The Relationship Between Dyspnea and Pulmonary Functions, Arterial Blood Gases and Exercise Capacity in Patients with COPD

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SUMMARY

Dyspnea is described as a sensation of awareness of difficulty in breathing. Clinical techniques for rating dyspnea include Medical Research Council (MRC) scale, Baseline Dyspnea Index (BDI) and Borg scale. The aim of this study was to investigate the relationship between clinical dyspnea ratings and pulmonary functions, exercise capacity. 20 patients with moderate COPD (group 1) and 12 healthy controls (group 2) were included to the study. MRC scale, BDI and Borg scales were applied to all patients and pulmonary function tests, maximal inspiratory pressure (Pimax), mouth occlusion pressure ($P_{0.1}$), breathing pattern (BP), arterial blood gases (ABG) and symptom-limited exercise on a cycle ergometer were performed. All patients with COPD terminated the test because of dyspnea. The patients with COPD had moderate COPD [FEV_1(pred%): 56.00 ± 15.03%]. The clinical dyspnea ratings of the patients were; MRC scale: 2.10 ± 0.55, BDI: 5.65 ± 1.60 and Borg scale: 4.55 ± 1.23. The BDI showed significant correlation with airflow rates, PaO_2 and SaO_2 ($p< 0.05$, $p< 0.01$), Borg scale showed significant correlation with airflow rates ($p< 0.01$), whereas they did not show significant correlation with Pimax and $P_{0.1}$. There was a only significant correlation between MRC scale and peak oxygen uptake [VO_2/kg (pred%)]; other dyspnea scales lacked any correlation with exercise testing parameters. In this study, clinical dyspnea scales and ratings during exercise were correlated with mainly airflow rates and ABG parameters. But they were not significant correlation with exercise capacity.

Key Words: *COPD, dyspnea, exercise capacity.*

ÖZET

KOAH'lı Hastalarda Dispne ve Pulmoner Fonksiyonlar, Arter Kan Gazları ve Egzersiz Kapasitesi Arasındaki İlişki

Dispne, solunum güçlüğünün hissedilmesi olarak tanımlanır. "Medical Research Council (MRC)" skalası, "Baseline Dyspnea Index (BDI)" ve Borg skalası dispnenin derecelendirilmesi için kullanılan klinik yöntemlerdir. Bu çalışmanın amacı, kronik obstrüktif akciğer hastalıklarında (KOAH) klinik dispne skalaları ile solunum fonksiyonları, egzersiz kapasitesi arasındaki ilişkiyi araştırmaktı. Yirmi KOAH'lı olgu ve 12 sağlıklı kontrol olgusu çalışmaya alındı. Tüm olgulara MRC skalası, BDI ve Borg skalası uygulandı. Solunum fonksiyon testleri, maksimal inspiratuvar basınç (P_{imax}), ağız içi tıkanma basıncı ($P_{0.1}$), solunum paterni (SP), arter kan gazları ve semptom-sınırlı bisiklet egzersiz testi yapıldı. KOAH olgularının *tümü dispne nedeniyle testi sonlandırdılar. KOAH olguları orta şiddetli grupta yer alıyordu (ortalama FEV_1: %56.00 ± 15.03). Klinik dispne skalaları; MRC skalası: 2.10 ± 0.55, BDI: 5.65 ± 1.60 ve Borg skalası: 4.55 ± 1.23 idi. BDI Pimax ve $P_{0.1}$ ile ilişkili değilken, hava akım hızları, PaO_2 ve SaO_2 ile ($p< 0.05$, $p< 0.01$); Borg skalası ise hava akım hızlarıyla anlamlı derecede ilişkiliydi ($p< 0.01$). Diğer dispne skalaları egzersiz testi parametreleriyle ilişkili değilken, sadece MRC skalası ise pik oksijen tüketimi (VO_2/kg%) ile önemli derecede ilişkiliydi ($p< 0.05$). Sonuç olarak, bu çalışmada klinik dispne skalalarının ve egzersiz dispne skalasının özellikle hava akım hızları ve AKG ile ilişkili olduğu gösterildi. Fakat bu skalalar egzersiz kapasitesiyle anlamlı derecede ilişkili değildi.*

Anahtar Kelimeler: *KOAH, dispne, egzersiz kapasitesi.*

Dyspnea is a common complaint of patients with chronic obstructive pulmonary disease (COPD). It has been defined as awareness of difficulty in breathing (1,2). Exercise dyspnea can be defined as the perception, during muscular exercise, of the imbalance between the ventilatory demand and the ability of the chest-lung mechanics to fulfil this demand (3). Abnormalities in gas exchange, pulmonary circulation and respiratory mechanics usually accompanies this unpleasant sensation (4). Perception of dyspnea, ventilatory demand and the inability of the chest-lung mechanics to fulfil this demand are three consecutive causes of exercise dyspnea (3,5).

Although dyspnea is the most frequent symptom in COPD patients, due to its subjective nature, it is difficult to assess. Psychophysical methods and several clinical scales have been applied to assess the severity of breathlessness. Medical Research Council (MRC) Scale and Baseline Dyspnea Index (BDI) have been in use for many years for grading the effect of breathlessness on daily activities (6-9). Borg Scale is used in the assessment of the exertional dyspnea (10).

Although these scales have been used as quantitative measure of dyspnea, the correlation of these clinical scales to physiologic parameters such as pulmonary function tests, arterial blood gas analysis and exercise testing need to be defined. Our goal was to evaluate these relations between the physiologic parameters and several scales of dyspnea.

MATERIALS and METHODS

Subjects

Twenty patients with COPD (group 1) and 12 healthy subjects (group 2) have been included in the study. ERS guidelines have been used for the diagnosis of COPD (11). All the patients had moderate COPD, FEV_1/FVC ratio below 75%. At the time of testing, all the patients were in a stable clinical and functional state.

Patients with concomitant disease such as vascular, rheumatologic, neuromuscular or cardiac disease and patients with $FEV_1 < 30\%$, $PaO_2 < 40$ mmHg and $PaCO_2 > 70$ mmHg excluded from the study (12).

Control group were nonsmoker, healthy subjects with similar age distrubution.

Evaluation of Dyspnea

MRC scale, BDI and Borg scales were applied to all patients and all ratings were performed without knowledge of results of pulmonary function tests (6-10). MRC scale is a five-point scale based on degrees of various physical activities that precipitate dyspnea. BDI recognises five grades for each of the following categories: Functional impairments, magnitude of task and magnitude of effort. Borg scale was used to evaluate the exertional dyspnea in which 0 indicated easy breathing and 10 represented maximal dyspnea.

Evaluation of Physiologic Parameters

Pulmonary function tests [including ventilatory tests, diffusing capacity for carbon monoxide (DLCO), maximal inspiratory and expiratory pressures, mouth occlusion pressure, breathing pattern], exercise testing and arterial blood gas analysis were performed in all COPD patients. In healthy subjects maximal expiratory flow maneuver and exercise testing were performed. To avoid any potential influence of medication, aminophylline and beta agonists were with held for 12 hours and 6 hours, respectively and caffeine and heavy meal was restricted for four hours before the test.

Pulmonary function testing (PFT): Spirometric parameters (FEV_1, FVC, FEV_1/FVC%, FEF_{25-75}) were measured at rest using Vmax 229 Pulmonary Function/Cardiopulmonary Exercise Testing Instruments (SensorMedics, Bilthoven, The Netherlands). Lung volumes (TLC, FRC, RV, RV/TLC%, EELV) were measured by a plethysmograph (SensorMedics 6200 Autobox, Bilthoven, The Netherlands). Single breath method has been used in the assessment of DLCO. All these tests were performed in the sitting position and the best of three attempts was considered. The tests were compatible with ATS criteria (13). Predicted values were calculated using the ECCS reference values (14).

Respiratory muscle strength; Pimax was measured near residual volume (RV), Pemax was measured near total lung capacity (TLC). Percentage Pimax and Pemax were calculated according to Black and Hyatt's reference values (15). The mouth occlusion pressure developed 0.1 second after the start of inspiration was recorded as the mouth occlusion pressure ($p_{0.1}$) (1).

Breathing pattern; tidal volume, respiratory frequency, inspiratory time (Ti), total breathing time (Ttot) and Ti/Ttot (inspiratory time/total breathing time) and VT/VC ratios were evaluated.

Exercise testing: Progressive cycle exercise tests to symptom limitation were conducted on an electronically braked cycle ergometer (Vmax 229 Pulmonary Function/Cardiopulmonary Exercise Testing Instruments, SensorMedics, Bilthoven, The Netherland). All the patients were monitored continuously in terms of ECG, arterial pressure, and saturation of oxygen while performing the tests. After the initial evaluation, subjects began cycling at a pedalling rate of 50-60 rpm/min for three minutes and afterwards the work was increased by 16.3 watts every minute. The patients were strongly encouraged to perform maximally. The test was terminated at the point of symptom limitation. The reason for ending the test was recorded (i.e. dyspnea, chest pain, leg pain, fatigue etc.). Peak heart rate, workload (watt), peak oxygen consumption (VO_2), peak oxygen consumption/kg (VO_2/kg), peak CO_2 output (VCO_2), gas exchange ratio (R, VCO_2/VO_2), minute ventilation [VE(BTPS)], VT, f, VD/VT rate (est), Ti/Ttot were recorded. Metabolic parameters of the exercise test (VO_2 and VCO_2) were compared with predicted normal values of Jones (16).

Arterial blood gas analysis (ABG): Analysis was performed at rest with a Rapidlab 348 pH/Blood Gas Analyser (Chiron Diagnostics Ltd., Essex,UK). pH, PaO_2, $PaCO_2$ and SaO_2 were measured.

Statistical Analysis

Statistical analysis was performed through SPSS (Statistical Package for Social Sciences for Windows, SPSS, Inc., Chicago, IL, USA). Results are expressed as means ± SEM; $p< 0.05$ was accepted as significant for all analysis. Descriptive group data were compared using student's t statistics. Spearman's rank correlation test was used to evaluate the relations between the clinical dyspnea ratings and physiologic parameters.

RESULTS

The average age of COPD group (group 1) was 60.55 ± 9.92 years (2 female, 18 male). According to ERS guidelines all the patients had moderate COPD (11). During the exercise test all the patients exhibited severe exercise curtailment due to dyspnea. Additionally four of these patients had leg fatigue. The average exercise duration was 7.55 ± 1.68 minutes.

Control subjects (group 2) were all male. The average age of this group 45.89 ± 8.85 years. The test was ended due to leg fatigue (83%) and leg pain (17%). The exercise duration was 9.65 ± 1.70 minutes.

The dyspnea scales of COPD patients were shown in Table 1. The patients had dyspnea with activities of daily living.

The results of the pulmonary function test and arterial blood gas analysis are shown in Table 2

Table 1. The dyspnea scales in COPD patients.

Scale	Mean ± SD
MRC scale	2.10 ± 0.55
BDI	5.65 ± 1.60
Borg scale	4.55 ± 1.23

MRC scale: Medical Research Council Scale

Table 2. Pulmonary function tests at rest.

Parameters	Group 1 (n: 20) Mean ± SD	Group 2 (n: 12) Mean ± SD	P
FVC (pred%)	73.25 ± 13.90	101.92 ± 12.24	< 0.001
FEV_1 (pred%)	56.00 ± 15.03	101.58 ± 10.80	< 0.001
FEV_1/FVC%	60.75 ± 10.80	83.50 ± 5.44	< 0.001
FEF_{25-75} (pred%)	30.80 ± 10.94	95.92 ± 20.17	< 0.001
MVV (pred%)	42.00 ± 10.37	78.09 ± 14.58	< 0.001

and 3, and peak exercise ventilatory and metabolic parameters are presented in table 4. In patients with COPD; Mean FEV_1(pred%): 56.00 ± 15.03%. Exercise capacity was decreased [Mean VO_2 (pred%): 46.15 ± 10.18%, Mean VO_2/kg (pred%): 53.70 ± 11.72%].

The correlation between the dyspnea scales and pulmonary function tests, arterial blood gas analysis are shown in table 5 and the correlation between the peak exercise metabolic and ventilatory parameters with the dyspnea scales are presented in table 6. BDI and Borg scales have been found to correlate with FVC (pred%), FEV_1 (pred%), FEV_1/FVC (%), PEF (pred%), FEF_{25-75} (pred%), MVV (pred%); and MRC scale with FEF_{50} (pred%), PEF (pred%), MVV (pred%), Ti, Ttot. Additionally BDI showed correlation with EELV (TLC%).

When these scales were correlated with each other, significant correlations were observed (MRC scale and BDI: r: -0.62, p< 0.01; MRC and Borg scales: r: 0.46, p< 0.05; BDI and Borg scale: r: -0.67, p< 0.01).

DISCUSSION

Dyspnea is the sensation of breathlessness. It is result of mismatch between central respiratory motor activity and incoming afferent information from receptors in the airways, lungs and chest wall structures. The disassociation between the motor command and the mechanical response of the respiratory system may produce a sensation of respiratory discomfort. The mismatch of neural activity, mechanical and ventilatory response affects the severity of dyspnea (17).

COPD patients feel restrictions in their daily activities due to respiratory discomfort and reductions in their exercise capacity and quality of life, further leading long-term disability for the patient (17). The increase in ventilation in order to compensate the increased dead space; increase in airway resistance; abnormal breathing pattern; the mechanical inefficiency of the respiratory muscles; and the effects of hypoxemia and hypercapnia on peripheral and central chemoreceptors cause the sensation of dyspnea in COPD patients. Patients usually define this feeling as chest tightness, air hunger or increased effort of breathing (4,17).

Table 3. Lung volumes, diffusing capacity of CO, respiratory muscle strength, breathing pattern and arterial blood gas analysis of COPD patients.

Parameters	Group 1 (n: 20) Mean ± SD
VC (pred%)	70.26 ± 9.99
TLC (pred%)	105.21 ± 15.04
FRC (pred%)	194.26 ± 45.05
RV/TLC%	56.63 ± 9.28
IC (L)	1.23 ± 0.45
EELV (TLC%)	78.74 ± 8.10
DLCO (pred%)	72.78 ± 26.65
DLCO/VA (pred%)	99.31 ± 26.24
Pimax (pred%)	57.25 ± 18.53
$P_{0.1}$ (cmH_2O)	3.80 ± 1.35
VE/$P_{0.1}$%	14.07 ± 7.05
Ti (sec)	0.91 ± 0.30
Ti/Ttot	0.39 ± 0.06
pH	7.43 ± 0.04
PaO_2 (mmHg)	66.33 ± 9.01
$PaCO_2$ (mmHg)	39.69 ± 4.35
SaO_2%	93.00 ± 3.32

Table 4. Peak metabolic and ventilatory parameters of COPD patients during the exercise testing.

Parameters	Group 1 (n: 20) Mean ± SD	Group 2 (n: 12) Mean ± SD	p
Heart rate (/min)	131.50 ± 14.62	157.25 ± 14.41	< 0.001
Work (watt)	117.78 ± 37.45	167.17 ± 41.53	< 0.01
VO_2 (L/min)	1.03 ± 0.32	2.31 ± 0.50	< 0.001
VO_2 (pred%)	46.15 ± 10.18	74.33 ± 16.57	< 0.001
VO_2/kg (ml/kg/min)	14.09 ± 3.92	29.05 ± 6.98	< 0.001
VO_2/kg (pred%)	53.70 ± 11.72	70.00 ± 16.24	< 0.01
VCO_2 (L/min)	1.24 ± 0.43	2.46 ± 0.65	< 0.001
R	1.19 ± 0.13	1.06 ± 0.12	< 0.01
VT peak (L)	1.26 ± 0.41	2.21 ± 0.62	< 0.001
VE peak (BTPS) (L/min)	46.48 ± 13.80	74.87 ± 21.81	< 0.001
VE peak/MVV%	88.53 ± 18.02	-	-

Dyspnea is a subjective terminology, in order to assess it objectively several clinical scales have been put forward since 1950. The most popular ones are MRC scale, The Oxygen Cost Diagram (OCD), BDI, Transitional Dyspnea Index (TDI), University of California at San Diego Shortness of Breath Questionnaire (UCSDQ). These are mostly used in order to assess dyspnea during daily activities. Borg Scale and Visual Analogue Scale (VAS) are used to define the dyspnea felt during exercise. In this study, we used BDI, MRC and Borg scales in order to define the severity of dyspnea. According to MRC scale the patients were between grade 0-3, mostly grade 2. BDI score of the patients was 5.65, which meant that most of them were grade 1-2 in each of category. These two scales seemed to correlate significantly with each others (r: -0.61, $p< 0.01$). According to Borg scale the score changed between 3-7 with an average of 5. Again this scale also seemed to correlate significantly with the other two scales ($p< 0.01$, $p< 0.05$).

Pulmonary function tests are important in evaluating the dyspnea in COPD patients, also it helps to discriminate patients with obstructive and restrictive lung diseases (17). There are some reports evaluating the correlation between the dyspnea scales and pulmonary function tests. Hajiro et al, have shown that MRC and BDI correlates with airway obstruction (FEV_1) and hyperinflation (RV/TLC%); and Mahler et al, had concluded that both of these scales correlated with FEV_1 and FVC (9,19). Bestall et al, have reported that when the COPD patients were clustered according to MRC scale, FVC seemed to decrease significantly especially in grade 3-4 patients (20). In our study we observed that BDI and Borg scales have significant correlation with expiratory flow rates and MRC scale with only FEF_{50}, PEF, MVV (Table 5).

The MRC sclae has been used extensively as a method to define an characterize the patient population. The BDI, a discriminative instrument, describes specific criteria for each of the three components at a single point in time. Both have been in use for grading the effect of breathlessness on daily activities. But, BDI a multidimensional instrument, describes multibl factor that influence the sensation of dyspnea. Borg scale has been used by patients with respiratory disease to rate their intensity of breathlessness during exercise. The measurement of dyspnea during exercise can be used for discriminative purpose (identifying patients with more severe exertional breathlessness) (21). Especially, Borg scale and BDI show good correlation with the severity of obstruction as was the case in our study.

We also observed that MRC scale showed significant correlation with breathing pattern (Ti, Ttot; $p< 0.05$, $p< 0.01$). There is little direct evi-

Table 5. The Correlation of MRC, BDI, Borg scales of the patients with PFT and ABG analysis.

	MRC scale	BDI	Borg scale
Parameters	r	r	r
FVC (pred%)	-0.35	0.45*	-0.70**
FEV_1 (pred%)	-0.44	0.70**	-0.86**
FEV_1/FVC%	-0.33	0.67**	-0.65**
FEF_{25-75} (pred%)	-0.41	0.68**	-0.77**
FEF_{50} (pred%)	-0.46*	0.72**	-0.72**
PEFR (pred%)	-0.53*	0.41	-0.60**
MVV (pred%)	-0.46*	0.58*	-0.69**
VC (pred%)	-0.02	0.13	-0.37
TLC (pred%)	0.15	-0.36	0.22
IC (L)	0.15	-0.20	0.10
EELV (TLC%)	0.24	-0.55*	0.44
DLCO (pred%)	-0.05	0.19	-0.10
Pimax (pred%)	-0.15	0.10	-0.07
$P_{0.1}$ (cmH_2O)	-0.10	0.03	0.09
VE/$P_{0.1}$%	0.17	-0.01	-0.20
Ti (sec)	0.56*	-0.14	0.27
Ttot (sec)	0.60**	-0.28	0.35
Ti/Ttot%	0.24	0.15	-0.37
VT (L)	0.24	-0.26	0.42
VE (L/min)	-0.11	0.06	-0.13
VEpeak/MVV%	0.17	-0.23	0.33
PaO_2 (mmHg)	-0.10	0.47*	-0.19
$PaCO_2$ (mmHg)	0.23	-0.43	0.23
SaO_2%	-0.11	0.48*	-0.22

* $p< 0.05$
** $p< 0.01$

dence that pulmonary vagal receptors contribute directly to dyspnea. Vagal inputs are important in shaping the pattern of breathing (17). The changes in level and pattern of breathing may contribute to the sensation of dyspnea (1,3,22). Leblanc et al, in their study with different clinical disorders, have observed that dyspnea showed correlation with breathing pattern (especially VT/VC, Ti/Ttot and f) (2).

It is an acknowledged truth that dyspnea has positive correlation with lung volumes. The lowest dyspnea scores showed correspondence to the lowest end-expiratory lung volumes (3). Dynamic hyperinflation was shown to be the most important factor in limiting the exercise capacity in O'Donnell's study (23,24). In our study resting EELV showed inverse correlation with BDI and no correlation with Borg scale. Borg scale was found to correlate with expiratory flow rates and maximal breathing capacity.

As for the relation with the dyspnea scales and ABG analysis, only BDI showed correlation with PaO_2 and SaO_2 ($p< 0.05$). Hypoxemia results in dyspnea either directly or through the stimulation of the peripheral receptors causing an increase in the respiratory motor activity. Also hypoxemia contributes to exertional symptoms and exercise limitation (25). In our patients, mild hypoxemia was observed at rest (PaO_2: 66.33 mmHg, SaO_2: 93%), supporting the role of hypoxemia in the occurrence of dyspnea.

Table 6. The Correlation of MRC scale, BDI, Borg scales with peak exercise parameters.

	MRC Scale	BDI	Borg scale
Parameters	**r**	**r**	**r**
Work (watt)	-0.10	0.41	-0.30
VO_2 (L/min)	0.41	-0.03	0.10
VO_2 (pred%)	0.40	-0.11	0.14
VO_2/kg (ml/kg/min)	0.43	-0.04	0.06
VO_2/kg (pred%)	0.47*	-0.34	0.19
VCO_2 (L/min)	0.42	-0.01	0.08
VTeg (L)	0.38	-0.04	0.05
VEeg (BTPS)(L/min)	0.18	0.03	-0.04

* $p< 0.05$

In cycle ergometer, all COPD patients terminated the test due to dyspnea. The exercise capacity in COPD patients was significantly decreased compared to the control group (peak VO_2: 46.15 ± 10.18%, VO_2/kg: 53.70 ± 11.72%). Only MRC scale showed positive correlation with VO_2/kg (pred%) (Table 6, r: 0.47, $p< 0.05$). In several studies, dyspnea is found to be the most important symptom in the limitation of exercise capacity (2,18,19,24-26). Mahler and Harver showed that BDI was an important factor in determining VO_2, Silverman et al, presented that Borg scale correlated with physiologic parameters such as VO_2 and VE (26,27). In some of the studies the relation between exercise dyspnea and oxygen consumption have been shown, supporting the role of exercise dyspnea in the limitation of exercise capacity (19,23,24).

In our study, we found relation between the airflow rates and Borg scale, whereas no correlation was found with the exercise capacity and the Borg scale, with exercise capacity and BDI. At the present time, there is no concensus as to which independent variable should be used as the presumed stimulus to relate to the response of dyspnea (21). In addition it has been shown that there is generally greater variability for dyspnea ratings at submaximal exercise intensities compared with maximal values (21). The lack of correlation between exercise testing parameters and clinical dyspnea scales in our study may be explained by these facts.

In conclusion, both clinical scales and ratings during exercise are used to measure the impact of dyspnea in symtomatic patients. The BDI generates a score that can indicate the severity (mild, moderate, severe) of dyspnea. This scale shows correlation with expiratory airflow rates and hypoxemia. Borg scale, despite its correlation with airflow rates, showed no relation with exercise capacity. Although BDI and Borg scale seemed to inform us about the airway obstruction of COPD patients, the ability to reflect exercise capacity in these patients seems to be poor.

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