Correlation of the Ventilation and Perfusion Aspects of Chronic Obstructive Pulmonary Disease: A Review of 100 Cases*

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An irreversible change of the pulmonary perfusion was observed in a series of 100 chronic obstructive pulmonary disease patients studied with a pulmonary artery perfusion scan (PAPS). This perfusion involvement was greater in patients in whom the major respiratory component was pulmonary emphysema as opposed to either chronic bronchitis or bronchial asthma. A statistically significant correlation was noted between the extent of the perfusion changes, ventilatory and physical impairment of the individual. The PAPS offers an additional method for evaluating patients with chronic obstructive pulmonary disease. An original classification of the extent of the perfusion abnormalities as detected by the PAPS is presented.

Although the ventilatory aspects of chronic lung diseases have been carefully studied, less is known about the concurrent changes present in the pulmonary perfusion. The pulmonary artery perfusion scan (PAPS) is a relatively simple technique for evaluating the physiologic status of the pulmonary circulation.1-4

This study applies the particle distribution technique of pulmonary artery perfusion scanning to investigate the extent of the perfusion involvement in chronic obstructive pulmonary disease (COPD);† to correlate the perfusion changes with the degree of ventilatory impairment; and to learn whether these perfusion changes are fixed or can be affected by a period of medical treatment, chest physiotherapy and the passage of time or all of these.

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§Chronic obstructive pulmonary disease refers to a heterogeneous group of chronic respiratory disorders, including chronic bronchitis, asthma and emphysema. The criteria for defining these diseases are those recommended in a statement to the Committee on Diagnostic Standards for Non-Tuberculous Respiratory Diseases, American Thoracic Society (9).

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Materials and Methods

The first 100 COPD patients admitted to the Regional Chest Center, University of Nebraska College of Medicine for participation in a 24-day interdisciplinary program designed to evaluate their pulmonary status were included in the study. Ninety-one of the patients were men and nine were women ranging in age from 30 to 69 years. Among other measurements, their interdisciplinary work-up included an admission and discharge PAPS study, chest radiography (PA and left lateral, midcoronal planigraph) and pulmonary physiology studies.

For at least 3 days prior to each PAPS study stable iodine was prescribed to block the absorption into the thyroid gland of metabolized iodine-131. Three hundred microcuries of a macroaggregated albumin labeled with iodine-131 (MAA-131) was used for each study. The nuclide was injected intravenously during resting breathing with the patient lying in the supine position. A four-plane projection scan was completed with a dual five-inch detector rectilinear scanner using 51 hole focusing collimators with a focal length of 3 inches and a radius resolution of one-half length. The anterior and posterior projections were simultaneously recorded as were the right and left lateral projections.

The changes in the PAPS were classified both as to distribution and extent of the perfusion deficit. A Roman numeral (I-IV) was used to record the distribution of the perfusion deficit and the extent of total lung area involved graded on a scale ranging from zero to four plus. The distribution pattern was recorded in a manner described by Lopez-Majano and co-workers,10 using four major groups: I. patchy distribution of radioactivity distributed throughout both lung fields; II. unilateral, in which one lung was predominantly involved; III. predominant unilateral component with a patchy involvement of the contralateral lung; IV.

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normal perfusion pattern.

The extent of involvement (an original classification) was defined by us as follows: 0—no involvement (no change observed in two planes of the PAPS); 1+ — a perfusion deficit is observed in only one plane of the PAPS and between 0 percent to 25 percent of the total lung area is affected; 2+ — the perfusion deficit involved less than 25 percent of the total lung area and a deficit were apparent in two planes of the perfusion scan; 3+ — the perfusion deficit was estimated as including between 25 percent to 50 percent of the total lung area and again was observed in two planes; 4+ — impaired perfusion was seen in greater than 50 percent of the total lung area and the changes in perfusion was present in two planes. As an example, combining the Lopez-Majano classification with ours the changes in perfusion if equally distributed throughout both lungs and involving 25 percent and 50 percent of the total lung area could be written as 1.3+. In this study we will be primarily concerned with the extent of the perfusion abnormalities as opposed to the distribution of the perfusion involvement.

The pulmonary physiology studies included: vital capacity (VC), residual volume (RV), total lung capacity (TLC), residual volume to total lung capacity ratio (RV/TLC), first-second forced expiratory volume (FEV1.0), as percent of observed forced expiratory volume (FEV), maximal voluntary ventilation (MVV), the arterial pH and partial pressures of oxygen (PaO2) and carbon dioxide (PaCO2) and a measurement of the maximum work energy expended while walking on the treadmill (Ew Max). A closed circuit valveless spirometer was used to measure the VC, FEV1.0 and the MVV. The helium dilution technique was used to calculate the functional residual capacity (FRC); and the RV was determined by subtracting the expiratory reserve volume (ERV) from the FRC. The pH, PaO2, and the PaCO2 were measured directly by microelectrodes. The diffusing capacity was determined by the

\[ Ew = \frac{(29.0 + 0.0035v) - \text{time}}{\text{speed}} \]

*Energy expenditure in level walking has been expressed by the formula \( Ew = (29.0 + 0.0035v)t \), where \( v \) is velocity and is expressed in meters per minute, and \( t \) is time and refers to the number of minutes that the subject walked on a motor driven treadmill. The term \( Ew \text{ Max} \) refers to the maximum energy (expressed as cal/kg) expended by a patient following a 24-day treatment regimen.*


†Radiometer, The London Company, West Lake, Ohio.

steady state method. After the initial studies the patients participated in a 24-day chest rehabilitation program which in addition to medical treatment included: (1) bronchial hygiene, (2) breathing exercises, and (3) physical hardening. The details of the latter program have been published elsewhere.

**RESULTS**

The initial PAPS distribution studies revealed a bilateral patchy generalized perfusion deficit (type I) in 64 of 100 patients studied. A predominant change in one lung with patchy involvement in the contralateral lung (type III) was found in the 32 patients and a type II distribution (one lung predominantly involved) in the remaining four patients.

Of the 100 patients 38 percent (38) were judged to have minimal-moderate 1+ or 2+ perfusion involvement of their total lung area. Moderate perfusion defects involving between 25 percent to 50 percent (3+) of the total lung area were observed in 44 percent (44) of the patients. A severe perfusion defect involving more than 50 percent (4+) of the total lung area was recorded in 18 percent (18) of the 100 patients.

The chest roentgenograms and the PAPS changes recorded in one of the patients in the most involved group can be seen in Figure 1A and B, Figure 2A,B,C and D, Figure 3A,B,C, and D; and Figure 4A,B,C,D. In this patient the unrelenting nature of the perfusion changes is observed when one compares the PAPS scans obtained in February with those completed in June and July of the same year. The marked decrease in perfusion confined to the bases of both lungs as noted in these figures has been observed by us in the homozygote patients with a marked serum alpha1 antitrypsin deficiency. (The diagnosis was confirmed in this patient.)

With the exception of one case, (an asthmatic)

![Figure 1A and B. Patient with severe involvement of lung perfusion. Chest roentgenogram, frontal and left lateral projections.](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/21537/)
the same distribution pattern and extent of involvement noted on the initial scan was present in the repeat PAPS study obtained in all the 100 patients following the 24-day period of medical treatment and chest physiotherapy. There was no statistically significant difference (Pearson’s r) noted in the results of the pulmonary physiology studies obtained at the same time as the initial and repeat scan studies.

Eighty-eight patients had one or more types of COPD (emphysema, chronic bronchitis, bronchial asthma).

Twelve patients were diagnosed as having only one etiologic form of COPD. Sixty-eight of the patients had asthmatic symptoms but in 65 subjects this was always with chronic bronchitis or emphysema or with both.

Table 1 shows the association between the following tests of ventilation and physical function; FEV₁, MV, MVV, RV/TLC, Ew Max and the extent of the pulmonary perfusion impairment as defined by the PAPS subgroups. There was no similar relationship between the distribution of perfusion changes by use of the Lopez-Majano classification, and the degree of pulmonary physiologic abnormalities.

A statistical analysis of the relationship between the extent of perfusion involvement and the degree of ventilatory and physical impairment is expressed in Table 2. We used the correlation coefficient eta* to assess the relationship between the extent of involvement on the PAPS and many variables associated with the degree of ventilatory and functional impairment. The F Test* was used to see

* A description of eta and the F Test will be presented in the section following Acknowledgments.
Table 1—The Extent of Perfusion Abnormality Associated with Ventilatory and Physical Impairment.

<table>
<thead>
<tr>
<th>No. Pts</th>
<th>PAPS Subgroup</th>
<th>FEV₁₀ (L)</th>
<th>MVV (L/min)</th>
<th>RV/TLC (percent)</th>
<th>Eₜ Max (Cal/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1+</td>
<td>2.28 ± 0.6*</td>
<td>63.0 ± 16.4</td>
<td>48.1 ± 11.5</td>
<td>671.4 ± 283.4</td>
</tr>
<tr>
<td>30</td>
<td>2+</td>
<td>1.39 ± 0.8</td>
<td>47.7 ± 30.2</td>
<td>49.8 ± 9.26</td>
<td>706.3 ± 387.4</td>
</tr>
<tr>
<td>44</td>
<td>3+</td>
<td>0.89 ± 0.4</td>
<td>29.6 ± 13.9</td>
<td>61.3 ± 10.3</td>
<td>459.9 ± 215.6</td>
</tr>
<tr>
<td>18</td>
<td>4+</td>
<td>0.69 ± 0.3</td>
<td>26.1 ± 13.5</td>
<td>64.5 ± 8.6</td>
<td>345.0 ± 168.9</td>
</tr>
</tbody>
</table>

*Arithmetic mean and standard deviation.

whether there were any significant differences between the means recorded for each of the PAPS subgroups for any of the given variables. The probability values associated with the F Test are presented. The most statistically significant relationship appeared to exist between the actual FEV₁₀ and the extent of perfusion involvement. This was followed by the RV/TLC ratio, FEV₁₀ expressed as percent of FEV and MVV.

DISCUSSION

While evaluating the perfusion defects observed on the PAPS one must consider the following possibilities:

1. Vasocostriction
   a. Decreased PaO₂
   b. Increased Paco₂
   c. Decreased pH
   d. Vasocostrictive agents eg, serotonin

2. Organic obstruction
   a. Necrotizing arteritis
   b. Intimal fibrosis
   c. Thrombosis
   d. Embolism

3. Localized destruction, compression, or displacement
   a. Airway obstruction
   b. Emphysematous bullae
   c. Surgery
   d. Tumors, cysts, cavities, abscess
   e. Fibrosing alveolitis
   f. Trauma
   g. Atelectasis

4. Gravity

A decrease in the partial pressure of oxygen or pH or both can cause a vasoconstriction of the pulmonary vascular bed and the same can be said for an increase in the partial pressure of arterial CO₂. In 10 of our 100 patients the PAPS was repeated during the inhalation of pure oxygen for 20 minutes and no changes were noted in the preexisting perfusion defects. Changes in pulmonary perfusion have been attributed to mitral steno-
Table 2—Statistical Analysis of the Relationship between the Extent of Perfusion Abnormalities, Ventilatory and Physical Impairment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation Coefficient</th>
<th>P Associated with F Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Vital capacity (VC) % predicted</td>
<td>.483</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>2 Residual volume (RV) % predicted</td>
<td>.353</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>3 RV/TLC ratio expressed as %</td>
<td>.542</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>4 First-second forced expiratory volume (FEV1)</td>
<td>.614</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>5 FEV1 predicted as % forced expiratory volume (FEV)</td>
<td>.511</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>6 Maximum voluntary ventilation (MVV) (L/min)</td>
<td>.495</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>7 Oxygen partial pressure (PaO2) (mm Hg)</td>
<td>.460</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>8 Diffusing capacity (ml CO/min/mm Hg) (DLco)</td>
<td>.246</td>
<td>&lt;.100</td>
</tr>
<tr>
<td>9 Ew Max (cal/kg)</td>
<td>.448</td>
<td>&lt;.005</td>
</tr>
</tbody>
</table>

our capacity to classify the extent of involvement on the PAPS is a highly reproducible one. We have encountered no difficulty with the technical aspects of the study i.e., quality of nuclide, reliability of the equipment, patients' tolerance, and ability to compare serially performed studies.

As we reviewed our cases we noticed that in patients with mixed forms of COPD, especially those with a predominant chronic bronchitic component there was a tendency for far less perfusion involvement than in those with a predominance of emphysema. In fact, we believe that we can differentiate between the two entities on the basis of the PAPS even though we cannot always do so with the routine pulmonary function studies. This observation is further supported by Weiner and coworkers, who suggested that scanning may be useful in differentiation of emphysema from chronic bronchitis and asthma.

Although the degree of ventilatory and functional impairment can be predicted by the PAPS and vice versa, we have observed no correlation between the distribution of perfusion (Lopez-Majano) and the degree of pulmonary physiologic abnormality. We found the patterns of distribution helpful in diagnosing an alpha antitrypsin deficiency, homozygote type or in mapping the areas of the lung that are involved. In four of the 100 cases the perfusion abnormality was entirely confined to one lung (type II distribution). The possibility of unilateral emphysema (McLeod syndrome) could not be completely ruled out. Only one perfusion change was recorded after a 24-day medical and rehabilitative regimen directed primarily towards improvement of the ventilatory aspects of respiration.

Because asthma by definition is a paroxysmal disorder one may ask why patients did not show improvement on the PAPS following treatment. This is probably because their asthma was complicated by chronic bronchitis or emphysema or both. Thus the improvement (if any) recorded in the pulmonary functions of these patients following the 24-day treatment was very small and we believe that this was not of the magnitude to be detected by the PAPS.

Based upon the data presented in this study we believe that PAPS studies using the new classification to define the extent of perfusion involvement adds another facet to the clinical evaluation of the COPD patient. Because of the relationship between the perfusion involvement and the ventilatory and physical impairment (Tables 1 and 2); the irreversibility of the perfusion changes following medical treatment; the ability in some cases to use the PAPS in identifying the predominant component in mixed forms of COPD as well as mapping the area of perfusion impairment we believe that a PAPS study should be included in the routine work-up of almost any chest patient and particularly those with COPD.

ACKNOWLEDGMENT: We wish to thank Robert S. Innes, Ph.D., Associate Professor, Medical Psychology, Nebraska Psychiatric Institute, Omaha, for his assistance in the statistical analysis of the data presented.

A Description of Eta and F Test

\[
\eta^2 = \frac{\sum_{i=1}^{k} \sum_{j=1}^{n_i} (\bar{y}_{ij} - \bar{y})^2}{\sum_{i=1}^{k} \sum_{j=1}^{n_i} (\bar{y}_{ij})^2}
\]

where \( \bar{y}_{ij} \) = number in jth subgroup
\( k \) = number in subgroups, and
\( \bar{y} \) = within subgroups sum of squares

Computation of \( \eta^2 \) was according to the formula

\[
\eta^2 = \frac{\sum_{j=1}^{n} \sum_{i=1}^{k} (\bar{y}_{ij} - \bar{y})^2}{\sum_{j=1}^{n} \sum_{i=1}^{k} (\bar{y}_{ij})^2}
\]
where $\bar{y}_j$ = the mean of the jth subgroup,
$\bar{Y}$ = the grand mean,
$y_{ij}$ = an individual observation, and
N = total number of observations.

After obtaining $\bar{y}$, the calculations for $F$ followed directly by
the use of the relationship:

$$F = \frac{\sum_{j=1}^{k} (y_{ij} - \bar{y}_j)^2}{k-1}$$
$$\sum_{j=1}^{k} (y_{ij} - \bar{y}_j)^2 / (N-k)$$

With $N - k = df$ within and $k - 1 = df$ between subgroups.

REFERENCES

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Discovery of Science

The word "science" is derived from the Latin word *scire* which means "to know". The philosophy of how to know and understand how to discover the truth came into being quite suddenly in the sixth century BC in Miletus, a city of the Ionian coast. There Thales (640-546 B C), a military engineer, predicted that on a certain day there would be an eclipse of the sun. It occurred as he predicted. Modern astronomers have set the date as May 28, 585 BC. Thales made the revolutionary generalization that the universe was ordered and therefore that careful observation of any group of phenomena could lead to similar understanding and similar predictions.

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