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DISCRIMINANT ANALYSIS OF PULMONARY FUNCTION PARAMETERS —— MILD ASTHMATICS VERSUS MODERATE ASTHMATICS ——

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Abstract. Maximal expiratory volume-time and flow-volume (MEVT and MEFV) curves were constructed from the measurements of young male nonsmoking, mild and moderate asthmatic patients (mean age, 29.7 yrs.). Eleven parameters of the pulmonary function tests, two MEVT, six MEFV, and three mean time constant (MTC) parameters, were calculated from the curves. These parameters were used in 15 analyses through the all possible selection procedure (APAP) discriminating between mild and moderate asthmatics. The probability of misclassification was computed with each of the eleven parameters, and all eleven probabilities thus obtained were compared with each other. This procedure showed us that the probability of misclassification ranged from 30.83 % to 45.40 % and that the most useful parameter was MTC_{50-25}. The probability of misclassification computed using all eleven parameters (total parameter group) was 15.90 %. The discriminant analysis indicated that the flow-volume patterns varied according the severity of bronchial asthma, thus, the flow-volume curve was considered to be important in analyzing the severity of bronchial asthma.

Key words : discriminant analysis, the volume-time and flow-volume curve, the all possible selection procedure (APSP), asthmatic severity, the probability of misclassification.

It is generally understood that the results of the forced expiration curve (spirogram) of asthmatic patients in the asymptomatic stage are almost the same as those of healthy adults. Takishima (1) reported that the maximal expiratory flow-volume (MEFV) curves (3, 4) of asthmatic patients were distinct from those of patients with other chronic obstructive lung diseases (COLD), in that during the asthmatic attack stage flow rates suddenly fell concavely at high lung volumes (70-80 % of FVC). Takishima did not mention, however, flow changes in the asthmatic attack free stage (1). During the non-attack stage, the sudden drop just below the peak flow rate (PFR) is not remarkable, and therefore it is difficult to distinguish the MEFV patterns of asthmatic patients in the non-attack stage from healthy subjects. In recent studies, we have performed discriminant anlayses between healthy subjects and asthmatic patients using MEFV patterns.

We (5-7) reported the results of a discriminant analysis of healthy adults and asthmatic patients in the asymptomatic stage with eight MEVT and MEFV parameters. The analysis was performed with the forward selection procedure (ESP) (8). In this procedure, independent parameters are ordered step by step, based on the multiple correlation coefficients of the dependent parameters. In the first step, the parameter shown to have the lowest probability of misclassification is selected out of all the parameters used, and from the second to the final, the lowest parameter is selected out of the remaining parameters. In previous papers (5-7), we reported that the parameters of the pulmonary function of patients in the asymptomatic stage was different from that of healthy males, and compared the order of the selected parameters, the probabilities of misclassification and the discriminant function equations. But since with FSP, parameters selected at each step were not always the best, we performed the discriminant analysis using the all possible selection procedure (8) in our most recent papers (9-10).

In these papers (9-10), we added three MTC parameters to the eight MEVT and MEFV parameters. We showed which parameters were most useful, for example, MEFV parameters $\dot{V}_{75}$, $\dot{V}_{50}$, and $\dot{V}_{25}$, and the probabilities of misclassification. Thus MEFV parameters were shown to be important in analyzing bronchial asthma.

The use of MEFV curve in attempting to distinguish mild asthmatics from moderate ones, is not conclusive, but it was hoped that discriminant analysis would lead to a clear differentiation of the two.

In this paper, we wanted to investigate four points, the first being to compare the probabilities of misclassification using each of the eleven parameters, the second being to evaluate the discriminatory ability of the four parameter groups (the MEVT, the MEFV, the MTC, and the total parameter group) by comparing their respective probabilities of misclassification, the third being to select the best parameters, and the fourth, to compute the probabilities of misclassification at each step using the eleven parameters and to evaluate the extent of their decrease.

MATERIALS AND METHODS

The subjects were 26 nonsmoking asthmatic young males (15 mild asthmatics and 11 moderate) (Table 1). Significant differences were not found in age or height.

TABLE 1. ANTHROPOMETRIC DATA

Group	Number	Mean age (Yrs.)	Height (cm) (m ± U)
Mild asthmatics	15	28.6	166.1 ± 4.5
Moderate asthmatics	11	31.3	167.1 ± 5.9

m: Mean value, U: Unbiased standard deviation.

The patients were chosen while they were under medical supervision at the Allergy Outpatient Clinic of the Department of Internal Medicine of Okayama University Medical School Hospital. They had been given brocnchodilators. Before the pulmonary function tests they had no asthmatic attacks for two more consecutive days including the test day.

The severity of bronchial asthma was classified according to Oshima's classification (2), which depends on the frequency of monthly attacks and the intensity of asthmatic attacks as shown by dyspnea and its effects on daily life. The patients were under medical supervision more than six months before severity of their bronchial asthma was determined.

A flow-volume curve recorder (OST-70D, Chest Co. Ltd.) was used for the maximal expiratory procedure, which consisted of MEVT and MEFV measurements. MEVT and MEFV curves were measured with the patients in a sitting position a few times. One of the larger MEFV patterns with a sharp peak flow rate was selected out of those obtained, but the chart obtained at the first measurement was never used for calculation. MEVT parameters (% FVC and $FEV_{1.0\%}$), MEFV parameters (Peak flow rate (PFR), $\dot{V}_{75}$, $\dot{V}_{50}$, $\dot{V}_{25}$, $\dot{V}_{10}$, and $\dot{V}_{50}/\dot{V}_{25}$), and MTC parameters ($MTC_{75-50}$, MTC_{50-25}, and MTC_{25-RV}) were calculated from the curves.

In this study, these eleven parameters were used for the discriminant analysis. In the analysis, APSP was performed using the electronic computer (NEC ACOS 700-S) in the Okayama University Computer Center.

RESULTS

The Pulmonary Function Data

TABLE 2. RESULTS OF PULMONARY FUNCTION TESTS IN EACH GROUP

Parameters		Mild asthmatics		Moderate asthmatics		t-test
		Mean value	U.S.D.	Mean value	U.S.D.	
1. % FVC	(%)	108.0	15.7	101.4	16.0	(−)
2. $FEV_{1.0\%}$	(%)	78.0	11.4	65.8	16.4	(+)
3. PFR	(L/sec)	9.2	2.3	7.4	2.3	(−)
4. $\dot{V}_{75}$	(L/sec)	6.5	2.5	4.3	2.3	(+)
5. $\dot{V}_{50}$	(L/sec)	3.8	1.8	2.4	1.7	(−)
6. $\dot{V}_{25}$	(L/sec)	1.5	0.7	1.1	1.0	(−)
7. $\dot{V}_{10}$	(L/sec)	0.5	0.3	0.4	0.5	(−)
8. $\dot{V}_{50}/\dot{V}_{25}$		2.6	0.5	2.8	0.9	(−)
9. MTC_{75-50}	(1/sec)	2.48	0.81	1.80	0.63	(+)
10. MTC_{50-25}	(1/sec)	2.09	0.99	1.23	0.62	(+)
11. MTC_{25-RV}	(1/sec)	1.38	0.65	0.95	0.81	(−)

% FVC : per cent of forced vital capacity, $FEV_{1.0\%}$: per cent of first one second volume in forced expiration curve, PFR : peak flow rate in maximal expiratory flow volume curve (MEFVC), $\dot{V}_{75}$: flow rate at 75% of FVC in MEFVC, $\dot{V}_{50}$: flow rate at 50% of FVC in MEFVC, $\dot{V}_{25}$: flow rate at 25% of FVC in MEFVC, $\dot{V}_{10}$: flow rate at 10% of FVC in MEFVC, $\dot{V}_{50}/\dot{V}_{25}$: ratio of $\dot{V}_{50}$ to $\dot{V}_{25}$, MTC_{75-50} : mean time constant (MTC) in the level of 75-50% of FVC, MTC_{50-25} : MTC in the level of 50-25% of FVC, MTC_{25-RV} : MTC in the level of 25-0% of FVC, U.S.D. : unbiased sample standard deviation.

The results of the tests using pulmonary function parameters. The results of the pulmonary function tests are shown in Table 2. Seven mean values of the pulmonary function parameters obtained from the moderate asthmatic patients (%FVC, $FEV_{1.0\%}$, PFR, $\dot{V}_{75}$, $\dot{V}_{50}$, MTC_{75-50}, and MTC_{50-25}), were lower than those from mild asthmatic patients.

The t-tests of the differences in mean values. The results of the t-tests are shown in Table 2. The parameters, $FEV_{1.0\%}$, $\dot{V}_{75}$, MTC_{75-50}, and MTC_{50-25}, were statistically significant.

Discriminant Analysis with Single Parameter

The order of the parameters. The parameters were arranged as follows in the order of the probability of misclassification: MTC_{50-25}, $\dot{V}_{75}$, MTC_{75-50}, $FEV_{1.0\%}$, $\dot{V}_{50}$, and PFR.

The probability of misclassification. The results are shown in Table 3. MTC_{50-25} showed 30.83%, the lowest probability of misclassification, $\dot{V}_{75}$, showed 32.03%, MTC_{75-50} 32.40%, $FEV_{1.0\%}$ 32.81%. The results of the remaining parameters are shown in Table 3.

Discriminant Analysis with the Four Parameter Groups (MEVT, MEFV, MTC and Total Parameter Group)

The probabilities of misclassification computed with the parameter groups are shown in Table 3.

The probabilities of misclassification. The probability with the two MEVT parameters was 31.18%. The probability with the six MEFV parameters was

TABLE 3. THE PROBABILITIES OF MISCLASSIFICATION BETWEEN MILD AND MODERATE ASTHMATICS USING THE ALL POSSIBLE SELECTION PROCEDURE

Parameter or parameter group	Probability of misclassification
%FVC	41.75 %
$FEV_{1.0\%}$	32.81
PFR	35.11
$\dot{V}_{75}$	32.03
$\dot{V}_{50}$	34.46
$\dot{V}_{25}$	39.55
$\dot{V}_{10}$	45.40
$\dot{V}_{50}/\dot{V}_{25}$	44.64
MTC_{75-50}	32.40
MTC_{50-25}	30.83
MTC_{25-RV}	38.17
Volume-time parameter group	31.18
Flow-volume parameter group	18.63
Mean time constant parameter group	28.14
Total parameter group	15.90

TABLE 4. PARAMETERS SELECTED AT EACH STEP AND PROBABILITY OF MISCLASSIFICATION BETWEEN MILD AND MODERATE ASTHMATICS USING THE ALL POSSIBLE SELECTION PROCEDURE

Step	Parameters selected at each step											Probability of misclassification
	1	2	3	4	5	6	7	8	9	10	11	
1	—	—	—	—	—	—	—	—	—	*	—	30.83 %
2	—	—	—	*	—	*	—	—	—	—	—	27.31
3	—	—	—	*	—	*	—	*	—	—	—	20.59
4	—	—	—	—	*	*	—	*	*	—	—	17.63
5	—	—	—	*	—	*	—	*	*	—	*	16.86
6	—	—	—	*	*	*	—	*	*	—	*	16.51
7	—	*	—	*	*	*	—	*	—	*	*	16.37
8	*	*	—	*	*	*	—	*	—	*	*	16.24
9	*	*	*	*	*	*	—	*	—	*	*	15.96
10	*	*	*	*	*	*	—	*	*	*	*	15.91
11	*	*	*	*	*	*	*	*	*	*	*	15.90

Parameters: 1) %FVC, 2) $FEV_{1.0\,\%}$, 3) PFR, 4) $\dot{V}_{75}$, 5) $\dot{V}_{50}$, 6) $\dot{V}_{25}$, 7) $\dot{V}_{10}$, 8) $\dot{V}_{50}/\dot{V}_{25}$, 9) MTC_{75-50}, 10) MTC_{50-25}, 11) MTC_{25-RV}. (*): Parameter selected. (—): Parameter not selected.

18.63 %. The probability with the MTC parameters was 28.14 %. The probability with the total parameter group was 15.90 %.

Discriminant Analysis with the Total Parameter Group

Results are shown in Table 4.

The probability of misclassification at each step. The probability at the first step was 30.83 % ; at the second, 27.31 % ; at the third, 20.59 % ; at the fourth, 17.63 %, and at the fifth, 16.86 %. A gradual decrease in the probability of misclassification was shown from the fifth to the final step. The final probability was 15.90 %.

The selection of the best parameters at every step. MTC_{50-25} was selected at the first step, but was not selected from the second to the fifth step, and was selected again from the sixth to final step. $\dot{V}_{75}$ was selected at the second and third step, but was not selected at the fourth step, and selected again from the fifth to final step. $\dot{V}_{25}$ was selected from the second to final step. The ratio $\dot{V}_{50}/\dot{V}_{25}$ was selected from the third to final step. MTC_{75-50} was selected at the fourth and fifth step, but was not selected srom the sixth to ninth step, and selected again at the tenth and the final step (Table 4).

DISCUSSION

In the supervision of asthmatic patients, it is useful to perform the maximal expiratory volume-time and flow-volume tests in order to estimate the extent of ventilatory abnormality. In the field of public health, it is difficult to perform

further pulmonary function tests, such as the closing volume measurement and the measurement of frequency dependence of dynamic compliance, and tests for respiratory allergy, such as skin tests, a bronchial hypersensitivity reaction test, and measurement of total and specific serum IgE level.

The flow-volume curve is useful because it easily indicates the severity of bronchial asthma, and also because it estimates the extent of bronchoconstriction. The sudden drop in flow near $\dot{V}_{75}$ and the change in the flow rates from $\dot{V}_{75}$ to $\dot{V}_{50}$ were characteristic in asthmatic patients of MEFV patterns. The subjective nature of the estimation of differences in MEFV patterns, however, is of disadvantage.

Therefore we attempted discriminant analysis using the forward selection procedure (FSP) with six pulmonary function parameters (two V-T, and four MEFV parameters) and determined that $\dot{V}_{50}$ showed the lowest probability of misclassification (5). In using eight parameters ($\dot{V}_{75}$ and $\dot{V}_{10}$ added), $\dot{V}_{75}$ showed the lowest probability of misclassification (7). $\dot{V}_{75}$, $FEV_{1.0\%}$, PFR, and $\dot{V}_{50}$, selected at the fourth step, were effective in the discriminant analysis. The probability of misclassifying healthy adults as asthmatics was 15.8 % at the fourth step. The decrease in the probability was slight from the fifth to the final step.

We performed the analysis using the all possible selection procedure (APSP) (9-10) because the parameters selected and the probability of misclassification computed at each step were not always the best with FSP, but those using APSP were always the best.

In our previous paper (9), three MTC parameters of ventilatory mechanics were added to the eight parameters because they were considered to be important and effective in discriminant analysis. At higher steps the MTC parameters were selected with the total parameter group, but not with any of the eleven parameters, while at the three highest steps, the flow-volume parameters ($\dot{V}_{75}$, $\dot{V}_{50}$, and $\dot{V}_{25}$) were selected. The probabilities of misclassification using all the parameters (the total parameter group) was 15.49 %. Thus discriminant analysis demonstrated the importance of flow-volume curves.

In our last paper (10), we attempted the discrimination between healthy adults and mild asthmatics and also between healthy adults and moderate asthmatics. We thought that this would provide a basis for a sequential discrimination of bronchial asthma.

In the analyses we considered the order of use of the eleven parameters, the probabilities of misclassification, and the best selection parameters. In the two analyses, the order of the parameters selected at every step was slightly different, but the probabilities of misclassification were remarkably different.

In this paper, we attempted the discrimination between mild asthmatics and moderate asthmatics. First, we compared the probabilities of misclassification using each of the eleven parameters. Next, we compared the probabilities of misclassification obtained from the four parameter groups. Finally, we selected

the best parameters out of the eleven at each step, computed the probabilities of misclassification at each step and evaluated the extent of the decrease in the probabilities.

In this analysis of the severity of bronchial asthma, the parameters selected at each step were remarkably different from those of previous analyses (9, 10). In addition, the probability of misclassification gradually decreased after the fourth step. The final probability of misclassification was 15.90 %, and nearly equal to that of the analysis between healthy adults and total asthmatics. Thus the discriminant analysis showed that flow-volume curves can be used to distinguish between mild and moderate asthmatics.

When a sequential discrimination is performed in the further, the discrimination of mild and moderate asthmatics, which were well distinguished in this analysis, will be necessary. The sequential discrimination of bronchial asthma using APSP will be discussed in a paper soon to follow.

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