Failure of Body Plethysmography to Reflect Functional Deterioration Seen in Chronic Obstructive Pulmonary Disease*

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Measurements of lung volumes, airway conductance (Ca) and expiratory flow rates were compared in 40 patients with chronic obstructive pulmonary disease (COPD) who were observed for an average of 3.3 years. The first and final study of each patient were compared and the average changes for the group were analyzed statistically. Although a diminution in expiratory flow rate was an almost invariable finding, changes in Ca, specific conductance, residual volume, residual volume/total lung capacity, functional residual volume and expiratory reserve volume did not show any consistent change. Patients who were more severely impaired in terms of expiratory flow tended to show more consistent deterioration in Ca and Ca/V'TTO. However, the initial level of Ca and Ca/V'T; did not indicate in which direction these functions would change with time. It is concluded that at least for the short term follow-up of COPD body plethysmography does not reflect the clear deterioration manifested by the reduction in expiratory flow rate seen in this disease.

In 1967 Mitchell and co-workers,† when they measured specific conductance by means of body plethysmography, suggested that the plethysmograph might not be any more sensitive in detecting early obstructive lung disease than the measurement of expiratory flow rates by routine spirometric methods. Other workersⅡ-Ⅶ have pointed out that expiratory flow rate may be diminished by the loss of lung retractive force without producing abnormality in the measured airway resistance. The present work points up the additional disadvantage of the plethysmograph in that although diminution in expiratory flow, even with short periods of follow-up, is an almost universal finding, there are no clear directional changes in either conductance or specific conductance.

Methods

Patients were selected from a group of 91 subjects with chronic obstructive pulmonary disease (COPD) who have been observed in this laboratory for up to 13 years.Ⅲ Forty of these patients, studied by means of body plethysmography two or more times, form the basis of this report. The duration of follow-up with body plethysmography for these 40 patients was from 0.8 to 5.8 years, average 3.3 years. These patients, as with the parent group of 91, were considered to have COPD on the basis of physiologic tests. The first second timed vital capacity, (FEV1 percent) was less than 70 percent or the MMF was below 1.8 L/sec or both.ⅢⅣ Two patients who did not fit these criteria when first seen were included because they have shown consistent decline in expiratory flow over four and eight years. No patient had asthma or an identifiable cause of COPD such as pulmonary tuberculosis and no patient was included with chest wall deformity, significant systemic disease or heart disease other than cor pulmonale. No patient was studied during acute respiratory failure.

Ventilatory studies were performed on a Pulmonor with the subject seated and the nose occluded. The best of three slow vital capacities (VC) was taken to be the patient’s VC. The best of three or more forced vital capacities (FVC) was used for the calculation of the MMF, the FEV1 percent and the first second volume (FEV1). Studies in the body plethysmograph were performed according to methods previously published.ⅢⅤ-ⅢⅧ Spirometric and plethysmographic

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studies were performed in random order in the morning during the same visit. Plethysmographic studies were performed only by one of us, JW, for the years covered by this work. Total lung capacity (TLC) and residual volume (RV) were calculated from the expiratory reserve volume (ERV) and the VC spirometrically determined, and from the functional residual capacity (FRC) determined plethysmographically, as follows: TLC = FRC - ERV + VC; RV = FRC - ERV. Functional residual capacity was determined during quiet breathing while thoracic gas volume (VGT) was determined at the volume at which the subject panted during the determination of Ca. FRC is set by the subject's end-expiratory volume during quiet breathing. However, RV is an indeterminate volume which may vary widely from FRC, particularly in patients with COPD who may involuntarily pick a volume at which to pant which is a liter or more above FRC. It was, therefore, this latter volume which was used to determine specific conductance (Ca/VGT).

For the purpose of analysis the 40 patients were considered as a group. They were also subdivided into two subcategories based on the level of the initial MMF. Group 1: MMF ≥ 0.5 L/sec; Group 2: MMF < 0.5 L/sec. These divisions may appear somewhat arbitrary; however, in this laboratory an MMF below 0.5 L/sec is considered to indicate severe COPD. There were too few subjects with an MMF above this level to subdivide further group 1 into mild and moderate disease.

The initial spirometric study used was the one which coincided with the initial plethysmographic study although many of these patients had been followed by means of spirometry for years prior to the first plethysmographic study. The final value for each function was obtained from the patient's most recent study.

**RESULTS**

Table 1 summarizes the clinical, physiologic and statistic data on all 40 subjects (two subjects had no lung volume measurements except VGT). There are two measures of airway conducance, Ca and Ca/VGT, five measures of volume, RV, TLC, RV/TLC, ERV and FRC, and three measures of expiratory flow, FEV1, FEV1 percent and MMF. All statistical analyses reported here are on the

| Table 1—Analysis of Changes in Function between the Initial and Final Study |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Age | Moe | I | F | I | F | I | F | I | F | I | F | I | F |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| **Group 1** |
| Range | 27-71 | 23-71 | .18 | .22 | .03 | .03 | 1.5 | 2.3 | 4.6 | 4.4 | 30 | 39 | 2.5 | 3.2 | 0.6 | 0.5 | 1.05 | 0.9 | 41 | 34 | 0.5 | 0.24 |
| n/N | 15/16 | 10/16 | 9/14 | 11/14 |
| M | 54 | 46 | 46 | 42 | 4.9 | 1.1 | 1.0 | 1.5 | 57 | 50 | 10.0 | 7.7 |
| SD | 13 | 18 | 0.12 | 0.23 | 0.04 | 0.06 | 1.36 | 1.42 | 10.03 | 9.87 | 1.13 | 1.30 |
| Δ M | 0.1 | 0.02 | 0.7 | 0.4 | 0.6 | 0.7 | -0.1 | -0.3 | 7.0 | 7.4 |
| p | <0.05 | >0.5 | 0.05 | >0.1 | >0.05 | >0.02 | >0.6 | 0.005 | 0.005 | 0.005 | 0.005 | 0.005 |
| **Group 2** |
| Range | 30-74 | 10-64 | .15 | .13 | .02 | .02 | 2.9 | 2.8 | 5.1 | 4.5 | 41 | 47 | 3.8 | 3.7 | 0.3 | 0.3 | 0.6 | 0.35 | 22 | 18 | 0.10 |
| n/N | 17/24 | 18/24 | 15/24 | 10/24 |
| M | 61 | 35 | 35 | 27 | 2.7 | 0.4 | 0.4 | 0.5 | 65 | 65 | 5.3 | 2.1 |
| SD | 8 | 15 | 0.08 | 0.06 | 0.02 | 0.01 | 1.59 | 1.46 | 1.39 | 8.43 | 8.18 | 1.45 |
| Δ M | -0.03 | -0.01 | 0.4 | 0.1 | 5.0 | 0.5 | 0.1 | 0.3 | -6.0 | -0.1 |
| p | <0.02 | <0.05 | >0.1 | >0.8 | <0.005 | >0.05 | >0.1 | >0.005 | <0.005 | <0.005 | <0.005 | <0.005 |
| **Combined Group 1 and Group 2** |
| Range | 27-74 | 10-71 | .15 | .13 | .02 | .02 | 1.5 | 2.3 | 4.6 | 4.4 | 30 | 39 | 2.5 | 3.2 | 0.3 | 0.3 | 0.6 | 0.35 | 22 | 18 | 0.10 |
| n/N | 20/40 | 24/38 | 19/38 | 28/38 |
| M | 58 | 40 | 40 | 31 | 0.31 | 0.06 | 0.06 | 4.3 | 4.9 | 7.3 | 5.8 | 64 | 5.4 |
| SD | 11 | 16 | 0.11 | 0.19 | 0.03 | 0.05 | 1.57 | 1.47 | 1.53 | 1.44 | 12.00 | 11.53 |
| Δ M | 0.2 | 0 | 0.5 | 0.5 | 2.2 | 0.6 | 0.6 | 0 | -0.3 | -0.2 |
| p | >0.3 | >0.6 | >0.02 | >0.3 | >0.001 | >0.01 | >0.6 | <0.001 | <0.001 | <0.001 |

All statistical analyses were performed prior to rounding off. The rounding off has produced some minor discrepancies between pairs of means and the delta mean.

I—Initial
F—Final
n—Number of subjects whose function changed in the same direction as the average for the group
N—Total number of subjects in the group
M—Mean value
ΔM—Difference between mean of initial and final
p—Probability
Moe—Duration between the initial and final studies
I—Initial study

Ca—Conductance, liters/sec/cm of H2O
Ca/Vt—Specific conductance, liters/sec/cm H2O/liter
RV—Residual volume, liters
TLC—Total lung capacity, liters
RV/TLC—Residual volume: Total lung capacity ratio, percent
FRC—Functional residual capacity, liters
ERV—Expiratory reserve volume, liters
FEV1—Forced expiratory volume, 1 second, liters
FEV1 Percent—First second timed vital capacity, percent
MMF—Maximal mid-expiratory flow, liters/sec

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FIGURE 1. I-increase; D-decrease. The small horizontal line represents the mean for each group. This is a plot of the value for the individual functions when the subject was first seen. For those in whom this function rose, the plot is over (I), for those in whom the function fell, the plot is over (D). In only one instance, RV, was the mean for these values significantly different at the p ≤ 0.01.

observed values of these functions rather than the percent predicted. This was done because of the short period of follow-up and because of the generally wide variation in predicted values, particularly for lung volumes. However, the analyses which follow were also performed with the use of the predicted values and there was no substantial difference from that found with the observed values and they are therefore not presented here.

In the interpretations which follow, the level of significance was set at a p value of 0.01 or less. For the entire group there was no significant change in Ca or Ca/V_{TLC} despite significant deterioration in all measures of flow (Table 1). RV, TLC and ERV did not change significantly while RV/TLC and FRC did. In those patients who had not reached severe disease, group 1, at the time of the initial study, there was no significant change in any plethysmographic function, while for group 2, RV/TLC was the only function other than the expiratory flow rates which changed significantly.

In terms of the numbers of patients showing improvement or deterioration, without regard to the magnitude of the change, for the group as a whole Ca rose in 20 and worsened in 20 while Ca/V_{TLC} improved in 16 and worsened in 24. In group 1, 13 of the 16 patients had an improvement in Ca and 10 in Ca/V_{TLC}. Three cases were normal in terms of Ca or Ca/V_{TLC} or both (Ca ≥ 0.5, Ca/V_{TLC} ≥ 0.155) on the initial or final visit or both. On the other hand, of the patients in group 2 all were abnormal in terms of Ca and Ca/V_{TLC} and only about 20 percent (seven and six patients respectively) showed improvement in Ca and Ca/V_{TLC}.

Since the interval between the initial and final study was variable and since group 1 had an average duration of follow-up which was significantly longer than group 2, changes between the initial and final study were analyzed in terms of percent change per year. Because a longer follow-up tends to minimize the changes due to the tests themselves, the analysis was limited to those subjects with a follow-up of three or more years. However, there were only minor differences between this analysis and that presented in Table 1 and they are, therefore, not presented.

Since directional changes may be obscured by the fact that the group was heterogeneous, ie, contained patients with predominant bronchitis or predominant emphysema, efforts were made to determine the course of plethysmographic changes on this basis. However, separating the patients by the
severity of the diffusing capacity did not serve to clarify the deterioration or lack thereof in plethysmographic functions.

In an effort to determine whether there was some level of severity for each plethysmographic function which would indicate the direction that the change would take, the initial value for each function was compared in those in whom that function rose to those in whom it fell. However, there was no significant difference between the initial and final values for any function save RV (p = <0.001) (Fig 1). Of particular note in this regard is Ca, in which the average initial value for those in whom this function improved was indistinguishable from those in whom it worsened.

**Discussion**

Previously published reports\(^8,14-17\) indicate that in terms of expiratory flow, the MMF, FEV\(_1\) and FEV\(_{0.75}\), pulmonary function in COPD deteriorates with time. Although the present study was conducted over a short period of time, expiratory flow, in terms of the FEV\(_1\), FEV\(_1\) percent and MMF showed significant deterioration. For the MMF this occurred in 39 out of 40 cases. Such deterioration was not true for the group for Ca or Ca/V\(_{To}\), although it is true that for those patients with severe disease when first seen, Ca deteriorated in 71 percent. However, since the initial level of Ca gave no indication of whether Ca would deteriorate or not (Fig 1) the level of the initial MMF gave a better indication of the progression of Ca than did Ca itself.

Ca/V\(_{To}\), which should worsen whether the underlying lung disease is bronchitis or emphysema or a combination of the two, did not show any significant change in either group or the two groups combined. The change in all the plethysmographic functions, which from patient to patient tended to be very variable, is the more surprising in that in a general way the abnormality in most of the functions (Table 2) parallels the abnormality in expiratory flow. Although this parallelism exists between functions it did not occur between the initial and final study. The apparent paradox of two functions relating to each other yet not changing together over the period of observation presented here is elucidated in Figure 2. The change with the short period of this study is variable and generally small. Thus, although the direction of change for two functions may not be consistent over the period of this study, the over-all relationship is significant both at the beginning and end of this study. The failure of some plethysmographic functions to show a trend may, therefore, be due to the short duration of the study, i.e., these functions deteriorate at a slower rate or may fluctuate more as they deteriorate, or both. Whatever the reason, those in whom Ca will deteriorate is best indicated by the level of the MMF when first seen and not by the level of the initial Ca. Such being the case, at least

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<th>Table 2—Correlations between Various Measures of Pulmonary Function</th>
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Abbreviations as in Table 1. These correlations were determined using the initial studies on all subjects.

![Figure 2](https://example.com/figure2.png)

FIGURE 2. Abbreviations as in Table 1. One end of the line represents the initial value of the function while the end of the line with the closed circle represents the final value for the function. As is obvious from this graph, although these two functions did not vary together during the period of this study, for the group both the initial and final values of each function correlate to the same degree with each other.

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for the group of patients presented here, the measurement of Ca or Ca/V\textsubscript{TG} adds nothing to the delineation of the subject's progression, the nature of which is more easily obtained by the measures of expiratory flow.

Two things should be borne in mind in considering this work. In the first place, the variability of the tests may exceed the deterioration which one would expect to see in a few years. However, since variability is presumably random, this should not vitiate the validity of the statistical analysis. The second factor is that change in function was not quantitated. Since the rate of deterioration for plethysmographic functions is not known, there was no way of separating those patients in whom a change was due to the variability of the test from those in whom the change was a true change.

Regardless of the above considerations, which apply to measures of expiratory flow as well as to plethysmographic measurements, there was little, in the short term, to indicate a clear trend in the latter despite the clear trend in the former in this and previous work.\textsuperscript{9,14-17} There was little indication that the change in plethysmographic functions were internally consistent, i.e., that directional changes in Ca or Ca/V\textsubscript{TG} would be accompanied by appropriate changes in the volumes. However, the failure of this to occur in a substantial percentage of cases may be due to the mixed nature of COPD combining loss of retractive force with intrinsic airway disease and varying rates of progression of both. It may also be due to the variability of the tests themselves.

This work does not shed light on the manner in which mechanical factors will alter with time in COPD. However, it does confirm the observations of Mitchell and associates\textsuperscript{1} that the plethysmograph may not be more sensitive in detecting early disease than the spirogram. Three patients presented here had normal Ca or Ca/V\textsubscript{TG} on either the initial or final study or both, despite abnormalities in expiratory flow. From this work and from other observations in this laboratory it is not rare to find patients with COPD with normal Ca, Ca/V\textsubscript{TG} or both. The reverse, abnormal Ca or Ca/V\textsubscript{TG} or both with normal expiratory flow, appears, in our hands, to be limited to a small percentage of patients with asthma. Thus, despite the many fruitful uses of the plethysmograph it appears to be less helpful than the spirometer both for the early detection of COPD and for monitoring its course.

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REFERENCES


