

INTRA-INDIVIDUAL AND DIURNAL VARIATION OF LUNG FUNCTION MEASUREMENTS IN HEALTHY SRI LANKANS

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Summary. Maximum expiratory flow-rates in the latter part of the flow-volume curve are considered to be useful in the diagnosis of early small airways obstruction. For this objective, it is essential to determine the degree of intra-subject and diurnal variation of these variables in healthy individuals. This study measures intra-individual variation of dynamic lung function tests, including indexes derived from the flow-volume curve, in a group of healthy Sri Lankans.

Eleven subjects (4 women) of age range 22 to 48 years were studied. Spirometric tests (FVC, FEV₂, and FEF_{25-75%}) peak expiratory flow rates (using the mini-Wright peak flow meter) and flow-volume curves were performed in the morning and in the afternoon on 10 consecutive days. The mean morning-afternoon differences and mean coefficients of variation were calculated for each test.

There was no morning-afternoon variation in any of the tests. The intra-individual variations detected for FVC and FEV₁ and the the peak expiratory flow rate were of the order of 3 to 4%. The variations of the maximum expiratory flow rates at 50% and 25% lung volume and the the forced mid-expiratory flow rate (FEF_{25-75%}) were about 7 to 10%. The results were similar to those reported in other populations.

It is concluded that the indexes derived from a volume-time tracing during a forced expiratory manoeuvre were more reproducible and therefore more suited for population screening. The high variability inherent in the indexes derived from the flow volume curve may limit their usefulness in detecting early airways obstruction.

Key words: Lung function measurements, adults, diurnal variation

INTRODUCTION

One of the purposes of lung function testing is to identify early airways disease, specially those involving the small airways of the lungs which constitute the "silent zone". For this purpose, it is essential not only to establish normal values for a given population, but also to investigate the variability of the tests concerned and to establish whether a diurnal variation is present; and if so, to find out the extent of this variation.

John Hutchinson was the first to report the existence of a day-to-day variation of lung function with respect to vital capacity (1). Since then, several studies of reproducibility of some spirometric measurements have appeared in the

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literature (2, 3, 4). Some reports (5) are available with regard to intra-individual variation of indexes derived from the flow-volume curve. No data are available for Sri Lankans.

The aim of this investigation was to determine the morning-evening and day-to-day variation of a number of lung function tests in a group of healthy Sri Lankan subjects, both men and women.

METHOD

Fourteen normal subjects (4 women) of age range 22 to 48 years, volunteered for the study. They were employees of the department of Physiology at the Faculty of Medicine, Peradeniya, familiar with the testing procedure and accustomed to performing forced expiratory manoeuvres. The subjects had no history of upper respiratory infection in the three weeks immediately preceding the test. None gave a past history of chronic respiratory illness. Three of the male subjects developed upper respiratory tract infections during the test period and were excluded from the final analysis.

The mean age and height of the 7 remaining men were 32.3 (SD 8.96) years and 159.8 (SD 1.84) cm respectively. They had a mean smoking history of 0.9 pack years (the pack-year indicates the number of cigarettes smoked per day divided by 20 and multiplied by the number of years the subject has been smoking). Five were never-smokers and one, an ex-smoker. The mean age of the four women was 29.3 (SD 2.50) years and the mean height was 151.6 (SD 4.53) cm. None of the women smoked.

As the subjects chosen were highly motivated, familiar with the testing procedure and experienced in the performance of lung function tests, the effect of training and learning on the results was minimized.

To eliminate inter-observer error, all the tests were carried out by a single operator.

The following tests were performed:

1. Peak expiratory flow rate (PEFW)
2. Indexes derived from the forced expiratory spirogram which included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced mid-expiratory flow rate (FEF 25-75%) and the FEV_1 /FVC ratio
3. Indexes derived from the flow-volume curve which were instantaneous peak expiratory flow rate (PEF), flow rate at 50% lung volume ($V_{max 50}$) and the flow rate at 25% lung volume ($V_{max 25}$).

A new mini - Wright peak flow meter was used to measure peak expiratory flow rate - as the instrument had been observed to lose calibration with time (6). A single instrument was used to obtain all the readings in order to eliminate differences in readings between instruments. Measurements were taken with the subjects in the standing position and the flow meter held horizontally. The subjects were watched for faults in technique such as acceleration of air-flow at the mouth which is known to give spuriously high readings (7). They were exhorted to perform the test to the best of their ability and the highest result of three acceptable blows was taken as the correct reading, as recommended in the ACCP Scientific Recommendations (8).

The forced expiratory manoeuvres were performed using Morgan "Spiroflow" spirometer (obtained from PK Morgan Ltd., 4, Bloors Lane, Rainham, Gillingham, Kent, United Kingdom). The spirometer conformed to the recommendations of the American Thoracic Society 1987 Update (9). Tests were performed with the subject seated and without a nose-clip, as stated in the ACCP Scientific section recommendations (8), the largest value of three acceptable readings which varied by less than 5% of the highest reading was selected as the correct reading. The "end of test" criteria were as recommended by the American Thoracic Society (9). The FEV₁ was calculated using the back - extrapolation method (10).

A Rikedensky X-Y recorder (obtained from Rikedensky Mitsui Electronics Ltd., Oakcroft Road, Chessington, Surrey, England) was used in series with the spirometer to record flow-volume curves. The curve resulting from the forced expiratory manoeuvre giving the largest sum of FVC and FEV₁ was selected for calculating forced expiratory flow rates (9).

The ambient temperature of the laboratory recorded to an accuracy of $\pm 1^{\circ}\text{C}$ was between 24 to 29 $^{\circ}\text{C}$. The results were converted to BTPS using a nomogram (10).

Tests were performed between 7.30 and 8.30 in the morning following a 30 minute period of rest after arriving in the laboratory, and between 4.00 and 4.30 in the afternoon following a 30 minute rest period after the day's work. Those who were smokers did not smoke for 2 hours prior to the test.

RESULTS

The readings obtained for eleven subjects for each lung function test (expressed as the mean of the readings for the 10 test days) for the morning and afternoon separately, were used to calculate the mean morning and afternoon difference. These values (and SD and 95% confidence intervals of the differences) with respect to each lung function test, are shown in Table 1. The

Table 1. Morning: afternoon variation of respiratory function tests

Test	Morning and	95%	t	P
	afternoon difference Mean (SD)	confidence intervals of the difference		
PEF (Wright) (l/min)	-2.70 (8.08)	8.10 to -2.70	1.10	0.293 (NS)
FVC (l)	0.021 (0.043)	0.05 to -0.01	0.621	0.136 (NS)
FEV ₁ (l)	-0.001 (0.028)	0.02 to -0.02	0.107	0.917 (NS)
FVC/FEV ₁ %	-0.688 (1.198)	0.11 to -1.50	1.905	0.086 (NS)
FEF _{25-75%} (l/s)	-0.007 (0.145)	0.09 to -0.11	1.660	0.871 (NS)
PEF (l/s)	-0.113 (0.185)	-0.08 to -0.17	2.018	0.071 (NS)
V _{max} 50 (l/s)	-0.055 (0.106)	-0.02 to -0.09	1.736	0.113 (NS)
V _{max} 25 (l/s)	-0.054 (0.084)	-0.03 to -0.08	2.119	0.060 (NS)

Means (and SD) of the morning and afternoon differences for eleven subjects for ten days are given in column 2. NS = not significant; PEF (Wright) = peak expiratory flow rate measured by the mini-Wright peak flow meter.

peak expiratory flow rate recorded by the flow meter, FEV₁, the FVE₁ / FVC ratio and the indexes derived from the flow-volume curve were observed to have afternoon readings which were marginally higher than the readings obtained in the morning. The data obtained in the afternoons gave slightly lower readings for FVC. The differences, however, were very small and were not statistically significant.

The "within-subject" coefficients of variation (CV) for each test were calculated as the means of all the readings obtained for the ten days for all eleven subjects; The mean coefficients of variation (and 95% confidence intervals) are shown in Table 2. The within-subject CV was lowest (being of the order of 3%) for FEV₁ and the FEV₁ / FVC ratio. High coefficients of variation (of the order of 10%) were seen in FEF_{25-75%}, and V_{max25} measurements,

Table 2. "Within-subject" coefficient of variation of respiratory function

Test	Coefficient of variation % (SD)	95% confidence intervals
PEF (Wright) l/s	3.03 (1.41)	3.34 to 2.72
FVC (l)	3.48 (1.70)	3.85 to 3.11
FEV ₁ (l)	4.01 (2.06)	4.46 to 3.56
FVC/FEV ₁ (%)	2.49 (0.73)	2.65 to 2.33
FEF _{25-75%} (l/s)	10.09 (2.69)	10.6 to 9.76
PEF (l/s)	5.46 (2.74)	6.06 to 4.86
V _{max50} (l/s)	7.74 (2.35)	8.25 to 7.23
V _{max25} (l/s)	10.32 (3.63)	11.1 to 9.53

Mean coefficients of variation (and SD) obtained for 10 days for eleven subjects are given in column 2. NS = not significant; PEF (Wright) = Peak expiratory flow rate obtained by the mini-Wright peak flow meter

DISCUSSION

A small group of subjects was studied as it was impracticable to repeatedly test a large group over a one hour period in the mornings and evenings daily. Since the results of this study confirmed the findings of other authors (who also tested small groups of subjects) in other population groups, it was decided not to extend the study to a larger group.

The study showed no significant variation in respiratory function (as measured by FVC, FEV₁, FEF 25-75%, V_{max}50, V_{max}25 and PEF estimated by flow-volume curves and the mini-Wright peak flow meter) between the morning hours (7.30 to 8.30 am) and the afternoon hours (4.00 to 4.30 pm). This is in agreement with the results of Cochrane, Prieto and Clark (5) and Hruby and Butler (11) who showed that there was no consistent statistically significant pattern of variation of FVC, FEV₁ and FEF25-75% between the hours of 9 am and 6 pm in normal individuals, although a diurnal variation was demonstrable in patients (11, 12). The latter authors showed that the above findings were also applicable to vital capacity and airways resistance.

The existence of a variation between the morning hours and the late evening hours cannot be ruled out in the present study. Patients are generally tested during working hours (between 8 am and 4 pm). Within these times, this study shows that there is no significant morning: afternoon difference in the measurements. Therefore it can be concluded that respiratory function tests can be carried out in the laboratory throughout a working day without loss of precision.

Several studies are available concerning the day-to-day variability in lung function tests in normal subjects. Table 3 shows the coefficient of variation for repeated measurements of FEV₁ in various studies reported in the literature. Rozas, Allen and Goldman (21) have reported coefficients of variation observed in five subjects with regard to FVC and FEV₁ for five days to be 2.8 (SD 1.7)% and 2.8 (SD 2.1)% respectively. Recent studies that have reviewed the existing data have suggested that the "within subject" coefficients of variation for FVC and FEV₁ are between 3-4% (23, 24). Hankinson and Paterson (17) have reported that the "intra-subject" coefficient of variation over a one to two year period was less than 3% for FVC and 3.68% for FEV₁. These results compare favourably with the present study where the coefficients of variation were 4.01 (SD 2.06)% and 3.49 (SD 1.41)% respectively.

The coefficients of variation of the tests show considerable variation from person to person (Table 4). This is in agreement with the findings of Black, Offord and Hyatt (24) and McCarthy, Craig and Cherniack (4). The significance of this variability is unclear. Longitudinal studies are necessary to determine whether there may be implications such as increased susceptibility to lung damage in response to environmental pollutants, cigarette smoke and other noxious stimuli.

The results of the present study show that the more sensitive tests of airways obstruction such as FEF_{25-75%} and tests of small airways obstruction such as V_{max50} and V_{max25} have large intra-subject variations (of the order of 8-10 per cent). It has been shown that the maximum expiratory flow rate is effort-independent over the latter half of the FVC, due to the fact that airway compression and collapse occurs with increasing effort, which causes progressive increase in intra-thoracic pressure (25). Thus, tests such as FEF_{25-75%}, V_{max50} , and V_{max25} would be expected to be highly reproducible. However, tests that are considered effort-dependent such as FVC and FEV₁ demonstrated much less variability. These findings are in agreement with Dawson (2), Leullen and Fowler (26) and Clement and Van de Woestijne (27). It is possible that slight differences in FVC on successive expirations may contribute to the variability noted in effort-independent flow rates (27). The high variability inherent in these tests may limit their usefulness in clinical practice. The considerably smaller coefficients of variation for FEV₁, FVC and FEV₁/FVC ratio reported here suggest that these measurements may be more useful for routine screening of patients than the more modern tests of airway dysfunction,

Table 3. Intra - individual variation of FEV₁ values reported in the literature

Reference	CV%
Dawson (2)	3.0
Carey, Dawson & Merrett (13)	1.6-4.9
Guberan, Williams & Smith (14)	4.1
Stebbins (15)	8.2
Lapp, Hankinson, Burgess & O'Brian (16)	9.1
Hruby & Butler (11)	3.0
McCarthy, Craig & Cherniack (4)	3.0
Cochrane, Prieto & Clark (5)	2.7
Hankinson & Peterson (17)	3.68
MacDonald & Cole (18)	3.8
Pennock, Rogers & McCaffree (19)	6.7-8.1
Pham et al (20)	5.1
Rozas, Allen & Goldman (21)	2.8
Groth, Dirksen, Dirksen & Rossing (21)	4.7

CV = Coefficient of variation

Table 4. Within - subject coefficient of variation (%) (with respect to each subject for each lung function measurement) in 11 healthy subjects

Subject	PEF	FVC	FEV ₁	FVC/ FEV ₁	FEF 25-75%	PEF	V _{max50}	V _{max25}
	Wright							
1	3.79	2.62	3.67	2.65	9.28	3.06	9.59	10.3
2	3.90	2.89	2.26	2.70	7.61	3.24	4.95	12.1
3	2.12	2.97	3.61	3.53	14.45	3.17	8.98	13.33
4	2.49	2.03	2.41	2.27	8.97	3.20	4.86	8.55
5	3.17	3.08	4.21	2.75	8.89	5.01	6.53	9.98
6	2.30	3.67	3.06	3.17	10.73	5.27	8.89	7.21
7	2.79	5.85	5.24	2.25	11.15	10.52	10.24	10.24
8	1.45	4.43	4.46	1.84	11.48	7.45	9.81	10.32
9	2.69	4.15	3.54	3.34	6.90	6.77	7.72	4.17
10	2.11	2.13	2.27	1.90	11.5	3.41	4.91	12.0
11	3.67	4.50	9.36	2.29	10.01	8.96	9.63	9.80

Mean coefficients of variations for 10 days for each subject are given for each lung function test

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