The relationship between pulmonary function tests, thorax HRCT, and quantitative ventilation-perfusion scintigraphy in chronic obstructive pulmonary disease

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ÖZET

Kronik obstrüktif akciğer hastalığı olgularında solunum fonksiyon testleri, toraks YRBT ve kantitatif ventilasyon-perfüzyon sintigrafisi arasındaki ilişki

Çalışmamızda yaş ortalamaları 65.6 ± 5.5 yıl olan 16 kronik obstrüktif akciğer hastalığı (KOAH) olan erkek olguda, solunum fonksiyon testleri, toraks yüksek rezolüsyonlu bilgisayarlı tomografi (YRBT) incelemesi ve kantitatif ventilasyon-perfüzyon (V/Q) sintigrafisi arasındaki ilişki incelenmiştir. Olguların ortalama FVC değeri 2352 ± 642 mL (%65.4 ± 15.8), FEV_1 değeri 1150 ± 442 mL (%40.8 ± 14.9), DLCO/VA değeri 3.17 ± 0.88 mL/dakika/mmHg/L, PaO_2 ve $PaCO_2$ değerleri sırasıyla 68.5 ± 11.04 mmHg, 38.9 ± 5.8 mmHg idi. Her hastanın toraks YRBT ve V/Q sintigrafi imajları, sağ ve sol akciğerde üst, orta ve alt alanlara bölünerek incelenmiştir. Toraks YRBT'de amfizem skorlaması için Visual skorlama yöntemi kullanılmış ve bu yöntemle amfizem derecesi hafiften ağıra doğru skorlanmıştır (≤ %25 - ≥ %76). Amfizem skorlarının her iki akciğerin üst alanlarında en yüksek olduğu, aynı alanlarda V/Q oranlarının da en düşük olduğu bulunmuştur. DLCO/VA, DLCO değerleri ile total amfizem skoru ve üst, orta, alt akciğer alanlardaki amfizem skorları arasında korelasyon tespit edilmiştir. Çalışmamızda; KOAH'lı olgularda amfizematöz değişikliklerin üst akciğer alanlarında daha belirgin olduğunu ve aynı alanlarda V/Q oranının en düşük olduğunu saptadık.

Anahtar Kelimeler: *KOAH, yüksek rezolüsyonlu bilgisayarlı tomografi, ventilasyon-perfüzyon sintigrafisi.*

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SUMMARY

The relationship between pulmonary function tests, thorax HRCT, and quantitative ventilation-perfusion scintigraphy in chronic obstructive pulmonary disease

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We have evaluated the relationship between pulmonary function tests (PFT), thorax high resolution computed tomography (HRCT) images and quantitative ventilation-perfusion (V/Q) scintigraphic studies in 16 male patients (mean age 65.6 ± 5.5 years) with chronic obstructive pulmonary disease (COPD). The mean forced vital capacity (FVC) value of the patient group was 2352 ± 642 mL (65.4 ± 15.8%), whereas mean forced expiratory volume in one second (FEV_1) was found to be 1150 ± 442 mL (40.8 ± 14.9%). The ratio of carbon monoxide diffusion capacity to alveolar ventilation (DLCO/VA) was 3.17 ± 0.88 mL/min/mmHg/L, and the mean partial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) pressures were 68.5 ± 11.04 mmHg and 38.9 ± 5.8 mmHg respectively. For each patient, thorax HRCT and V/Q scintigraphic images of both lungs were divided into upper, mid and lower zones during examination. Visual scoring for the assessment of emphysema on thorax HRCT were used and images were graded from mild to severe (≤ 25%-≥ 76%). Emphysema scores were found to be higher on upper zones with accompanying lowest V/Q ratios. DLCO/VA, DLCO, total emphysema scores, and individual emphysema scores of the upper, mid and lower zones were found to be correlated. As a conclusion, it can be stated that emphysematous changes in COPD patients are more apparent in the upper lung zones, which also have the lowest V/Q ratios.

Key Words: *Chronic obstructive pulmonary disease (COPD), thorax high resolution computed tomography (HRCT), ventilation-perfusion scintigraphy.*

It is recognized that the generic term chronic obstructive pulmonary disease (COPD) includes patients with a variety of conditions including emphysema and chronic bronchitis which may occur alone or in combination (1). Cigarette smoking is the dominant risk factor the development of COPD (2). Emphysema implies loss of elastic recoil producing airway collapse and gas trapping, resulting in hyperinflation which is a useful but non-specific feature on chest X-ray, whereas loss of lung tissue and alterations in the pulmonary vasculature can only be accurately assessed by thorax high resolution computed tomography (HRCT) (3). Centrilobular emphysema with upper lobe predominance is the most common type of emphysema in smokers. Thorax HRCT scanning is also sensitive and accurate in the diagnosis of emphysema (4). Many studies have shown a correlation between thorax HRCT images and diffusion tests in emphysematous patients (5).

Ventilation/perfusion (V/Q) mismatch is a well known feature of COPD. Emphysema impairs both ventilation and perfusion of the lung tissue. In mild to moderate COPD with a normal chest X-ray, multiple small matched defects may be found on V/Q scans (6).

We have evaluated the relationship between pulmonary function tests (PFT), thorax HRCT images and quantitative V/Q scintigraphic studies in 16 patients with COPD.

MATERIALS and METHODS

The Methodology of Pulmonary Function Tests

Sixteen patients with COPD were enrolled from the outpatient COPD clinic of the Pulmonary Diseases Department in Cerrahpasa Medical Faculty. They were clinically stable with no acute exacerbations of COPD at least for three weeks prior to enrollment. All the patients enrolled met the European Respiratory Society criteria for the diagnosis of COPD and airflow obstruction ranging from mild (n= 4 cases) to severe (n= 12 cases) (7). All of the patients were on inhaled glucocorticosteroid, long-acting inhaled β_2 agonist

and sustained-release theophylline therapy at the initation and through the study period. Written informed consent was obtained from each patient at beginning of the study.

Forced spirometry (FVC, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$), lung volumes (FRC, TLC, RV, RV/TLC) and carbon monoxide transfer (DLCO, DLCO/VA) were measured using a Sensor Medics Vmax series 22 spirometre. The spirometry test procedure uses the forced expiratory vital capacity (FVC) maneuver, in which the subject inhales maximally and then exhales as rapidly and completely as possible. Patients were considered to have fixed expiratory flow limitation if FEV_1 values, measured after two inhalations of salbutamol (400 μg) from a metered-dose inhaler, increased by less than 12% (or < 200 mL) of the baseline value. Even with complete exhalation, some air still remains in the lungs. This remaining volume is the residual volume (RV). The RV can be measured and added to the vital capacity (VC) to obtain the total lung capacity (TLC). To measure the lung volumes we used nitrogen washout method (8). Carbon monoxide transfer was measured by the single-breathe method using a 10 second breath-hold time (9). Duplicate measurements were accepted where estimates of transfer factor (DLCO) and effective alveolar volume (VA) were within 5%. The CO transfer coefficient was derived (DLCO/VA). Arterial blood gas (ABG) analyses measurements were carried out using a Rapid lab 248, Chiron/Diagnostics diagnostic device.

The Methodology of Ventilation/Perfusion Studies

Ventilation and perfusion studies were performed in different days with three days interval. Five mCi Tc 99m Macroaggragated Albumin (MAA) was used for perfusion study. The radiopharmaceutical was injected to the patient in supine position and during quiet respiration. Tc 99m diethylene triamin penta acetic acid (DTPA) aerosol was used for ventilation study. 30 mCi Tc 99m DTPA was placed in to the nebulizer of an aerosol delivery system. Oxygen tubing was connecred to the side port, and oxygen was supplied through flow meter. Flow rates were in the range of 7 to 10 L/min. A mouthpiece with a nose clip was used to administer the aerosol. The patient was asked to breathe 5 minutes in sitting position. Siemens large field of view gamma camera equipped with low energy all purpose collimator was used for both studies. Anterior and posterior lung images were obtained for 30 seconds with the patient in supine position and with the collimator nearly tight to the bodysurface of the patient and stored on the computer with 256 x 256 matrix size.

During processing, pixel reregistration program was called to provide the two images that are to be aligned. Computer generated conjugated image from anterior and pixel reregistrated posterior image. During calculation of the conjugated image the posterior image is flipped along Y-axis to be in anterior view. Flipped posterior image was manually aligned with the anterior image, by means of the built in pixel reregistration software. Anterior and flipped posterior image are multiplied to produce the product image. The square root of each pixel in the product image is calculated to build the conjugated image. The sum of the pixels in all six rectangles in a view is 100%, each rectangular region comprices a percentage of this total. Left and right regions are summed to give a left and right total percentage.

The Methodology of Radiographic Studies

Thorax HRCT scans were performed on a Siemens Somatom Plus (Siemens, Erlangen, Germany) scanner during breath-holding at full inspiration according to Gevenois and collegues (10). None of the patients received contrast medium intravenously. In the beginning of the procedure radiographic fields were marked in patients digital topograms. Choosing cross sectional thickness of 1 mm and cross sectional interval of 10 mm deep inspiration images of the whole lung parenchema, from apex to base, were taken. Images were obtained by using high reconstruction bony algorithm. Every sections over the diaphragm and both lungs were evaluated separately.

Pulmonary emphysema was visually assessed by an expert chest radiologist unaware of the clinical and lung function data. Visual observation was quantified using a semiquantitative visual score according to Sakai and Goddard co-workers (11,12). Emphysema is characterized by fo-

cal areas of abnormally low attenuation usually without visible walls, and sometimes with a persistent vessel in the center of the lesion. An appropriately low window setting is essential for diagnosing emphysema (13). In every HRCT sections emphysema scores were calculated separately for both lungs. All sections were divided equally among three lung fields; lower, mid and upper. The scores of every lung sections were summed up. The maximum score for every section was 4 and the possible maximum score was calculated by multiplying section number by 4. The proportion of patients total score to the possible maximum score were expressed as emphysema scores. According to the emphysema scores patients lung parenchyma were classified as follows: no damage, mild damage (≤ 25%), moderate damage (26-50%), severe damage (51-75%) and very severe damage (≥ 76%).

Statistical Methods

In the analysis of the data obtained, SPSS (Statistical Package of Social Sciences) 10.0 for Windows was used. The results were defined as mean value ± standard deviation. Correlations between variables were assessed by Spearman Correlation. A p value smaller than 0.05 was considered to be significant.

RESULTS

Demographic characteristics of our cases were summarized in Table 1. All patients were not smoking for 7.06 ± 8.2 years. Patients mean hemoglobin and hematocrit values were 14.5 ± 1.21 g/dL and 42.4 ± 3.88% respectively. Neither anemia nor polycythemia was observed.

The PFT, lung volume, diffusion capacity and ABG mean values were given in Tables 2.

Table 1. The demographic characteristics.

Total number of cases	16
Age (years)	65.44 ± 5.69
Sex	16 M
Smoking history (pack-years)	56.68 ± 34.1
Disease of duration (years)	10.25 ± 5.29

M: Male.

Table 2. Pulmonary function tests, lung volumes, diffusion capacities and arterial blood gases values of patients*.

FVC (mL)	2351.87 ± 642.54
FVC (%)	65.43 ± 15.89
FEV_1 (mL)	1150.62 ± 442.68
FEV_1 (%)	40.81 ± 14.98
FEV_1/FVC (%)	48.21 ± 10.5
TLC (mL)	7200.62± 1922.88
TLC (%)	113.56 ± 26.1
RV (mL)	4690 ± 1652.44
RV (%)	193.37 ± 67.33
FRC (mL) (%)	5359.37 ±1718.11
FRC (%)	154.8 ± 46.84
RV/TLC (%)	63.93 ± 9.5
DLCO (mL/mmHg/min)	14.71 ± 4.7
DLCO (%)	61.15 ± 21.2
DLCO/VA (mL/mmHg/min/Liter)	3.17 ± 0.88
DLCO/VA (%)	62.76 ± 20.56
PaO_2 (mmHg)	68.53 ± 11.04
$PaCO_2$ (mmHg)	38.93 ± 5.85
SaO_2 (%)	93.03 ± 4.3

* Values are expressed as mean.

FVC: Forced vital capacity, FEV_1: Forced expiratory volume in 1 second, TLC: Total lung capacity, RV: Rezidual volume, FRC: Functional rezidual capacity, DLCO: Carbonmonoxide transfer factor, DLCO/VA: Carbonmonoxide transfer coefficient, PaO_2: Arterial partial oxygen pressure, $PaCO_2$: Arterial partial carbondioxide pressure, SaO_2: Oxygen saturation.

FEV_1/FVC ratio and FEV_1 (%) values was found to be lower in the patient. Lung volumes of the COPD patients tend to increase with increasing percentage of emphysematous component. The RV, TLC and FRC (%) values of the cases were found to be increased. DLCO and DLCO/VA values of the COPD patients tend to decrease with increasing percentage of emphysematous component (14). The DLCO ve DLCO/VA values of the COPD patients were found to be decreased. The ABG analyses of the patients enrolled in the study reveal that most of them were hypoxic and normocarbic.

The visual HRCT scores ventilation and perfusion scintigraphic values of patients mean values given Table 3. It can be stated that emphysematous changes in COPD patients are more appa-

Table 3. Visual HRCT scores and ventilation/perfusion values of patients.

		HRCT scores (%)*	V (%)*	P (%)*	V/Q
Right	Upper	60.87 ± 28.38	9.43 ± 3.5	11.3 ± 6.2	0.83
	Mid	36.7 ± 26.37	27.3 ± 4.7	28.8 ± 4.9	0.94
	Lower	20.93 ± 19.18	15.5 ± 5.1	16.8 ± 6.3	0.92
Left	Upper	57.7 ± 29.14	8.8 ± 3.0	10.1 ± 3.5	0.87
	Mid	40.56 ± 30.78	24.9 ± 6.1	22.3 ± 5.4	1.11
	Lower	24.93 ± 24.97	13.9 ± 3.6	12.5 ± 4.2	1.11

* Values are expressed as mean.

rent in the upper lung zones, which also have the lowest ventilation and perfusion values. Correlation analysis between visual HRCT scores and diffusion capacity values of COPD patients shown Table 4. Between HRCT total scores and DLCO and DLCO/VA values were found to be correlated ($p< 0.05$).

In COPD patients, V/Q values and emphysema scores of upper, mid and lower zones in both lungs were found to be correlated ($p< 0.001$). But, we found no correlation between total V/Q ratio and PaO_2, $PaCO_2$, SaO_2 values and diffusion parameters ($p> 0.05$). COPD cases were classified into two subgroups according to V/Q ratio values. Group I (n= 8 cases) consisted of patients whose $V/Q < 1$ and group II (n= 8 cases) consisted of patients whose $V/Q \geq 1$. In both groups, no statistically significant difference is found in DLCO, DLCO/VA and emphysema scores of upper, mid and lower zones in both lungs (Table 5).

DISCUSSION

Emphysema scores were found to be higher on upper zones with accompanying lowest V/Q rations. Taking heavy smoking history of our patients into account, it is not suprising to find high emphysema scores on upper zones. Many studies evaluating HRCT images of COPD patients have emphasized that the most frequent localization of emphysema was in upper lobes (15). DLCO, DLCO/VA values and emphysema scores of upper, mid and lower zones of both lungs were found to be correlated ($p< 0.01$). The correlation between diffusion tests and visual scoring of emphysematous fields is pointing out to sensibility of these test in determining emphysematous fields. O'Brien et al found that emphysematous changes in mid and lower lung zones were correlated with low DLCO and DLCO/VA values. As our study included only mild and severe COPD patients, O'Brien et al constituded their study group with COPD patients in every stages (1). Baldi et al fo-

Table 4. Visual HRCT scores and diffusion test values of patients.

	DLCO		DLCO/VA	
	r	p	r	p
Right HRCT scores				
Upper	-0.611	0.012	-0.662	0.005
Mid	-0.657	0.006	-0.697	0.003
Lower	-0.62	0.010	-0.758	0.001
Left HRCT scores				
Upper	-0.733	0.001	-0.716	0.002
Mid	-0.651	0.006	-0.737	0.001
Lower	-0.583	0.018	-0.747	0.001

Table 5. Visual HRCT scores and diffusion capacities of groups.

	Group I (n= 8) V/Q < 1		Group II (n= 8) V/Q ≥ 1		
	Mean	SS	Mean	SS	p
DLCO (mL/mmHg/min)	16.4875	4.7954	12.9375	4.1407	0.130
DLCO/VA (mL/mmHg/min/L)	3.5588	0.9385	2.7850	0.6872	0.083
Right HRCT scores					
upper	57.625	23.089	64.125	34.195	0.798
mid	31.375	22.608	40.750	30.476	0.505
lower	16.625	14.050	25.250	23.426	0.574
Left HRCT scores					
upper	51.500	24.611	62.625	33.823	0.574
mid	34.875	24.562	46.250	36.784	0.505
lower	16.125	17.707	33.750	29.070	0.234

und a highly significant correlation between pulmonary emphysema, as assessed by HRCT quantitative analysis, and % predicted values of FEV_1, DLCO, DLCO/VA in patients with COPD (5).

In their study which was taken in COPD patients with lung volume reduction Cleverley et al, established strong correlation between lung perfusion on scintigraphy and HRCT images (16). We found no correlation between ventilation, perfusion values and emphysema scores on upper, mid and lower zones of both lungs. But V/Q values and emphysema scores on upper, mid and lower zones of both lungs were found to be correlated ($p< 0.001$). V/Q values and emphysema scores were found positively correlated. Besides lowest V, Q and V/Q values were obtained in upper zones of both lungs. So we can claim that emphysematous changes are one of the important reasons of V/Q mismatch in COPD patients.

Emphysema scores decreased from upper to lower lung lobes and ventilation/perfusion ratios were higher in mid lung fields than lower portions of the lung. One possible explanation for this observation could be the horizontal pozition of the patients during V/P scanning. In horizontal position movements of the diaphragm decreases, it moves up and volumes of lower lung lobes diminishes (17).

In conclusion smoking related COPD results emphysematous changes especially in upper lung lobes,visual scoring on thorax HRCT correlates with difusion tests and V/P mismatch exist in emphysematous lung fields.

REFERENCES

1. *O'Brien C, Guest PJ, Hill SL, Stockley RA. Physiological and radiological characterization of patients diagnosed with chronic obstructive pulmonary disease in primary care. Thorax 2000; 55: 635-42.*
2. *Hanrahan JP, Sherman CB, Bresnitz EA, Emmons KM. Cigarette smoking and health. Am J Respir Crit Care Med 1996; 153: 861-5.*
3. *Gevenois PA, de Maertelaer V, De Vuyst P, et al. Comparison of computed density and microscopic morphomtery in pulmonary emphysema. Am J Respir Crit Care Med 1996; 154: 187-92.*
4. *Stern EJ, Frank MS. CT of the lung in patients with pulmonary emphysema; diagnosis, quantification, and correlation with pathologic and physiologic findings. Am J Roentgenol 1994; 162: 791-8.*
5. *Baldi S, Miniati M, Bellina CR, et al. Relationship between extent of pulmonary emphysema by high-resolution computed tomography and lung elastic recoil in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001; 164: 585-9.*
6. *Anderson PO, Secker Walker RH, Forrest JV. Detection of obstructive pulmonary disease. Relative sensitivity of ventilation-perfusion studies and chest radiography. Radiology 1974; 112: 643-8.*
7. *Siafakas NM, Vermeire P, Pride NB. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). ERS-Consensus Statement. Eur Respir J 1995; 8: 1398-402.*

8. *American Thoracic Society. Standardization of spirometry-1994 update. Am J Respir Crit Care Med 1995; 152: 1107-36.*
9. *American Thoracic Society. Single-breath carbon-monoxide diffusing capacity: Recommendations for a standard techique-1995 update. Am J Respir Crit Care Med 1995; 152: 2185-98.*
10. *Gevenois PA, de Maertelaer V, De Vuyst P, et al. Comparison of computed density and macroscopic morphomtery in pulmonary emphysema. Am J Respir Crit Care Med 1995; 152: 653-7.*
11. *Sakai FG, Gamsu JG, Ray CS. Pulmonary function abnormalities in patients with CT determined emphysema. J Comput Assist Tomogr 1987; 11: 963-8.*
12. *Goddard PR, Nicholson EM, Laszlo G, et al. Computed tomography in pulmonary emphysema. Clin Radiol 1982; 33: 379-87.*
13. *Webb WR, Müller NL, Naidich DP. High Resoluation CT of the Lung. 3rd ed. New York. Lippincott Williams & Wilkins, 2000.*
14. *Senior RM, Shapiro SD. Chronic obstructive pulmonary disease: Epidemiology, pathophysiology, and pathogenesis. In: Fishman AP (ed). Fishman's Pulmonary Diseases and Disorders. 3rd ed. McGraw-Hill, 1998: 659-81.*
15. *Gurney JW, Jones KK, Robbins RA, et al. Regional distribution of emphysema; correlation high-resolution CT with pulmonary function tests in unselected smokers. Radiology 1992; 183: 457-63.*
16. *Cleverly JR, Desai SR, Wells AU, et al. Evaluation of patients undergoing lung volume reduction surgery: Ancillary information available from computed tomography. Clin Radiol 2000; 55: 45-50.*
17. *Roisin RR, Barbera JA, Roca J. Pulmonary gas exchange. In: Calverly EMA, Mac Nee W, Pride NB, Rennard SI (eds). Chronic Obstructive Pulmonary Disease. 2nd ed. London: Arnold, 2003: 175-93.*