatory impairment by spirometric analysis which plays main role to pulmonary insufficiency.

From clinical standpoint preventive care against infection is most important. Enzyme therapy, recently developed, will be a hopeful method against pulmonary insufficiency. Inhalation therapy should be done more positively, but treatment using surface active material should be done more carefully for their harmful effect to alveolar stability.

VII. Conclusion

In this paper some of the recent problems of cardiopulmonary physiology and their clinical adaptation were discussed. Although a complete description of the functional studies in cardiopulmonary disorders was not intended, it is hoped that this manuscript added some advantage to this field.