Studies on Prognosis of Chronic Pulmonary Emphysema with Special Reference to Abnormalities in Pulmonary Circulation and Arterial Blood Gases

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In evaluating the prognostic significance of pulmonary function tests performed on the patients with chronic pulmonary emphysema, authors studied the relationship of main values of lung volumes, ventilatory capacities, arterial blood gases and pulmonary hemodynamics to the prognosis for 5 to 8 years.

Although further studies are necessary, the arterial carbon dioxide tension in combination with the maximal breathing capacity was a simple practical index of both ventilatory and circulatory disturbances and was a useful guide to prognosis in chronic pulmonary emphysema.

In general, the clinical manifestations of chronic pulmonary emphysema depend on the degree of the pulmonary insufficiency. Physiological tests performed on the patients demonstrate various abnormalities which range from simple disturbances in ventilation in early stage, to chronic hypoxia, hypercapnia, respiratory acidosis, pulmonary hypertension, pulmonary arteriosclerosis and chronic cor pulmonale with heart failure in later stage. However, in each individual patient, each of these abnormalities does not always develop to the same degree, as the disease progresses. Therefore, the prognosis in chronic pulmonary emphysema is very complicated, and it is not easy to determine the prognosis only by clinical investigations. Nevertheless, it is necessary to assess the severity and prognosis of this disease as early as possible, for establishing the accurate information about the treatment of this disease.

On this point of view, in determining the prognosis of chronic pulmonary emphysema, it may be important to estimate precisely the various values obtained by adequate pulmonary function tests together with clin-

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ical investigations. In recent years few reports have appeared on the prognostic value of pulmonary function tests, such as the maximal breathing capacity, arterial oxygen saturation, arterial carbon dioxide tension and diffusing capacity.

The purpose of the present investigation was to evaluate the prognostic significance of the pulmonary function tests, which were performed on patients with chronic pulmonary emphysema for confirming the clinical diagnosis and for determining the degree of severity of emphysema.

**Materials and Methods**

A total of 36 patients with chronic pulmonary emphysema were investigated, who had been diagnosed by clinical, radiological and functional investigations, and could be followed up for 5 to 8 years, by personal contacts, by letters or by informations from attending doctors.

All of the patients selected in this study had, at least, as the diagnostic criteria of chronic pulmonary emphysema, a history of dyspnea on exertion, the findings of decreased maximal breathing capacity below 70 per cent of predicted and of increased residual volume as a percentage of the total lung capacity above 40 per cent, and had no evidence of other disease.

The methods used for the assessment of pulmonary function were the same as that described previously by Murao. The vital capacity, its subdivisions and maximal breathing capacity were measured on a Knipping spirometer. Normal values for these tests were predicted according to age, sex, height and weight by the formulae of Baldwin et al. The residual volume was measured by Christie's closed circuit method. The contents of carbon dioxide and oxygen of the blood were measured by the manometric method of Van Slyke and Neill. The pH of the whole blood was measured with Cambridge pH meter. The oxygen saturation of the arterial blood was measured by Van Slyke-Sendroy's method. The carbon dioxide tension was then calculated from the nomogram of Singer and Hastings. Pulmonary arterial pressure was measured by the cardiac catheterization technique and the cardiac output was determined by the direct Fick's method during the catheterization. Total pulmonary resistance was calculated from the data of the mean pulmonary arterial pressure and cardiac output.

**Results**

A. Fatal cases.

As shown in Table I, 36 patients with chronic pulmonary emphysema were examined. There were 6 women and 30 men, with ages varying from 25 to 67 years, but most of them were the sixties, followed by the forties and the fifties.

Sixteen cases among 36 patients died within 5 years after the first
investigation, 7 within 2 years and 9 within 2 to 5 years: 7 due to pulmonary heart failure (1 confirmed by autopsy, 6 diagnosed clinically), each one due to the complication of pneumothorax, carbon dioxide narcosis, acute heart failure, acute pneumonia, acute severe enteritis (these 5 cases were confirmed clinically by other doctors), one due to suicide and 3 of unknown causes. The death of these patients was closely related to their advanced chronic pulmonary emphysema, except one suicide case and 3 of unknown cases.

B. Relationship of the disturbances in pulmonary function to the prognosis.

Fig. 1–8 summarized the results of this study. The largest number of deaths occurred in the group with vital capacity of less than 65 per cent of its predicted value (Fig. 1), or with maximal breathing capacity of less than 40 per cent of its predicted value (Fig. 2). But survivals over 5 years appeared not only in patients with vital capacity above 65 per cent of predicted or maximal breathing capacity above 40 per cent of predicted but also in patients with the former of less than 65 per cent or the latter of less than 40 per cent. On the residual volume as a percentage of the total lung capacity, as shown in Fig. 3, there was no significant difference between the two groups of patients who survived over 5 years and those who died within 5 years.

Fig. 4 and 5 indicated the relationship of the arterial blood gases to prognosis. The arterial oxygen saturation ranged from normal values to as low as 52 per cent and the arterial carbon dioxide tension ranged from normal values to as high as 84 mm Hg.

All the patients died within 5 years whose arterial oxygen saturation was lower than 87 per cent and especially those with the low values

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Table I. Age Distribution of Patients at First Observation and Number of Deaths within Five Years

<table>
<thead>
<tr>
<th>Age (yr.) at First Observation</th>
<th>Number of Patients</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>30-39</td>
<td>2 (2)</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>8 (1)</td>
<td>6</td>
</tr>
<tr>
<td>50-59</td>
<td>9 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>60-69</td>
<td>13 (3)</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>36 (6)</td>
<td>16 (1)</td>
</tr>
</tbody>
</table>

Note: Number of females in parentheses.
Fig. 1. Relationship of vital capacity to prognosis.

Fig. 2. Relationship of maximal breathing capacity to prognosis.
Fig. 3. Relationship of residual volume as a percentage of total lung capacity to prognosis.

Fig. 4. Relationship of arterial oxygen saturation to prognosis.
of less than 55 per cent died within 2 years, although considerable number of deaths occurred not only in the patients with subnormal values but also in those with normal values of arterial oxygen saturation. On the other hand, survivals over 5 years appeared only in the patients with the arterial oxygen saturation above 87 per cent (Fig. 4).

As to the arterial carbon dioxide tension (Fig. 5), all the patients died within 5 years whose arterial carbon dioxide tension was higher than 55 per cent and especially those with the high values of more than 60 per cent died within 2 years, although several number of deaths occurred in the patients with nearly normal value of higher than 45 per cent. The survivals over 5 years were noticed only in the patients with the arterial carbon dioxide tension below 55 mm.Hg.

Concerning the hemodynamics of the pulmonary circulation, the relationship of the pulmonary arterial pressure, pulmonary blood flow and total pulmonary resistance to prognosis was investigated.

As shown in Fig. 6, all the patients with mean pulmonary arterial pressure of higher than 30 mm.Hg died within 5 years, and especially those with the high values of more than 40 mm.Hg died within one year, while the deaths within 5 years occurred among the patients with the value of higher than 20 mm.Hg. The patients who survived over 5 years appeared only in those with mean pulmonary arterial pressure of lower than 30 mm.Hg.
Fig. 6. Relationship of mean pulmonary arterial pressure to prognosis.

Fig. 7. Relationship of pulmonary blood flow to prognosis.
As shown in Fig. 7, the range of pulmonary blood flow scattered widely from increased to decreased values in patients with chronic pulmonary emphysema, but no remarkable difference in the pulmonary blood flow was observed between those who died within 5 years and those who survived over 5 years.

In Fig. 8, the relationship of total pulmonary resistance to prognosis was shown. This relationship was almost similar to that of the mean pulmonary arterial pressure to prognosis, that is, although the deaths within 5 years occurred in those with total pulmonary resistance of higher than 280 dynes sec. cm$^{-5}$, all the patients with the value of higher than 500 dynes sec. cm$^{-5}$ died within 5 years. The survivals over 5 years were noticed in the patients with total pulmonary resistance of lower than 500 dynes sec. cm$^{-5}$.

**Discussion**

Concerning the diagnostic or prognostic significance of the pulmonary function tests, Sinclair$^6$ stated that, although the residual volume relative to total capacity changed less with increasing severity of emphysema, both of vital capacity and maximal breathing capacity gave reasonable indications, but the evaluation of these values was limited because of their wide normal variations. West and others$^7$ did not find a close
correlation between the severity of emphysema as judged by these tests and the development of pulmonary heart failure. Bates and co-workers and Cotes pointed out that these tests were of value in diagnosis but of less reliable to estimate the prognosis. On the other hand, Leiner and co-workers showed that in a group with the maximal breathing capacity of less than 50 per cent of predicted, the percentage of deaths increased sharply, corresponding to the observation of Gaensler, who stated increased risk of chest surgery in patients with the maximal breathing capacity of less than 50 per cent of predicted.

In the present study, it was noticeable that the deaths within 5 years in the patients with chronic pulmonary emphysema occurred among the patients with the vital capacity of less than 65 per cent of predicted or with the maximal breathing capacity of less than 40 per cent of predicted. But none of both tests was helpful by itself for establishing a prognosis in a patient with emphysema, because considerable number of survivals over 5 years appeared also in patients with such decreased vital capacity or maximal breathing capacity.

As to the residual volume as a percentage of the total lung capacity, no significant result for prognosis was obtained.

The abnormalities of arterial blood gases in patients with chronic pulmonary emphysema have been studied by many investigators. Although arterial blood gas analyses do not reveal any abnormalities in patients with mild pulmonary emphysema, they become abnormal as the disease progresses. At first, hypoxia occurs only after exercise, but later on, it does even at rest. In the advanced stage of the disease, hypercapnia is also observed, and eventually respiratory acidosis occurs in the final stage. Platts and Greaves, and Simpson pointed out the poor prognosis in patients with very low arterial oxygen saturation or with very high arterial carbon dioxide tension.

The present results showed apparently that both of the arterial blood oxygen saturation and carbon dioxide tension were the good information for establishing the prognosis.

The patients with advanced pulmonary emphysema frequently have pulmonary arterial hypertension. reported previously that most of all patients with severe chronic pulmonary emphysema, whose mean pulmonary arterial pressures were higher than 30 mmHg, showed roentgenographic and electrocardiographic evidences of right ventricular hypertrophy and other clinical signs consistent with the diagnosis of chronic cor pulmonale.

The present study indicated that the prognosis was unfavorable in patients with pulmonary arterial hypertension or with high pulmonary vascular resistance. The patients with pulmonary arterial pressure of higher
than 500 dynes sec. cm.$^{-5}$ died within 1 to 5 years, according to the degree of pulmonary hypertension or high pulmonary resistance in each individual patient.

The relationship of the pulmonary blood flow to prognosis was not evident. The pulmonary blood flow in the present patients scattered widely from low to high values. That is, although most of the values were higher than normal limits, reduced values were also observed particularly in some of patients with cor pulmonale$^{12}$ or in older patients.$^{5}$

As to the value of the pulmonary blood flow in chronic pulmonary emphysema, there is no agreement of opinion among observers, as Courand$^{13}$ stated that the pulmonary blood flow was high in chronic pulmonary emphysema, while Dexter$^{14}$ reported contrarily that the pulmonary blood flow was rather low. It seems likely that pulmonary blood flow and the progress of the disease do not always follow the same pattern in all patients. Consequently, the relationship of the pulmonary blood flow to prognosis considerably complicated and, inspite of important problem, remained unsolved in this report.

Thus, the studies of pulmonary hemodynamics through cardiac catheterization are helpful for confirming the disturbances in pulmonary circulation as earlier as possible, and are valuable for establishing the prognosis in patients with chronic pulmonary emphysema. However, it is not always possible to perform the circulatory studies through cardiac catheterization, especially on patients with severe clinical signs and symptoms, such as violent dyspnea, cough, wheezing and cyanosis.

In those cases, abnormally high carbon dioxide tension in the arterial blood indicates not only the impairment of pulmonary ventilation, but also suggests strongly the existence of pulmonary arterial hypertension, since a linear relationship has been demonstrated between the carbon dioxide tension or the arterial oxygen desaturation and the pulmonary arterial pressure in patients with chronic pulmonary emphysema by many investigators$^{1)-17}$ (Fig. 9). Consequently, it may be said that the degree of the arterial carbon dioxide tension is of major prognostic significance in clinical standpoint.

In addition, considering from the relationship between the maximal breathing capacity and the arterial carbon dioxide tension in both patients who died within 5 years and who survived over 5 years (Fig. 10), it was suggested for the present that (1) the prognosis in the patients with the maximal breathing capacity above 40 per cent of predicted was relatively good, (2) the prognosis in the patients with the arterial carbon dioxide tension above 60 mm.Hg was bad, and (3) the prognosis in the patients with the maximal breathing capacity of less than 40 per cent and the arterial carbon dioxide tension lower than 60 mm.Hg was relatively poor.
Fig. 9. Relationship between mean pulmonary arterial pressure and arterial carbon dioxide tension.

Fig. 10. Relationship between maximal breathing capacity and arterial carbon dioxide tension in both of deaths and survivals.
Finally, although Bates and co-workers emphasized that all the tests of pulmonary function was of value in diagnosis and only the diffusing capacity was the most sensitive guide to prognosis, the studies on this test was omitted in this paper, because the measurement of the diffusing capacity was not performed sufficiently on the present patients.

**SUMMARY**

Thirty-six patients with chronic pulmonary emphysema have been investigated by pulmonary function tests, and followed up for 5 to 8 years, and the results were as follows.

(1) Seven cases died within 2 years and 9 within 3 to 5 years, 7 died from cor pulmonale.

(2) In the patients with vital capacity of less than 65 per cent of predicted or with maximal breathing capacity of less than 40 per cent of predicted, the largest number of deaths occurred within 5 years, but considerable number of survivals were also noticed. The relationship of the residual volume as a percentage of the total lung capacity to prognosis was not evident.

(3) All the patients with the arterial oxygen saturation of lower than 87 per cent or with the arterial carbon dioxide tension of higher than 55mm.Hg died within 5 years, although considerable number of deaths occurred not only in patients with subnormal values but also in those with normal values of both tests. But the survivals over 5 years were noticed only in patients with the arterial oxygen saturation above 87 per cent or carbon dioxide tension below 55mm.Hg.

(4) All the patients with mean pulmonary arterial pressure of higher than 30 mm.Hg or total pulmonary resistance of higher than 500 dynes sec. cm.$^{-5}$ died within 5 years. On the other hand, the survivals over 5 years appeared in patients with the former lower than 30 mm.Hg or the latter lower than 500 dynes sec. cm.$^{-5}$ The relationship of the pulmonary blood flow to prognosis was not evident.

(5) The prognostic significance of the pulmonary function tests has been discussed and it was suggested that the arterial carbon dioxide tension in combination with the maximal breathing capacity was a useful guide to the prognosis.

**ACKNOWLEDGEMENT**

Grateful acknowledgement is made to Professor H. Ueda, director of the Second Department of Internal Medicine, for his constant encouragement and criticism, and to Drs. T. Uzawa and S. Fukasu for their collaboration.
REFERENCES