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Normal Predicted Values of Single-Breath Diffusing Capacity of the Lung in Healthy Nonsmoking Adults

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Prediction equations for the carbon monoxide diffusing capacity of the lung (DLCO) and diffusing capacity per liter of lung volume (DLCO/VA) were derived from 90 normal nonsmoking subjects (40 men and 50 women), using a standardized single-breath technique for determining carbon monoxide diffusing capacity.

The results obtained are as follows:

1) The mean values for DLCO and DLCO/VA were 28.05±5.07 ml/min/mmHg, 4.569 ±0.694 ml/min/mmHg/L for men and 20.79±4.03 ml/min/mmHg, 4.695±0.743 ml/min/mmHg/L for women, respectively.

2) The values for DLCO and DLCO/VA disclosed significantly negative correlation with advancing age and positive correlation with height.

3) Normal prediction formulas were obtained for diffusing capacity, using age and height.

Men: DLCO=0.3504 H−0.2156 A−23.168
DLCO/VA=−0.0205 H−0.0283 A+9.0919
Women: DLCO=0.2491 H−0.1533 A−11.662
DLCO/VA =0.0140 H−0.0216 A+3.413

Key Words: *Diffusing capacity*

INTRODUCTION

As diffusing capacity of the lung has been used widely as one of the routine pulmonary function tests, many studies have been done to establish a standardized technique for examination and normal predicted values.

Two methods for estimating DLCO have been reported, one of which is the single-breath test,[1,2] a modified Krogh's breath-holding maneuver, and the other is the steady state method, using Filey's maneuver.[3] It has been known that values of carbon monoxide-diffusing capacity of the lung vary according to the hemoglobin concentration, the height, the body position, exercise, and altitude.[4]

In 1975 the Intermountain Thoracic Society (ITS) proposed a standardized modification of the technique of Krogh,[5,6] and in 1981 Crapo et al.[6] established prediction equations for DLCO and DLCO/VA, using the ITS technique in normal nonsmoking adults. In this study, in order to establish normal predicted values for the pulmonary-diffusing capacity in Koreans, DLCO and DLCO/VA were measured in 90 healthy nonsmoking adults, and the correlation between diffusing capacity and various physical characteristics, such as age, height, weight, and body surface area were observed. Then regression equations for normal predicted values were derived.

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MATERIALS AND METHODS

Ninety subjects (40 men and 50 women) were studied. All subjects lived in Chonnam Province. They were mainly members of the Chonnam University Hospital, medical students, relatives of

patients, and persons visiting the hospital for regular physical checkups.

Subjects were screened to select a population of disease-free nonsmokers. Normal was defined as having no history of (1) smoking, (2) asthma, chronic bronchitis, pneumonia or cardiac disease, (3) persistent cough, (4) recent treatment for any respiratory or cardiac symptoms, (5) chest injury or operation, (6) working in a polluted atmosphere for any extended period, finally, no evidence of cardiopulmonary disease on a physical examination, an EKG, or a chest radiograph.

Height, weight, and hemoglobin concentration were measured. The DLCO was measured by the modified Krogh's single-breath method, using the SRL 1000IV Computerized Pulmonary Function Laboratory, Gould Co., USA.

With the subjects in the sitting position, their noses were clamped and initial maximal exhalation was followed by maximal inhalation of the test gas (contained 0.3%CO and 10%He). After a 10-second holding of the breath the exhaled gas was collected in a sample bag, and the sampling was analyzed for CO and He. Then the DLCO was calcualted as follows:

$$DLCO = \frac{VA \times 60}{(PB-47)(t2-t1)} \times Ln\frac{(FACOt\ 1)}{(FACOt\ 2)}$$

VA: Alveolar volume (STPD)

60: Correction from seconds to minutes

PB: Barometric pressure

47: Water vapor pressure (P_{H_2O})

t2−t1: Breath holding interval

Ln: Natural logarithm

FACOt1: Fraction of CO in alveolar gas before diffusion

FACOt2: Fraction of CO in alveolar gas at the end of diffusion

Because the inspired gas was dry, an ATPD to BTPS correction factor was used. Units for DLCO were ml CO(STPD)/min/mmHg, and for DLCO/VA, ml CO(STPD)/min/mmHg/L(BTPS). Because changes in the hemoglobin concentration have a calculable effect on total CO diffusion, the measured DLCO and DLCO/VA were normalized to a standard hemoglobin value according to Cotes equation.[8]

$$\text{Corrected DLCO} = \frac{Hgb + 10.22}{1.7\ Hgb} \times \text{measured DLCO}$$

The correlations based on the diffusion capacity of the lung and the physical characteristics, such as age, height, weight and body surface area were observed. And prediction formulas were derived from the variables for both sexes, using a computer system (SPSS Batch System).

Table 1. Distribution of Subjects by Decades

Age (years)	Number of subjects	
	Men	Women
20~29	11	10
30~39	14	12
40~49	8	16
50~59	4	6
60~69	3	6
Total	40	50

Table 2. Mean Values and Standard Deviations for Physical Characteristics and DLCO in Healthy Nonsmokers

	Men		Women	
	Mean	SD	Mean	SD
Age, years	37.15	13.01	41.44	12.94
Height, cm	169.00	4.62	155.78	3.72
Weight, kg	60.95	7.30	56.30	10.06
BSA, m^2	1.697	0.106	1.543	0.125
Hemoglobin, g/dl	14.93	0.73	13.78	1.06
DLCO, ml/min/mmHg	28.05	5.07	20.79	4.03
DLCO/VA, ml/min/mmHg/L	4.569	0.694	4.695	0.743

* BSA; body surface area

Mean temperature; 24.10±1.34°C in men, 24.48±1.07°C in women

Mean pressure; 750.20±2.73mmHg in men, 751.28±2.10 mmHg in women

RESULTS

A total of 90 healthy nonsmoking men and women were included in the study. The distribution by decades of age is shown in Table 1.

The mean and standard deviations for age, height, weight, body surface area, DLCO, DLCO/VA, and hemoglobin concentration for each sex are listed in Table 2. The mean DLCO was higher in men than in women, but there was no significant difference for DLCO/VA.

Correlation coefficients between DLCO and each physical characteristic for each sex are shown in Tables 3 and 4. Negative correlations were obtained between DLCO and age (Tables 3 and 4, Fig. 1 and 2). Height was directly related to DLCO, but not to DLCO/VA.

Because DLCO and DLCO/VA showed correlation with age and height, prediction equations were derived for the variables for both sexes. The prediction formulas are listed in Tables 5 and 6.

Comparisons of the present study with previous studies reported from abroad regarding prediction formulas are shown in Tables 7 and 8, which indicate the differences between the predicted mean and the observed mean values. The mean values of age and height from the present study were substituted in the formulas of

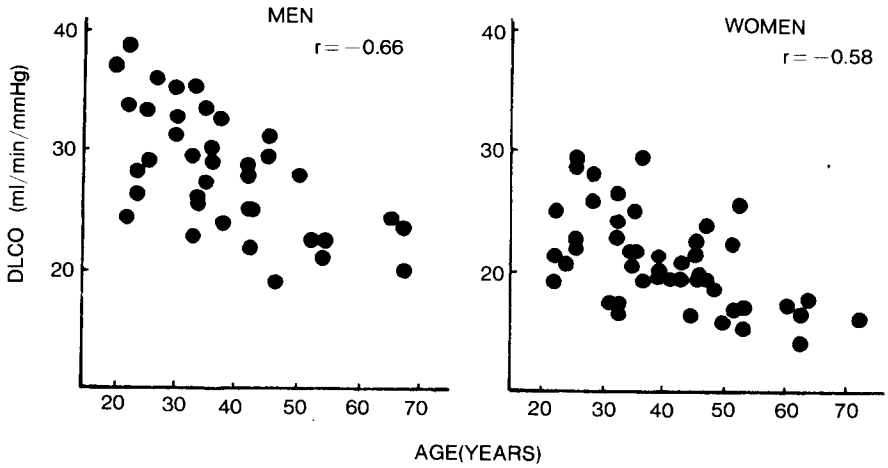

Fig. 1. *Correlation between DLCO and age in healthy nonsmokers.*

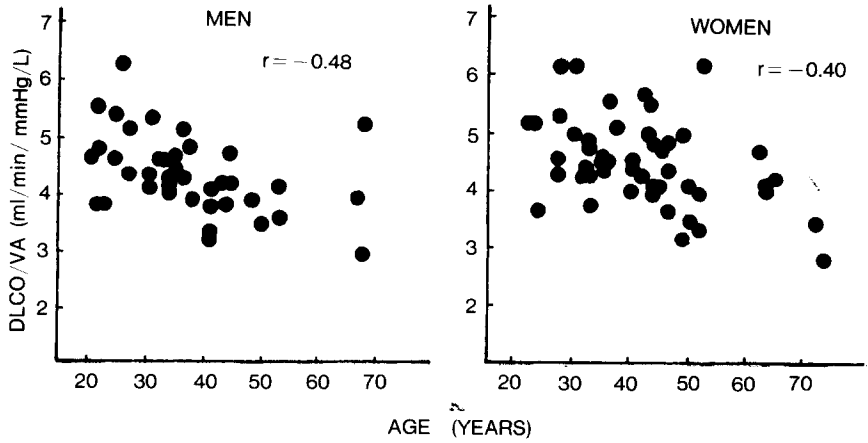

Fig. 2. *Correlation between DLCO/VA and age in healthy nonsmokers.*

Table 3. Correlation Coefficients of Physical Characteristics and DLCO for Healthy Male Nonsmokers

	Age	Height	Weight	BSA	DLCO	DLCO/VA
Age, years	1.00	−0.09	−0.17	−0.26	−0.66	−0.48
Height, cm	−0.09	1.00	0.09	0.15	0.51	0.04
Weight, kg	−0.17	0.09	1.00	0.95	0.19	−0.10
BSA, m^2	−0.26	0.15	0.95	1.00	0.33	−0.06
DLCO	−0.66	0.51	0.19	0.33	1.00	0.55
DLCO/VA	−0.48	0.04	−0.10	−0.06	0.55	1.00

* BSA; Body surface area

Table 4. Correlation Coefficients of Physical Characteristics and DLCO for Healthy Female Nonsmokers

	Age	Height	Weight	BSA	DLCO	DLCO/VA
Age, years	1.00	−0.40	−0.03	−0.11	−0.58	−0.40
Height, cm	−0.40	1.00	0.36	0.54	0.43	0.22
Weight, kg	−0.03	0.36	1.00	0.98	0.16	0.05
BSA, m^2	−0.11	0.54	0.98	1.00	0.24	0.11
DLCO	−0.58	0.43	0.16	0.24	1.00	0.70
DLCO/VA	−0.40	0.22	0.05	0.11	0.70	1.00

* BSA; Body surface area

Table 5. Prediction Formulas with Correlation Coefficient (r) and Standard Error of Estimate (SEE) for DLCO

Prediction formula	r	SEE
Men		
DLCO = −0.2563A + 37.545	0.661	3.835
DLCO = 0.3504H − 0.2156A − 23.168	0.727	3.578
DLCO = 8.1464B − 0.2392A + 23.091	0.681	3.791
Women		
DLCO = −0.1818A + 28.327	0.584	3.300
DLCO = 0.2491H − 0.1533A − 11.662	0.621	3.221
DLCO = 5.9807B − 0.1758A + 18.845	0.613	3.249

* A; Age in years, H; Height in cm, B; Body surface area in m^2

Table 6. Prediction Formulas with Correlation Coefficient(r) and Standard Error of Estimate(SEE) for DLCO/VA

Prediction formula	r	SEE
Men		
DLCO/VA = −0.0258A + 5.529	0.484	0.615
DLCO/VA = −0.0205H − 0.0283A + 9.0919	0.501	0.616
DLCO/VA = −1.3361B − 0.0286A + 7.900	0.523	0.607
Women		
DLCO/VA = −0.0232A + 5.658	0.405	0.686
DLCO/VA = 0.0140H − 0.0216A + 3.413	0.410	0.692
DLCO/VA = 0.4096B − 0.0228A + 5.009	0.410	0.692

* A; Age in years, H; Height in cm, B; Body surface area in m^2

previous studies in calculating the predicted mean. The observed means are those that were calculated from the total sample of the present study. The predicted mean using the formulas of the present study was lower than those using the formulas of previous studies for western peoples.[6,9-12]

The percentage of predicted values above which 95 per cent of the "normal" population fell were calculated as lower limits of the normal (Table 9).

Table 7. Comparison of Prediction Formulas for DLCO Using Mean Values for Age and Height from Present Study

Investigators	Sex	Prediction formula	SEE	Pred. Mean	Obs. Mean	Differ
Park et al*	M	0.3504H−0.2156A−23.168	3.578	28.05	28.05	0
Crapo et al[6]**	M	0.410H−0.210A−26.31	4.82	34.15	28.05	−6.10
Teculescu[9]	M	0.333H−0.298A−12.26	4.17	32.11	28.05	−4.06
Salorinne[10]	M	0.142H−0.232A+16.30	3.57	31.32	28.05	+3.27
Frans[11]	M	0.285H−0.140A+10.30	4.20	52.55	28.05	+24.50
Park et al*	F	0.2491H−0.1533A−11.662	3.221	20.79	20.79	0
Crapo et al[6]**	F	0.282H−0.157A−10.89	3.60	26.53	20.79	+5.74
Hall[12]	F	0.283H−0.185A−8.28	4.07	28.14	20.79	+7.35
Salorinne[10]	F	0.219H−0.115A−5.97	2.75	23.38	20.79	+2.59

Key; A: Age in years, H: Height in cm

* Corrected to a standard hemoglobin of 14.7 g/dl, according to Cotes

**Corrected to a standard hemoglobin of 14.6 g/dl, according to Cotes

Table 8. Comparison of Prediction Formulas for DLCO/VA Using Mean Values for Age and Height from Present Study

Investigators	Sex	Prediction formula	SEE	Pred. Mean	Obs. Mean	Differ
Park et al*	M	5.529−0.0258A	0.615	4.571	4.569	−0.002
Crapo et al[6]**	M	6.930−0.0030A	0.83	5.693	4.569	−1.124
Teculescu[9]	M	8.50−0.0510A	0.89	6.605	4.569	+2.036
Frams[11]	M	6.18−0.0296A+0.000157(A^2)	0.73	5.297	4.569	+0.728
Salorinne[10]	M	12.5−0.029A−0.0353H	0.63	5.545	4.569	−0.976
Park et al*	F	5.658−0.0232A	0.696	4.697	4.695	−0.002
Crapo et al[6]	F	6.940−0.0280A	0.80	5.780	4.695	+1.085
Salorinne[10]	F	12.39−0.0131A−0.0396H	0.74	5.678	4.695	−0.983

Key; A: Age in years, H: Height in cm

* Corrected to a standard hemoglobin of 14.7g/dl, according to Cotes

**Corrected to a standard hemoglobin of 14.6g/dl, according to Cotes

Table 9. The Normal Range (Low 95th percentiles of percent predicted)

Age, years	20~29	30~39	40~49	50~59	60~69	Total
Men						
DLCO	72.11	72.27	70.46	76.23	79.66	64.76
DLCO/VA	72.40	83.95	78.97	85.25	36.53	70.23
Women						
DLCO	69.04	65.69	75.21	58.08	73.43	62.01
DLCO/VA	68.81	80.64	76.29	53.12	66.08	68.98

DISCUSSION

As an index of pulmonary gas exchange, the test for DLCO, as well as the other lung function tests has been widely accepted in clinical practices or epidemiologic studies of disease of the respiratory system. It is quite valuable in the early diagnosis and evaluation of severity of pulmonary interstitial diseases and it may be used in epidemiologic studies of occupational lung diseases, such as asbestosis and berylliosis.[4]

Because the diffusing capacity of the lung depends chiefly on the area and thickness of the alveolar-capillary membrane available for diffusion (Dm) and the pulmonary capillary blood volume (Vc), it may decrease in patients with various cardiopulmonary disorders that affect Dm, Vc, or both.[13] And it depends also on changes in the hemoglobin concentration,[14] altitudes,[15] and the partial pressure of carbon monoxide in the blood.[16] For example, anemia reduces DLCO, the increased Vc by elevated pulmonary arterial pressures in persons who live at high altitudes increase and the high carbon monoxide blood level in smokers lowers it. These factors should be taken into account when the values are estimated.

There are many technical problems in measuring DLCO as in other lung function tests. They include the variability of the breath-hold-interval, and the difficulties in estimating the amount of exhaled gas, and the concentration of carbon monoxide.

Many studies have been done to establish normal predicted values for the diffusing capacity of the lung, but the normal standard values have not been settled on yet. An agreed upon set of normal standard values for Koreans is needed.

Ogilvie et al[4].(1957), Burrow et al[17].(1961), and Samet et al[18].(1979) have reported normal values already, but they selected subjects irrespective of smoking history. Recently Crapo et al[6].(1981) and Miller et al[19].(1983) measured DLCO for healthy nonsmoking adults. In these studies normal values for DLCO and DLCO/VA varied with sex, age and height, and the values for women were lower than those for men of the same age and height, and the values decreased with advancing age and increased with height.

Now, the use of the regression equations for normal predicted values by Crapo et al[6]. and Miller et al[19]. are widely recommended, and the normal values in these studies are slightly higher than those of authors. Although these differences are presumed to be due to racial difference, Cotes et al.[20] claimed that the estimated values for DLCO had no racial differencies; the inverse was the case in the estimated values for lung volumes and spirometry.

Miller et al.[19] reported that correlation coefficients between DLCO and age were −0.55 for men and −0.35 for women, and between DLCO and height, 0.27 for men and 0.28 for women. However, in the present study, the correlation coefficients between DLCO and age were −0.66 for men and −0.58 for women, and between DLCO and height, 0.55 for men and 0.43 for women. Thus, the values for DLCO showed negative correlation with age and positive correlation with height.

Ogilvie et al.[4] and Burrow et al.[17] reported that values for DLCO had significant correlations with body surface area, but in this study the correlation coefficients were low: 0.33 for men and 0.23 for women. Double correlation coefficients for DLCO with age and height were slightly higher (0.727 for men, 0.621 for women) than those of single correlations with age, and a_i similar result was obtained with age and body surface area.

As Crapo et al.[6] and Miller et al.[19] have suggested, better regression of DLCO could be obtained by using both age and height.

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