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SPECIAL COMMUNICATION

Changes in Measured Spirometric Indices*

What Is Significant?

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Pulmonary function testing in the last decade has moved from the research laboratory into the daily practice of internal medicine and surgery. The first report of a simple method of assessing airways obstruction was in the late 1940s.[1,2] It is not surprising that in this relatively young field the interpretation of the tests is still not universally clear. In recent discussions in the pulmonary section of the University of Oklahoma at Oklahoma City, one specific question stood out. In a subject with demonstrated abnormal measured spirometric values, how much acute or chronic change is required to be certain that improvement or deterioration has occurred? In searching the literature we concentrated on the evaluation of spirometry, since this has been examined in the greatest detail. The following assesses the data from the literature, as well as some of our own data, and attempts to answer the question. We recognize that this is not necessarily the final answer, but hope it will generate some interest and comments and make us pause and think about what we label improvement and deterioration.

Significance

The usual definition of a clinically significant difference from normal (an abnormal measured value) is a measured value that statistically would be expected in less than 5 percent of normal subjects. In a Gaussian population, this represents values that are more than 1.65 times the coefficient of variation below the mean. For example, the coefficient of variation for FVC determined in a large group of normal subjects (Table 1) is about 13 percent. A value 21.5 percent (1.65 × 13) smaller than the mean is considered abnormal.

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Population Significance

The application of this significance criterion to the parameters of spirometry in normal population studies is illustrated in Table 1. Coefficients of variation, using a 30-year-old, 173-cm tall man, are given from the studies of Morris et al,[3] Kory et al,[4] and Knudson et al.[5] The approximate average of the coefficients of variation for FVC, FEV_1, and FEF 25-75% are 13, 13, and 25 percent, respectively. Multiplying these coefficients of variation by 1.65 will give significance levels of about 21, 21, and 41 percent, corresponding to the commonly used criteria that values less than 80, 80, and 60 percent of the predicted values are normal values.[6]

Significant Changes in Time

One must identify coefficients of variation for multiple measurements within a day (acute changes) and for determinations from week to week (chronic changes) to develop criteria for the interpretation of time sequential changes in values for individual patients.

Acute Change

Three studies that have presented data with multiple daily spirometric values are listed in Table 2. McCarthy et al[7] tested 12 normal subjects ten times each day with a coefficient of variation calculated as shown in Table 2. Pennock et al[8] tested 20 subjects with reversible airways obstruction nine times

Table 1—*Population Coefficient of Variation**

Reference (No. in Study)	FVC	FEV_1	FEF 25-75%
Morris[3] (517)	14.5	13.6	26
Kory[4] (468)	12.1	13	
Knudsen[5] (128)	12.2	13.7	23.2
Summary	13	13	25

*Coefficient of variation calculated on the basis of a 30-year-old, 173-cm tall male.

Table 2—*Individual (Within Day) Coefficient of Variation*

Reference (No. of Patients, No. of Tests Each)	FVC	FEV_1	FEF 25-75%
McCarthy[1] (12, 10)	3	3	8
Pennock[6] (20, 9)	6.7	8.1	14
Hruby[*9] (15, 10)			
Normal	3	5	
Obstructive	6	7	
Restrictive	9	11	
Summary			
Normal	3	3	8
Obstructive	6.7	8.1	14

*Range, not coefficient of variation.

daily and found values for the coefficient of variation about twice those of McCarthy's normal subjects. Similarly, Hruby et al,[9] testing 15 subjects ten times per day, found that the ranges of coefficient of variation in both the obstructive and restrictive subjects were about twice those of his normal subjects. Multiplying each of the average values for coefficient of variation by 1.65 yields the result that a significant change within a day's time in a normal subject is 5 percent or greater in FEV_1 and FVC and 13 percent in FEF 25-75%. However, a significant change in an obstructive patient is about twice that of a normal subject, *ie* 11 percent of FVC, 13 percent in the FEV_1, and 23 percent in the FEF 25-75%. As a general rule of thumb, Tables 1 and 2 show that the daily individual variability in all tests is about one-fourth the population variability in normal subjects and about one-half of the population variability in chronically obstructed subjects.

Chronic Change

To evaluate long-term changes, one must look at the coefficients of variation from week to week.

Table 3—*Individual (Week-to-Week) Coefficient of Variation*

Reference (No. of Patients, No. of Tests Each)	FVC	FEV_1	FEF 25-75%
McCarthy[1] (20, 10) and (5, 25)	5	7	13
Spicer[*]			
Normal (11, 30-60)	7.8		
Bronchitic (7, 30-60)	13.5		
Asthmatic (10, 30-60)	14.1		
Pennock[6] (20, 5)			
Asthmatic	11.1	14.2	18.4
Summary			
Normal	6.4	7	13
Obstructive			18.4

Table 4—*Significance Level (Changes Greater than Percent Shown)*

	FVC	FEV_1	FEF 25-75%
Population mean	21	21	41
Within day			
Normal	5	5	13
Obstructive	11	13	23
Week-to-week			
Normal	11	12	21
Obstructive	21	23	30

Three studies have been identified in which these data are available (Table 3). In normal subjects significant week-to-week changes are 11 percent in the FVC, 12 percent in the FEV_1, and 21 percent in the FEF 25-75%. The patients with obstructive disease had greater variability than normal subjects, the variability being 21 percent in FVC, 23 percent in FEV_1, and 30 percent in FEF 25-75%. Again, in week-to-week changes, the subjects with obstruction showed about twice the variability of the normal subjects.

Table 4 summarizes the data for population studies and for longitudinal studies in individuals, both normal subjects and subjects with airways obstruction. These levels define significance at the 95 percent confidence limit, based on the cited population studies.

Application

As an example of the use of this type of information, one of the tests frequently used in evaluation of obstructed patients is the measurement of spirometric parameters before and after administration of a bronchodilator. From Table 4 it is apparent that an increase in FVC and FEV_1 by more than approximately 12 percent; 11 percent in FVC; 13 percent in FEV_1, or an increase in FEF 25-75% of greater than about 25 percent (23 percent) represents a statistically significant change from the baseline.

Similarly, if one is following up a patient over a long term, to assess a stable, deteriorating, or improving condition, the week-to-week change (Table 4) in FVC and FEV_1, must be greater than 20 to 25 percent or the change in FEF 25-75% greater than about 30 percent.

The identification of subjects with spirometric indices that are abnormal is commonly accomplished from a definition of clinical significance based on the concepts of statistical significance at the $P<0.05$ level. We have applied these concepts to measured data to derive criteria for clinical significance in relation to changes of measured spiro-

metric values in an individual subject within a day and from week to week. Again, we think this type of analysis yields clinically useful information, but we recognize that there may be better approaches. Whether or not better approaches exist, we hope to stimulate discussion of this very important question of improvement or deterioration in an individual patient.

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