Acta Medica Okayama

Volume 44, *Issue* 6 1990 *Article* 3

DECEMBER 1990

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Abstract

Pulmonary function tests were performed on 234 healthy non-smoking young subjects (189 males and 45 females free from respiratory and allergic symptoms). Maximal expiratory flow-volume (MEFV) curves were visually classified into five MEFV types: Type A, convex or straight flow changes; types B, C, and D, concave-convex-concave flow changes; and type E, sudden flow-fall and accompanying decreased flow rates at lower lung volumes. The reproducibility of MEFV patterns were shown by one way analysis of variance (ANOVA) of MEFV data obtained from 4 groups each consisting of 3-4 males and representing different MEFV types. Distribution of MEFV types was different between males and females; the rate of type A was higher in females than in males and those of types B and E were higher in males than in females. When analyzed in terms of three fractional flow rates, Fr-75, Fr-50, and Fr-25, these values could also be classified into 5 types similarly to the visual MEFV type analysis. It is concluded that MEFV type analysis is useful in assessing health conditions.

KEYWORDS: maximal expiratory flow-volume type, sex difference

*PMID: 2075828 [PubMed - indexed for MEDLINE]

Acta Med Okayama **44** (6) 293-300 (1990)

Classification of Maximal Expiratory Flow-Volume Types Observed in Non-Smoking Healthy Young Subjects

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Key words : **maximal expiratory flow-volume type, sex difference**

Maximal expiratory flow-volume (MEFV) curves are widely used in clinical and epidemiologic studies. Peters and Ferris have used MEFV data to analyze the effect of smoking on pulmonary function and respiratory system in a college-aged group (1), and Nishioka *et al.* have used MEFV curves in a study of nasal allergy (2). Landau *et al.* classified MEFV curves into five types according to their shape (3). Meguro and Ogata have obtained five reproducible and characteristic MEFV curves for the range from effort-dependence at high lung volume to effort-independence at low lung volume in patients with airway allergies such as bronchial asthma, allergic bronchitis and nasal allergy (4). Nishioka *et al.* reported that the percent distribution of type A was significantly lower in patients with nasal allergies than in a healthy control group, while the rate of type E was significantly higher in the patient group than in healthy controls and that of type B was particularly high in the patient group (2). They concluded that the MEFV curves in patients with nasal allergies are useful for differential diagnosis of the lower airway conditions. The reproducibility of MEFV types has not been demonstrated and differences in percent distribution of MEFV types between males and females have not been studied yet. The purpose

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of this study is to clarify the following: 1) the intra-individual and inter-individual variations of MEFV types; 2) the distribution of maximal expiratory volume-time (MEVT) and MEFV data in healthy nonsmoking young subjects of either sex; and 3) sex differences in the distribution of MEFV types in young healthy nonsmoking male and female subjects.

Materials and Methods

Materials. In this study, two groups of healthy young subjects were used. Group 1 (14 males, average age of 24.0) was used in a study of intra-individual and inter-individual variation in MEVT and MEFV data. Group 2 (220 non-smoking healthy young subjects) included 175 males, average age of 23.8 years, and 45 females, average age of 23.2 years. All the subjects in both groups were requested to complete a questionnaire made by the British Medical Research Council, and an airway allergy questionnaire. All were shown to be free from respiratory and airway allergy symptoms.

Pulmonary function testing. A flow-volume curve recorder (AS-4500, Minato Medical Co. Ltd., Osaka, Japan) was used for the maximal expiratory function tests, which consisted of the procedures to determine MEVT and MEFV. These procedures were repeated four times in a standing position for Group 1, and at least twice in a standing position for Group 2. A variety of incomplete expiratory efforts could give rise to inaccurate, unacceptable MEFV curve configurations.

Selection of MEVT and MEFV curves: For the analysis of curve types, MEFV charts were used which had peak expiratory flow rate (PEFR) values sufficiently high to visually evaluate MEFV curve types, and showed inter-determination variation of volume less than 150 ml in forced vital capacity (FVC) (usually less than 3 %) and less than 100 ml in forced expiratory volume in one sec (FEV_1) (usually less than 2 %). The three each MEVT and MEFV charts were obtained from each subject in Group 1 by repetition of determination and were used for the analysis of intra-individual and inter-individual variation. In Group 2, the MEFV chart with the largest PEFR and forced vital capacity (FVC) values obtained from each individual was used for the analysis.

Classification of MEFV types. MEFV curves were visually classified into five types from A to E (subtype

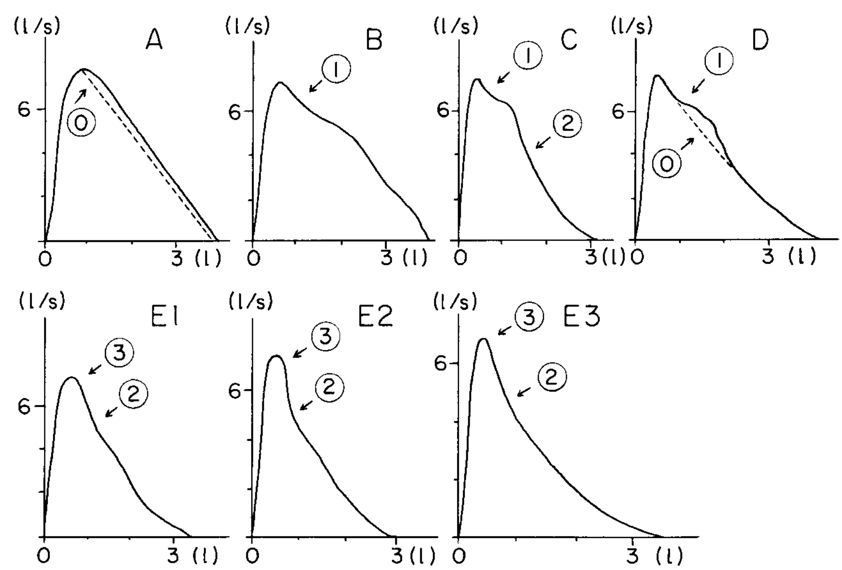

Fig. 1 Maximal expiratory flow volume (MEFV) type classification.
0: The broken straight line is considered to indicate flow changes in healthy subjects. 1: short concave flow changes. 2: long concave flow changes. 3: The slope of flow rates from PEFR (E1; a gentle slope, E2; a moderate sharp slope, and E3; a steep slope).

Table 1 One way ANOVA of pulmonary function indices in the four MEFV types found in Group 1

MEFV type	No.		%FVC	FEV1%	Fr75	Fr50	Fr25
A	3						
		Mean SQ (Inter)	204.344	72.227	61.328	38.937	64.607
		Mean SQ (Intra)	0.553	0.112	8.618	12.093	21.048
		F-value	369.26**	645.00**	7.13*	3.22⁻	43.07**
B	3						
		Mean SQ (Inter)	248.336	25.598	495.520	92.951	213.739
		Mean SQ (Intra)	3.962	4.238	33.288	6.922	4.089
		F-value	62.68**	6.04*	14.89**	13.43**	52.27**
E_1	4						
		Mean SQ (Inter)	58.535	35.231	198.336	55.238	8.108
		Mean SQ (Intra)	2.543	0.393	4.806	6.280	1.415
		F-value	23.02**	89.59**	41.27**	8.80*	5.73*
E_2	4						
		Mean SQ (Inter)	521.801	51.898	99.092	72.285	23.202
		Mean SQ (Intra)	2.701	1.739	34.595	9.983	2.430
		F-value	193.22**	29.85**	2.86⁻	7.24*	9.54*

Abbreviations: ANOVA, analysis of variance; MEFV, maximal expiratory flow volume; FVC, forced vital capacity; FEV, forced expiratory volume; Fr75, Fr50, and Fr25 indicate fractional flow rate at 75, 50 and 25 % of FVC to peak expiratory flow rate (PEFR), respectively (See Materials and Methods); Mean SQ (Inter), mean square of the interindividual data; Mean SQ (Intra), mean square of the intraindividual data. **, $p < 0.01$; *, $p < 0.05$; ⁻, $p < 0.05$. No.: numbers of subjects examined.

E1, E2 and E3) according to their shapes. The types of MEFV curves are shown n Fig. 1. Type A has a convex or straight shape and is considered to indicate normal pulmonary function. Type B has a concave-convex or concave-convex-straight shape and types C and D have concave-convex-concave shapes, and these three types are considered to indicate upper airway obstruction or nasal allergy. Type D is thought to be a transitional type between type B and type E. Type E, which can be divided into subtypes E1, E2 and E3, has a single concavity and is considered to indicate lower airway obstruction. MEFV curve classification was done according to the previously described criteria (2, 3).

Calculation of pulmonary function indices. Pulmonary function indices were simultaneously calculated from the curves using a microcomputer. Three fractional flow rates, Fr-75, Fr-50 and Fr-25 (flow rates at 75 %, 50 % and 25 % of FVC, respectively) were calculated from the following equation:

Fr-X = [Flow rate at X % of FVC/PEFR] × 100.0 (%)

(X = percent of lung volume to residual volume; 75, 50, and 25)

Statistical analysis. One way analysis of variance (ANOVA) of MEVT and MEFV indices was carried out for the four MEFV types found in Group 1 (Table 1). Mean values, standard deviations and coefficients of variation (CV) were calculated for each index. Chi-square test was performed for %-distribution of MEFV types in males and females. Student's t-test was done for MEVT and MEFV indices.

Results

Intra-individual and Inter-individual Variation

One-way ANOVA of pulmonary function indices for the four MEFV types found in Group 1. Results of the one-way ANOVA of pulmonary function indices for the four MEFV types found in Group 1 are shown in Table 1. Inter-individual differences in pulmonary function indices were significantly larger than intra-individual differences except for Fr-50 in type A and Fr-75 in type E2, showing the reproducibility of MEVT and MEFV data in individual subjects.

Table 2 Age, height and conventional spirometry data in non-smoking healthy young subjects

	Male (n=175)	Female (n=45)
Age (years)	23.8 ± 2.0 (8.4)	23.2 ± 1.1 (4.7)
Height (cm)	168.7 ± 5.1 (3.0)	158.2 ± 2.8 (1.8)
%FVC (%)	109.4 ± 10.8 (9.9)	103.8 ± 10.1 (9.7)
$FEV_{1\%}$ (%)	86.8 ± 5.3 (6.1)	91.7 ± 4.8 (5.2)

%FVC, measured forced vital capacity as a percent of predicted vital capacity calculated from Baldwin's equation (10); $FEV_{1\%}$, forced expiratory volume in 1.0 sec as a percent of measured forced vital capacity. Numbers in parentheses indicate coefficient variation (%).

Reproducibility of MEFV curves. Fig. 2 shows three MEFV curves obtained from four subjects, each showing one of the four types found in Group 1. Three MEFV curves obtained from each individual were not only similar visually, but also showed good reproducibility of indices of MEFV curves.

Comparison of MEFV Data obtained from Male and Female Medical students

Results of conventional spirometry. Table 2 shows demographic and conventional spirometry data for Group 2. There were no significant differences in percent forced expiratory volume in 1.0 sec ($FEV_{1\%}$) and % of measured FVC to predicted vital capacity (%FVC) between male and female subjects. Coefficients of variation in %FVC ranged from 4.8% to 11.7%, and those of $FEV_{1\%}$ ranged from 5.1% to 7.6%.

Percent distribution of MEFV types. Percent distribution of MEFV types is shown in Table 3. Chi-square test of percent distribution of

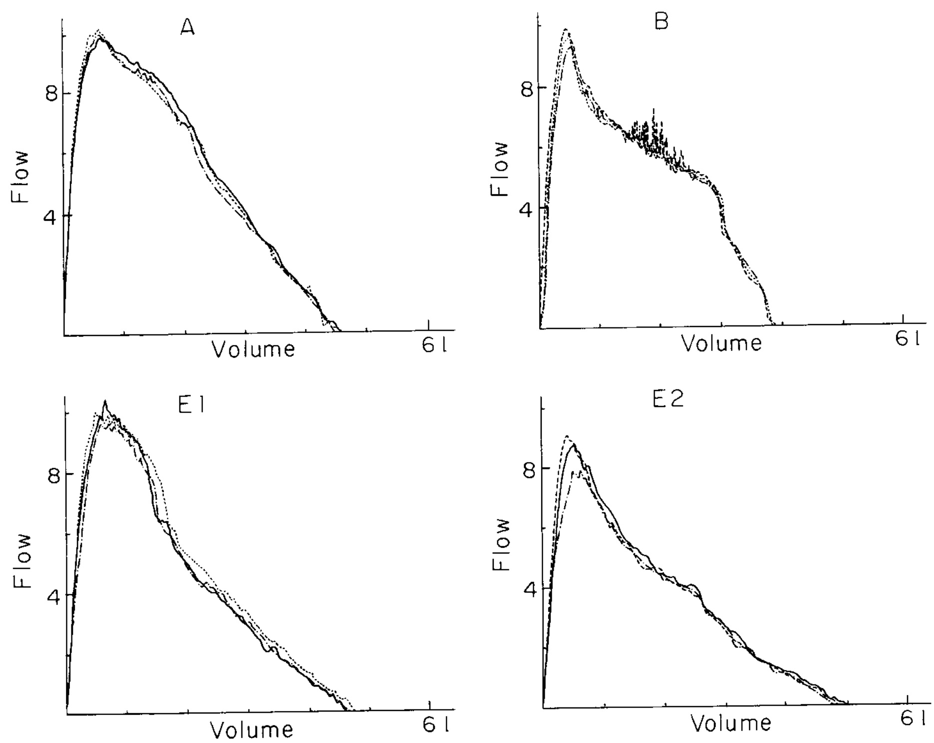

Fig. 2 Three maximal expiratory flow volume (MEFV) curves for each of four subjects representing four MEFV types. Solid line shows the first trial (——), broken line shows the second trial (- - - -), thin broken line shows the third trial (------), and the chain line shows the fourth trial (—·—).

five MEFV types showed a significant difference between male and female students. Percent distribution of type A in males was significantly lower ($P < 0.01$) than in females (29.7 % and 73.3 %, respectively), and percent distributions of types B, C and D, and E (subtypes E1 and E2) were significantly higher in males than in females.

Results of conventional spirometry in individuals showing different MEFV types. Results of conventional spirometry performed in individuals showing different MEFV types are presented in Table 4. There was no siginificant difference in % FVC values among the subject groups showing five different MEFV types. $FEV_{1\%}$ values in males of type E2 group were significantly different from the values in type A, B, C and E1 groups.

Fractional flow rates. Results of determination of fractional flow rates in MEFV types are shown in Table 5. In type A group, the values for all three fractional flow rates (Fr-75, Fr-50 and Fr-25) in females were higher than those in males. In males, the values for the three fractional flow rates in the group showing types E2 and E3 were significantly lower than those in groups showing the remaining types, and the

Table 3 Percent distribution of MEFV types in non-smoking healthy young subjects

Sex	Numbers of subjects showing MEFV types								Total
	A	B	C	D	E	E_1	E_2	E_3	
Male (%)	52 (29.7)	31 (17.7)	18 (10.3)	3 (1.7)	71 (40.6)	51 (29.1)	19 (10.9)	1 (0.6)	175 (100)
Female (%)	33 (73.3)	3 (6.7)	0 (0.0)	0 (0.0)	9 (20.0)	8 (17.8)	1 (2.2)	0 (0.0)	45 (100)

MEFV: Maximal expiratory flow volume.

Table 4 Conventional spirometry data in each MEFV types in healthy non-smoking young subjects

Index	MEFV type	Male		Female	
		Number	Mean ± USD	Number	Mean ± USD
% FVC (%)					
	A	52	108.6 ± 11.0 (10.1)	33	103.6 ± 9.7 (9.4)
	B	31	111.4 ± 11.2 (10.1)	3	107.1 ± 5.1 (4.8)
	C	18	112.7 ± 12.2 (10.8)	0	
	D	3	113.3 ± 13.3 (11.7)	0	
	E_1	51	107.7 ± 9.7 (9.0)	8	102.0 ± 16.0 (15.7)
	E_2	19	108.8 ± 12.2 (11.2)	1	112.0
	E_3	1	120.7	0	
$FEV_{1\%}$ (%)					
	A	52	88.7 ± 4.7 (5.3)	33	92.0 ± 4.7 (5.1)
	B	31	88.8 ± 5.5 (6.2)	3	89.9 ± 6.8 (7.6)
	C	18	85.6 ± 4.7 (5.5)	0	
	D	3	91.6 ± 6.9 (7.5)	0	
	E_1	51	85.0 ± 6.4 (7.5)	8	91.6 ± 5.4 (5.9)
	E_2	19	80.9 ± 4.2 (5.2)	1	88.0
	E_3	1	74.1	0	

Numbers in parentheses indicate coefficients of variation (%).
Mean, mean value ; USD, unbiased sample standard deviation.
Other abbreviations: See Table 1.

Table 5 Flow rate fraction in each MEFV type in healthy non-smoking young subjects

Index	MEFV type	Male		Female	
		Number	Mean ± USD (%)	Number	Mean ± USD (%)
Fr75 (%)					
	A	52	90.5 ± 7.5 (8.3)	33	94.8 ± 3.9 (4.1)
	B	31	86.0 ± 6.9 (8.0)	3	87.6 ± 10.8 (12.3)
	C	18	85.1 ± 5.7 (6.7)	0	
	D	3	87.8 ± 7.7 (8.8)	0	
	E_1	51	87.5 ± 9.9 (11.3)	8	94.1 ± 10.7 (11.4)
	E_2	19	73.8 ± 9.4 (12.7)	1	95.6
	E_3	1	9.6	0	
Fr50 (%)					
	A	52	57.1 ± 8.9 (15.6)	33	66.0 ± 9.6 (14.5)
	B	31	61.4 ± 8.0 (13.0)	3	63.9 ± 8.9 (13.9)
	C	18	56.0 ± 11.4 (20.4)	0	
	D	3	57.6 ± 12.9 (22.4)	0	
	E_1	51	45.7 ± 5.6 (12.3)	8	52.3 ± 6.8 (13.0)
	E_2	19	38.2 ± 6.2 (16.2)	1	48.1
	E_3	1	34.2	0	
Fr25 (%)					
	A	52	23.9 ± 5.8 (24.3)	33	28.7 ± 5.8 (20.2)
	B	31	28.4 ± 6.5 (22.9)	3	38.9 ± 13.5 (34.7)
	C	18	19.7 ± 3.6 (18.3)	0	
	D	3	28.7 ± 8.1 (28.2)	0	
	E_1	51	19.8 ± 4.5 (22.7)	8	24.7 ± 5.1 (20.6)
	E_2	19	15.1 ± 3.3 (21.9)	1	23.4
	E_3	1	14.0	0	

Numbers in parentheses indicate coefficients of variation (%).
Mean, mean value; USD, unbiased sample standard deviation; FrX (%), fraction of Flow-X to peak expiratory flow rate (PEFR) represented as per cent. Other abbreviations: See Table 1.

values for Fr-50 and Fr-25 in the group showing type B were higher than those in the groups showing the remaining types. Coefficients of variation were high in Fr-50 (13.0%–22.4%) and Fr-25 (18.1%–34.7%).

Discussion

Intra-individual and inter-individual variation of MEVT and MEFV data. Percent distribution of types of MEFV curves has been shown to be different between healthy subjects and patients with airway allergy, and the types of MEFV curves can usually be easily identified and classified (2, 4). But these types are thought to be modified by sex, aging, smoking habits, and other factors. Furthermore, patterns of MEFV curves are affected by the examinee's efforts. Thus, it is necessary to discuss intra-individual and inter-individual variations in MEVT and MEFV data. In the present study, the inter-individual reproducibility of MEFV patterns was confirmed by one way ANOVA of the pulmonary function indices calculated for the four types of MEFV curves (A, B, E1, and E2) observed in non-smoking healthy young subjects. Intra-individual reproducibility was shown by comparing the three test curves obtained from each subjects.

MEFV types in healthy subjects and patients with airway allergy. It is possible that so-called "healthy" subjects have subclinical airway allergies without subjective symptoms. Patients with bronchial asthma showed type E2 or E3 curves according to the asthmatic symptoms (4). In 77 % of patients with nasal allergy showing type B or C, hyperemic and hypertrophic membranes were observed in rhinoscopy, and in 52 % of patients with nasal allergy showing type E curves, exhibited pale edematous membranes. Thus, patients with nasal allergy and showing type E curves may have latent obstructions of the peripheral airways and developed latent hypersensitivity of the airways (2). However, it is necessary in the future to study the relationship between MEFV types and health conditions in healthy subjects as well as in patients with subclinical airway allergy.

Sex difference. Dockery *et al.* have reported that the FEV_1/FVC ratios in children were higher in girls than in boys (5). From their data, mean FEV_1/FVC ratios can be estimated to be about 86 % in girls, and about 83 % in boys. They reported estimated mean values for FEV_1/FVC ratios in nonsmoking adults aged 20–30; the values in females were about 88 % and those in males about 83 %. FEV_1/FVC ratio in females decreased remarkably between 20 and 40 years of age. Our calculated mean values for the FEV_1/FVC ratio was 93 % in females and 89 % in males. These mean values for FEV_1/FVC ratios were similar to those obtained by the extrapolation of the data of Dockery *et al.* (6).

In our previous report (2), percent distribution of MEFV types was determined in healthy controls (type A 40.5 %, type B 24.3 %, type C 8.1 %, type D 5.4 %, and type E 21.6 %), but sex differerences in the distribution of MEFV patterns have not been analyzed yet. The results of the present study performed in both sexes are similar to those obtained in our previous study made without discrimination between sexes. When the data obtained in this study for both sexes are combined, the percent distribution of MEFV types was as follows: type A 38.6 %, type B 15.5 %, type C 8.2 %, type D 1.4 %, and type E 36.4 %. But percent distribution of MEFV types in this study was remarkably different between males and females. Especially, the distribution of type A was 29.7 % in males and 73.3 % in females, and that of type E1, was 40.6 % in males and 17.8 % in females.

Type A in female students in this study was composed of 53.3 % convexed MEFV curves and 46.7 % straight curves. In a study of convexed MEFV curves, Green and Mead (7) have pointed out that deep inspiration has bronchodilating effects. On the bronchodilating effect of deep inspiration in yong healthy female subjects, Fujimura *et al.* (8) reported that deep inspiration in these subjects has a relaxation effect on the basic bronchomotor tone and that this sex difference disappeared by the blockage of cholinergic receptors. Fujimura *et al.* (9) also stated that the bronchodilating effect of deep inspiration in young healthy female subjects may depend on the intensity of basal bronchomotor tone caused by tonic vagus nerve activity. Therefore, airway hypersensitivity and vagus nerve activity are considered to be causal factors in the variation of MEFV curves based on sex differences.

Effects of aging. Lower airway obstruction may occur more easily in the aged than in younger adults, and changes in the shape of MEFV curves may proceed with aging. Data for young adults were obtained in this study which may be used as a basis of studies of MEFV types in older age groups.

Refinement of MEFV types. Types of MEFV curves were usually easily identified and classified visually, although sometimes intermediate type of curves were observed. We have often experienced concaved type A curves in lower lung volume ranges in nonsmoking subjects over 40 years of age or in smokers. Thus, this overlapping of MEFV curve types may mainly be due to smoking or aging. In order to solve the problem of this overlapping of types of MEFV curves due to smoking and aging, it is necessary to refine the classification of MEFV types. As more MEFV curve data for various populations become available, and the MEFV classification system is more refined, the MEFV curves will be demonstrated to be useful diagnostic and research tools.

Acknowledgment. Authors wish to thank Prof. B.G. Ferris Jr., M.D., Prof. F.E. Speizer, M.D., and Assistant Prof. D.W. Dockery, Ph.D., of Harvard School of Public Health, Department of Environmental Science and Physiology for helpful comments.

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Received April 18, 1990; accepted August 22, 1990.