# Effects of Pulmonary Rehabilitation for Patients with Chronic Pulmonary Diseases with Different Types of Ventilatory Defects: Relationships between Pulmonary Function Parameters and Exercise Torelance

Hidefumi Ishikawa<sup>1)</sup>, Kazunori Oishi<sup>1)</sup>, Hideaki Senjyu<sup>2)</sup>, Masashi Yamamoto<sup>3)</sup>

1) Department of Internal Medicine, Institute of Tropical Medicine, Nagasaki University

2) Department of Physical Therapy, The School of Allied Medical Science, Nagasaki University

3) Department of Medicine, Tagami Hospital

This prospective cohort study was conducted to determine which pulmonary function parameters are useful in the prediction of exercise torelance and exercise-induced hypoxemia (EIH) among patients with chronic pulmonary diseases with different types of ventilatory defects. Fifty one patients with chronic pulmonary diseases who underwent comprehensive pulmonary rehabilitation for periods of 4 to 8 weeks, and who were classified as to different types of ventilatory defects; obstructive, restrictive and mixed type based on their pulmonary functions. All patients were measured for pulmonary function parameters, 6-minute walking distance (6MD) and the activity of daily living (ADL) before and after pulmonary rehabilitation. After pulmonary rehabilitation, the patients demonstrated a significant (p<0.001) increase in 6 MD and ADL scores for all types of ventilatory defects. In the relationship between 6 MD and pulmonary function parameters, the forced expiratory volume in 1 sec. (FEV<sub>1.0</sub>) was significantly correlated with 6 MD for all types of ventilatory defect. Vital capacity (VC) and maximal voluntary ventilation (MVV) correlated with 6MD in the obstructive and the mixed ventilatory defects, and PaO<sub>2</sub> correlated with 6 MD relative to mixed ventilatory defects. In the relationship between EIH and pulmonary function parameters, VC significantly correlated with EIH relative to restrictive ventilatory defects. FEV<sub>1.0</sub> and MVV correlated with EIH relative to obstructive ventilatory defects. Our present data suggest that specific pulmonary function parameters which can be correlated with 6 MD and EIH for different types of ventilatory defects, may be useful in terms of devising pulmonary rehabilitation protocols for these patients.

ACTA MEDICA NAGASAKIENSIA 46:49-53, 2001

TEL: +81-95-849-7842 FAX: +81-95-849-7843

- **Key Words:** pulmonary rehabilitation; pulmonary function pa rameters; 6-minute walking distance; exerciseinduced hypoxemia; chronic pulmonary disease; activity of daily living
- Abbreviations: 6MD=6-minute walking distance; EIH=exercise -induced hypoxemia; ADL=activity of daily living; FEV<sub>1.0</sub>=forced expiratory volume in 1 sec.; FVC=forced vital capacity; VC=vital ca pacity; MVV=maximal voluntary ventilation; TB seq=sequela of pulmonary tuberculosis; SpO<sub>2</sub>=arterial oxygen saturation by pulse oximetry; PI max=maximal inspiratory pres sure; VO<sub>2</sub>max=maximal oxygen uptake

# Introduction

Two common types of chronic pulmonary diseases, such as chronic obstructive pulmonary disease (COPD) and restrictive lung diseases, are known<sup>1)</sup>. The restrictive lung diseases involve pulmonary fibrosis, pleural diseases including sequela of pulmonary tuberculosis (TB seq), and skeletal abnormalities<sup>1</sup>. With an increased number of elderly in the general population, the importance of pulmonary rehabilitation for chronic pulmonary diseases has been highlighted. However, the effectiveness of pulmonary rehabilitation for patients with chronic pulmonary diseases other than COPD has received less attention<sup>2-7)</sup>. No studies have been conducted relative to evaluating the effects of pulmonary rehabilitation for chronic pulmonary diseases which are associated with different types of ventilatory defects, although Foster, et al.<sup>7</sup> recently reported that pulmonary rehabilitation is beneficial for patients with severe chronic pulmonary diseases other than COPD, as well as for patients with COPD.

Pineda, et al.<sup>8)</sup> demonstrated that maximum oxygen consumption was correlated with  $FEV_{1.0}$  and MVV in

Address Correspondence: Hidefumi Ishikawa, M.D.

Department of Internal Medicine, Institute of Tropical Medicine, Nagasaki University, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan

patients with COPD. Furthermore, several studies<sup>9–11)</sup> have previously reported that the evaluation of pulmonary function parameters is helpful in predicting which patients are likely to develop increasing hypoxemia during exercise in cases of COPD. However, little is known about the relationship between pulmonary function parameters and exercise tolerance or exercise-induced hypoxemia (EIH) among patients with chronic pulmonary disease who have different types of ventilatory defects. Such information may provide us with a better way to predict exercise capacity of these patients, and may be helpful in prescribing exercise training.

In order to determine the effects of pulmonary rehabilitation for patients with chronic pulmonary disease with different types of ventilatory defects, we evaluated the pulmonary function parameters, 6-minute walking distance (6MD) and activity of daily living (ADL) before and after pulmonary rehabilitation among these patients in this study. We also analyzed the relationships between pulmonary function parameters and 6 MD or EIH in order to determine which pulmonary function parameters are useful in predicting the exercise torelance and EIH of patients with a specific type of ventilatory defect.

# **Patients and Methods**

#### Subjects

Fifty-one patients (33 male and 18 female; ranging in age from 32 to 84 year-old; mean age  $\pm$  SD: 68  $\pm$  12 yearold) with chronic pulmonary diseases were prospectively evaluated at Tagami Hospital, Nagasaki city, between 1991 and 1996. They were clinically stable during the period of study. Patients were admitted and then subjected to the comprehensive pulmonary rehabilitation including disease evaluation, educational programs as well as programming of exercise for a period of 4 to 8 weeks. The severity of breathlessness among these patients according to the definitions of Fletcher, et al.<sup>12)</sup> were 10 in grade II, 24 in grade III, 12 in grade IV and 5 in grade V, respectively. Diagnostic groups included pulmonary emphysema (n=8), TB seq (n=16), pulmonary emphysema with TB seq (n=19), chronic bronchitis (n=2), bronchiectasis (n=1), radiation pneumonitis (n=1), status post lung resection (n=1), TB seq with pulmonary fibrosis (n=1), pneumoconiosis (n=1), and pneumoconiosis with TB seq and lung resection (n=1). Eleven patients received supplementary oxygen during exercise because of chronic respiratory failure.

#### Programming of pulmonary rehabilitation

The rehabilitation program consists of multiple components<sup>2,4,13</sup>; (1) an education program, (2) physical therapy including bronchial drainage, pursed-lip breathing, diaphragmatic breathing and relaxation techniques, (3) exercise conditioning regimens involving the stationary bicycle riding, floor walking, step walking, muscle training of the extremities<sup>14</sup> and ventilatory muscle trainin  $g^{\scriptscriptstyle 15,16)}.$  Pulmonary function tests and 6 MD were examined, and the severity of breathlessness and ADL were assessed before and after pulmonary rehabilitation. ADL was assessed based on three parameters (velocity of motions, shortness of breath and oxygen demands) in daily activity with various grades of exertions including eating, defecation, face washing and brushing the teeth, bathing, dressing, walking in the room, walking in the ward, walking in the hospital, walking up the stairs, and shopping. Arterial oxygen saturation by pulse oximetry  $(SpO_2)$  was monitored for each patient during the 6 MD test.

Patients were classified into three groups; the obstructive type (n=15), the restrictive type (n=11) and the mixed type (n=22); obstructive and restrictive) of ventilatory defect. The obstructive and the restrictive type of ventilatory defect was defined when the the FEV<sub>1.0</sub>/FVC % was less than 70% and when the percentage of predicted VC was less than 80%, respectively. The mixed type of ventilatory defect was defined by a combination of FEV<sub>1.0</sub>/FVC % being less than 70% and the %VC being less than 80%.

#### Statistical analysis

Changes in pulmonary function parameters, the 6 MD and ADL score in patients with a specific type of ventilatory defect before and after pulmonary rehabilitation were compared by using Student's paired t tests. The data are presented as the mean  $\pm$  SD. Pearson's correlation coefficients were used to determine the relationships between pulmonary functions and 6 MD or EIH (the levels fall in SpO<sub>2</sub> in absolute values with 6 MD exercise) before pulmonary rehabilitation of different types of ventilatory defects. Significance was accepted if p<0.05.

## Results

Regarding the effects of pulmonary functions, 6 MD and the ADL score before and after pulmonary rehabilitation were compared to patients with chronic pulmonary diseases with different types of ventilatory Hidefumi Ishikawa et al : Effects of Rehabilitation for Chronic Pulmonary Diseases

**Table 1.** Comparison of pulmonary functions, 6 MD and ADL score among patients with chronic pulmonary diseases in different types of ventilatory defects before and after pulmonary rehabilitation.\*

		Restrictive	Obstructive	Mixed
		n=15	n=11	n=22
	Before	$1.32 \pm 0.46$	$2.70 \pm 0.57$	$1.66 \pm 0.49$
VC (L)	After	$1.61\pm0.50$	$2.59\pm0.54$	$1.90\pm0.62$
	р	p < 0.05	NS	p < 0.005
	Before	$1.03\pm0.39$	$1.03 \pm 0.39$ $1.32 \pm 0.58$	
FEV1.0 (L)	After	$1.14 \pm 0.39$	$1.30\pm0.57$	$0.83\pm0.42$
	р	NS	NS	NS
	Before	$35.0 \pm 12.4$	$49.5 \pm 26.6$	$25.6 \pm 11.1$
MVV(L/min)	After	$41.6 \pm 15.2$	$52.1 \pm 27.2$	$25.8 \pm 12.1$
	р	p < 0.001	NS	NS
	Before	$73.5 \pm 14.9$	$73.5 \pm 7.2$	$66.5 \pm 12.2$
PaO2 (mmHg)	After	$76.8 \pm 14.3$	$75.4 \pm 8.8$	69.0±11.1
	р	NS	NS	NS
PaCO2 (mmHg)	Before	44.7±8.9	42.8±4.1	$47.9 \pm 8.6$
	After	$45.0 \pm 7.2$	$41.4 \pm 4.6$	$47.4 \pm 7.0$
	р	NS	NS	NS
PI mov	Before	$34.9 \pm 25.0$	$45.6 \pm 23.5$	$31.5 \pm 15.6$
(cmH2O)	After	46.7±29.5	$57.5 \pm 31.8$	46.7±23.8
	р	p < 0.05	NS	p < 0.01
	Before	$275.6 \pm 86.5$	376.2±99.5	$268.1 \pm 94.2$
6 MD (m)	After	$347.8 \pm 86.3$	427.7±91.4	$313.7 \pm 78.3$
	р	p < 0.001	p < 0.001	p < 0.001
	Before	$72.0 \pm 19.4$	$81.2 \pm 8.1$	$59.0 \pm 21.4$
ADL score	After	$84.5 \pm 12.1$	90.8±6.3	$69.6 \pm 19.9$
	р	p < 0.001	p < 0.001	p < 0.001

\*Data represent the means  $\pm$  SD, NS = not significant.

**Table 2.** Correlation between 6 MD and pulmonary functions among patients with chronic pulmonary diseases in different types of ventilatory defects before pulmonary rehabilitation.\*

	Restrictive		Obstructive		Mixed	
	r	р	r	Р	r	р
VC	0.248	NS	0.686	p < 0.05	0.472	p < 0.05
FEV1.0	0.572	p < 0.05	0.742	p < 0.01	0.507	p < 0.05
MVV	0.292	NS	0.716	p < 0.05	0.587	p < 0.005
PaO <sub>2</sub>	0.174	NS	0.057	NS	0.760	p < 0.0001
PaCO <sub>2</sub>	0.08	NS	0.544	NS	0.369	NS
PI max	0.613	NS	0.368	NS	0.595	NS

\*r = coefficients of correlation; NS = not significant.

defects (Table 1). No differences in the values of FE  $V_{1,0}$ , PaO<sub>2</sub> or PaCO<sub>2</sub> were found before and after pulmonary rehabilitation. Significant increases in the values for VC and PI max, however, were observed in the

restrictive (p < 0.05 in VC and PI max) and in the mixed (p < 0.005 in VC and p < 0.01 in PI max) in ventilatory defects, but not in subjects with obstructive ventilatory defects. We also found a significant improvement in MVV only in the case of subjects with restrictive ventilatory defects (p < 0.001). On the other hand, a significant improvement for the 6 MD and the ADL score was observed for all types of ventilatory defects (p < 0.001). We next evaluated the relationship between 6 MD and pulmonary function parameters, for different types of ventilatory defects before pulmonary rehabilitation (Table 2). The  $FEV_{1,0}$  value was significantly correlated with 6 MD in all types of ventilatory defects (p < 0.05 in the restrictive type, p < 0.01 in the obstructive type, p < 0.05 in the mixed type). The clinical significance of FEV<sub>1.0</sub> as an exercise endurance index can, therefore, be confirmed<sup>8,17-19)</sup>. We also found a significant correlation between 6 MD and VC or MVV in the obstructive and the mixed ventilatory defects (p < 0.05; vs VC for both types and MVV in the obstructive type, p < 0.005; vs MVV in the mixed type). It is noteworthy that the PaO<sub>2</sub> value at rest was highly correlated with 6 MD only in the case of mixed ventilatory defects (p<0.0001)(Fig. 1).

The benefit of oxygen supplementation during exercise in patients with EIH has been reported<sup>20–22</sup>. The relationships between EIH (the fall in the percent SpO<sub>2</sub>) and pulmonary function parameters and arterial blood gases was investigated for the different types of vetilatory defects before pulmonary rehabilitation (Table 3). We also found significant correlations between EIH and VC in the case of restrictive ventilatory defects (p<0.05), and between EIH and FEV<sub>1.0</sub> or MVV in the case of obstructive ventilatory defects (p<0.05). No significant correlation between EIH and arterial blood gas tensions at rest was observed for any types of ventilatory defects.

**Table 3.** Correlation between exercise induced hypoxemia (the level fall in  $\text{SpO}_2$  in absolute values with 6 MD exercise) and pulmonary functions among patients with chronic pulmonary diseases in different types of ventilatory defects before pulmonary rehabilitation.\*

	Restrictive		Obstructive		Mixed	
	г	р	г	p	r	р
VC	0.765	p < 0.05	0.649	NS	0.413	NS
FEV1.0	0.575	NS	0.847	p < 0.05	0.535	NS
MVV	0.415	NS .	0.882	p < 0.05	0.463	NS
Pa O2	0.207	NS	0.443	NS	0.393	NS
Pa CO <sub>2</sub>	0.040	NS	0.756	NS	0.190	NS
PImax	0.523	NS	0.588	NS	0.511	NS

\* r = coefficients of correlation; NS = not significant.



**Fig. 1.** Correlation between 6 MD and PaO2 levels at rest among patients with chronic pulmonary diseases with mixed ventilatory defects.

### Discussion

Ambulation distance, as determined by 6 MD, is a simple exercise test that has been used in a number of previous studies as measure of exercise capacity, and has been shown to correlate with maximum oxygen uptake  $(VO_2max)$  in patients with  $COPD^{23, 24}$ . The performance of this test depends on several factors, including endurance, respiratory function, cardiovascular fitness, neuromuscular function, motivation, encouragement, and practice<sup>18,23,25)</sup>. In this study, we demonstrated a significant improvement in 6 MD and ADL as a result of pulmonary rehabilitation among patients with chronic pulmonary diseases with any type of ventilatory defect. Pulmonary rehabilitation improved VC and MVV to some extent, but the improvement in VC and MVV did not correlate with 6 MD (data not shown). Previous studies<sup>26-29)</sup> have reported that pulmonary rehabilitation results in significant improvement in physiologic exercise tolerance in contrast to those of pulmonary function for patients with COPD. In addition, Casaburi, et al.<sup>29)</sup> have described that patients with COPD are able to achieve a physiologic training effect, as manifested by a reduction in blood lactates and ventilation at given level of exercise. These findings are consistent with the improvement in 6 MD and ADL of patients with chronic pulmonary diseases in this study. We next examined the relationship between pulmonary function parameters and an initial 6 MD for patients with chronic pulmonary disease with different types of ventilatory defects (Table 2). The FEV<sub>1.0</sub> value correlated significantly with 6 MD for patients with each type of ventilatory defect. A highly significant correlation was found especially in patients with the obstructive type of ventilatory defect. Several investigators

have previously reported a relationship between exercise tolerance and pulmonary function parameters<sup>8,17-19</sup>. Jones et al.<sup>17)</sup> reported correlations between the maximal work load and FEV<sub>1.0</sub>, VC, airway resistance and DLco in patients with chronic airway obstruction. ZuWallack et al.<sup>18)</sup> similarly reported that the initial 12 MD correlated with FVC, FEV  $_{\scriptscriptstyle 1.0}$ , peak VO $_{\scriptscriptstyle 2}$  and peak PaO $_{\scriptscriptstyle 2}$  in patients with chronic pulmonary diseases. Furthermore, FEV<sub>10</sub>, VC and MVV values were significantly correlated with 6MD both in patients with the obstructive type and the mixed type of ventilatory defect in this study. This fact suggests that a limitation on ventilation is closely associated with exercise endurance in these patients. More interestingly, the levels of PaO<sub>2</sub> correlated with 6 MD for patients with chronic pulmonary diseases in the mixed type of ventilatory defect, although the specific reason for this remains unresolved. These data suggest that it may be possible to predict exercise tolerance in each patient with a certain type of ventilatory defect by examining pulmonary function tests and arterial blood gas prior to the start of pulmonary rehabilitation.

Breathing of supplemental oxygen improves exercise performance in patients with severe COPD<sup>20-22)</sup>. An indication of the need for O2 supplementation during exercise should be based on finding relative to exercise tests rather than on resting hypoxemia alone<sup>9)</sup>. Patients with a resting arterial oxygen tension of less than 55 mmHg as well as patients with arterial desaturation during exercise are recommended to receive oxygen therapy<sup>30)</sup>. Recent studies<sup>10,11</sup> have shown that some indexes which are helpful in determining which patients include desaturated during exercise. Owens, et al.<sup>11)</sup> have reported two indexes of diffusing capacity and FEV<sub>1.0</sub> are predictive of desaturation in patients with COPD. However, no reports have been conducted on the relationship between EIH and pulmonary function parameters for cases of chronic pulmonary diseases with different types of ventilatory defects. In this study, we found significant correlations between EIH and VC in the restrictive type, and EIH and FEV<sub>1.0</sub> or MVV in the obstructive type of ventilatory defect, respectively (Table 3). These pulmonary function parameters, which correlate with EIH are important as limiting factors in patients with chronic pulmonary disease who have restrictive and obstructive types of ventilatory defects, while many parameters did not correlate with EIH, in terms of the mixed type of ventilatory defect. This may be explained by circulatory insufficiency through pulmonary arterial vasoconstriction, since a low arterial blood oxygen pressure was found in these cases ( $PaO_2 \leq 60 \text{ mmHg}$  in 7 cases and  $PaO_2 \leq 70 \text{ mmHg in } 14 \text{ out of } 22 \text{ cases})^{31,32}$ . Therefore, each pulmonary function parameter which Hidefumi Ishikawa et al : Effects of Rehabilitation for Chronic Pulmonary Diseases

correlates with EIH in different types of ventilatory defects is also valuable for predicting arterial oxygen desaturation during exercise for patients with chronic pulmonary diseases.

In summary, a comprehensive pulmonary rehabilitation is clearly effective in patients with chronic pulmonary diseases which have any type of ventilatory defect. We also found certain specific pulmonary function parameters which were correlated with exercise torelance or EIH for patients with chronic pulmonary diseases with different types of ventilatory defect. These observations support the conclusion that the evaluation of pulmonary function parameters may lead to a prediction of exercise torelance and EIH in patients with chronic pulmonary diseases with different types of ventilatory defect. We wish to emphasize that the initial assessment of pulmonary function parameters is essential for patients who receive pulmonary rehabilitation. Further studies will be required for the development of individual plans for pulmonary rehabilitation.

## Acknowledgments

I am grateful to Dr. T. Nagatake (Department of Internal Medicine, Institute of Tropical Medicine, Nagasaki University) for his support and encouragement throughout this study.

## References

- Fishman AP. Approach to the patient with respiratory symptoms. In Fishman AP, Elias JA, Fishman JA, Grippi MA, Kaiser LA, Senior RM (eds). Fishman's Pulmonary Disease and Disorders. New York, McGraw-Hill, vol 1; 361-393, 1998
- 2) American Thoracic Society.; Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. Am Rev Respir Dis 136: 225-244, 1987
- 3) Petty TL. Pulmonary rehabilitation in perspective:historical roots, present status, and future projections. Thorax 48: 855-862, 1993
- 4) Fishman AP. Pulmonary rehabilitation research. Am J Respir Crit Care Med 149: 825-833, 1994
- 5) Couser JI Jr, Guthmann R, Hamadeh MA, Kane CS. Pulmonary rehabilitation improves exercise capacity in older elderly patients with COPD. Chest 107: 730-734, 1995
- 6) Fedro GSS. Pulmonary rehabilitation for the patient with severe chronic obstructive pulmonary disease. Am J Med Sci 318: 99-102, 1999
- 7) Foster S, Thomas HM. Pulmonary rehabilitation in lung disease other than chronic obstructive pulmonary disease. Am Rev Respir Dis 141: 601-604, 1990
- 8) Pineda H, Haas F, Axen K, et al. Accuracy of pulmonary function tests in predicting exercise tolerance in chronic obstructive pulmonary disease. Chest 86: 564-567, 1984
- 9) Minh V, Lee HM, Dolan GF, et al. Hypoxemia during exercise in patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 120: 787-794, 1979
- 10) Lebecque P, Lapierre J-G, Lamarre A, et al. Diffusion capacity and oxygen desaturation effects on exercise in patients with cystic

fibrosis. Chest 91: 693-697, 1987

- 11) Owens GR, Rogers RM, Pennock BE, et al. The diffusing capacity as a predictor of arterial oxygen desaturation during exercise in patients with chronic obstructive pulmonary disease. N Engl J Med 310: 1218-1221, 1984
- 12) Fletcher CM, Elmes PC, Fairbairn AS, et al. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. Brit Med J 29: 257-266, 1959
- 13) American Thoracic Society. Pulmonary Rehabilitation. Am Rev Respir Dis 124: 663-666, 1981
- 14) Martinez FJ, Vogel PD, Dupont DN, et al. Supported arm exercise vs unsupported arm exercise in the rehabilitation of patients with severe chronic airflow obstruction. Chest 103: 1397-1402, 1993
- 15) Larson JL, Kim MJ, Sharp JT, et al. Inspiratory muscle training with a pressure threshold breathing device in patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 138: 689-696, 1988
- 16) Harver A, Mahler DA, Daubenspeck JA. Targeted inspiratory muscle training improves respiratory muscle function and reduces dyspnea in patients with chronic obstructive pulmonary disease. Ann Intern Med 111: 117-124, 1989
- 17) Jones NL, Jones G, Edwards RHT. Exercise tolerance in chronic airway obstruction. Am Rev Respir Dis 103: 477-491, 1971
- 18) Zuwallack RL, Patel K, Reardon JZ, et al. Predictors of improvement in the 12-minute walking distance following a six-week outpatient pulmonary rehabilitation program. Chest 99: 805-808, 1991
- 19) Niederman MS, Clemente PH, Fein AM, et al. Benefits of a multidisciplinary pulmonary rehabilitation program. Improvement are independent of lung function. Chest 99: 798-804, 1991
- 20) Woodcock AA, Gross ER, Geddes DM. Oxygen relieves breathlessness in Pink puffers. Lancet 1: 907-909, 1981
- 21) Bye PTP, Esau SA, Levy RD, et al. Ventilatory muscle function during exercise in air and oxygen in patient with chronic air-flow limitation. Am Rev Respir Dis 132: 236-240, 1985
- 22) Payen JF, Wuyam B, Levy P, et al. Muscular metabolism during oxygen supplementation in patients with chronic hypoxemia. Am Rev Respir Dis 147: 592-598, 1993
- 23) Mcgavin CR, Gupta SP, Mchardy GJR. Twelve-minute walking test for assessing disability in chronic bronchitis. Brit Med J 1: 822-823, 1976
- 24) Butland RJA, Pang J, Gross ER, et al. Tow-, six-, and 12-minutes walking tests in respiratory disease. Brit Med J 284: 1607-1608, 1982
- 25) Guyatt GH, Pugsley SO, Sullivan MJ, Thompson PJ, et al. Effect of encouragement on walking test performance. Thorax 39: 818-22, 1984
- 26) Casaburi R, Wasserman K. Exercise training in pulmonary rehabilitation. N Engl J Med 314: 1509-1511, 1986
- 27) Mall RW, Medeiros M. Objective evaluation of results of a pulmonary rehabilitation program in a community hospital. Chest 94: 1156-1160, 1988
- 28) Casaburi R, Wasserman K, Patessio A, et al. A new perspective in pulmonary rehabilitation: anaerobic threshold as a discriminant in training. Eur Respir J 2, Suppl.7: 618s-623s, 1989
- 29) Casaburi R, Patessio A, Ioli F, et al. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. Am Rev Respir Dis 143: 9-18, 1991
- 30) Beers MF. Oxygen therapy and pulmonary oxygen toxicity. In Fishman AP, Elias JA, Fishman JA, Grippi MA, Kaiser LA, Senior RM (eds): Fishman's Pulmonary Disease and Disorders. New York, McGraw-Hill, vol 2; 2627-2642, 1998
- Voelkel NF. Mechanisms of hypoxic pulmonary vasoconstriction. Am Rev Respir Dis 133: 1186-1195, 1986
- 32) Jensen KS, Micco AJ, Czartolomna J, et al. Rapid onset of hypoxic vasoconstriction in isolated lungs. J Appl Physiol 72: 2018-2023, 1992