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Relationship between the Severity of Airway Obstruction and Inspiratory Muscles Dysfunction in COPD Patients

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ABSTRACT

Background: *COPD is known as the main cause of morbidity and mortality in the world. Morbidity in COPD patients is mainly due to the respiratory muscle dysfunction especially diaphragm and chest wall muscles. Respiratory muscle dysfunction is mostly seen in severe and progressive stages of the disease. COPD results in increased functional residual capacity (FRC). In severe cases of COPD, respiratory muscle dysfunction and FRC raise lead to the deterioration of hyperinflation.*

Materials and Methods: *In our study, 30 COPD patients (28 males, 2 females) referred to Masih Daneshvari Hospital were evaluated. All cases were studied with the exact same body plethysmography equipment and the same technician.*

Results: *The average age, height, weight and BMI of cases were 53 +/- 11 yrs,168.86+/-6.33 cm, 65.44+/-16.78 kg and 23.56+/- 6.32, respectively. The mean FEV1 according to the GOLD criteria was in the range of moderate to severe.*

Hyperinflation noted characterized by RV and reverse RV/TLC, was clearly noticed in our study (RV=225.9+/-82.11, RV/TLC%= 195+/-34.49).

Conclusion: *Based on our study results, there was a significant correlation between FEV1, hyperinflation (RV/TLC, RV), respiratory muscle function (PImax/P1) and respiratory time cycle Ti/Ttot .It should be mentioned that there was a significant correlation between PImax and Tension Time Index as well.* ***(Tanaffos 2009; 8(3): 37-42)***

Key words: *Airway obstruction, Muscle dysfunction, COPD, TI (inspiratory time), Tension-time index (TTI)*

INTRODUCTION

Function of respiratory muscles is significantly affected in COPD patients (1). The increased mechanical work load of respiration along with airway obstruction and inflation of the lungs might explain the weight loss seen in COPD patients. The oxygen cost is usually elevated in malnourished patients with COPD relative to the normally nourished group (2). In general, malnourished patients are characterized by a greater degree of hyperinflation (shown by the ratio of RV/TLC) and have a lower PImax.

Respiratory muscle dysfunction and hyperinflation in COPD patients result in exercise

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intolerance and dyspnea (3). Hyperinflation can enhance the dysfunction of respiratory muscles especially the diaphragm. It can also be a major compatibility factor in cases with severe obstructions (4, 5).

Also, in COPD patients with hypercapnia oxygen cost is inappropriately high and this is in direct correlation with pulmonary inflation (pulmonary inflation is confirmed by the RV/TLC ratio and flattening of the diaphragm on chest x ray).

Burrows et al (6) in their study on the mutual correlation between gas exchange indices and pulmonary function in COPD patients indicated that $PvCO_2$ measured by the re-breathing method was related with pulmonary inflation (determined by the RV/TLC method). However, he has emphasized on determining the significance of the inverse correlation between RV/TLC ratio and FEV1.

Rochester et al. (7) showed that $PaCO_2$ had an inverse correlation with PImax (although it is correlated with the severity of inflation). They also evaluated the correlation between decrease in PImax and primary weakness of respiratory muscles with gas exchange in COPD patients. They concluded that in a constant PImax, $PaCO_2$ was higher in COPD patients compared to those suffering only from weakness of respiratory muscles. Also, hypercapnia is correlated with the degree of dynamic inflation of the lungs (8). Other studies showed the importance of the inspiratory muscle threshold (and therefore hyperinflation) in determining the severity of hypercapnia. In a large number of under study patients, it was demonstrated that the best predictive of $PaCO_2$ among the measured variables was the imposed inspiratory load measured by the proportion of pulmonary resistance to PImax (9).

Also, it has been demonstrated that improving the endurance of respiratory muscles can result in halting the acute phase of the disease and potentially decreasing the morbidity and even mortality (10).

MATERIALS AND METHODS

In this prospective study 30 patients (28 men and 2 women) with stable COPD referred to Masih Daneshvari Hospital were evaluated. These patients were in a stable condition during the study and did not experience the exacerbation of symptoms for the past 2 weeks. There was no change in their medications and all patients were examined by the same body plethysmography device and the same technician. Results are presented as mean ± SD. Statistical analysis was performed by using student t-test. Linear regression test was used for evaluating the correlation between FEV1 and respiratory muscles and respiratory drive tests (especially TTI and its components).

RESULTS

In this study, 30 patients (28 males and 2 females) were evaluated. The mean age of patients was 53 ± 11 yrs (Table 1). The mean height, weight and BMI of patients was 168.85 ± 6.33 cm, 65.44 ± 16.78 kg and 23.56±6.32, respectively. Patients' BMI in this study was within the normal range.

Table 1. Demographic characteristics of patients (age, height, weight and BMI)

	AGE(year)	*HEIGHT(cm)*	*WEIGHT(Kg)*	*BMI(Kg/m²)*
Mean	53	168.85	65.44	23.56
SD	11	6.38	16.78	6.32
Max	75	183	102	39.84
Min	30	153	42	14.68

According to the Gold criteria, spirometric indices and the mean FEV1 in under study patients were in the range of moderate to severe (FEV1 = 36.3 ±13.9% , FEV1 /FVC = 57.66 ±13.97%). Also, there were significant differences in the severity of airway obstruction among patients (FEV1 ranged between 18 to 68% and FEV1/FV ranged between 32 to 70%).

Hyperinflation of the lungs determined by RV and inverse correlation of RV/TLC was significantly noticed in the under study patients (Table 2) (RV%=225.9±82.11, RV/TLC%=195±34.49). It was also detected that hyperinflation was frequent among patients (the frequency distribution of RV and RV/TLC ranged between 85-428 percent and 124-262 percent, respectively).

Table 2. Spirometric indices.

	VT	VT/Ti	FEV1	FVC	FEV1/FVC	Ti	Ti/Tt	RV%	RV/TLC%
Mean	0.54	0.57	36.3	48.9	57.66	0.34	0.39	225.9	195
SD	0.21	0.22	13.9	13.3	13.97	0.23	0.07	82.11	34.49
Max	1.1	1.06	68	66	70	0.11	0.54	428	262
Min	0.21	0.36	18	24	32	0.9	0.07	85	124

Table 3. Criteria for muscle function.

	PImax(Kpa)	*PIme*	*PI/PImax*	$P_{0.1}$	$P_{0.1}$*/PImax*	$P_{0.1}/P_{0.1}max$	$P_{0.1}$*Ti/TV	*TTI(S)*
Mean	3.93	0.87	0.27	0.47	16.95	29.2	0.77	0.11
SD	2.22	0.9	0.61	0.08	18.37	23	0.39	0.14
Max	10.51	3.42	0.61	1.19	73	72	1.95	0.56
Min	1.32	0.17	0.11	0.04	2	6	0.08	0.02

Table 2 demonstrates the mean ventilatory data in patients including VT (tidal volume), TI (inspiratory time) and Ti/Ttot (the ratio of inspiratory time to the total respiratory cycle time) which were 0.21±0.54, 0.34±0.23 and 0.39± 0.07, respectively.

Table 3 demonstrates data regarding respiratory drive and respiratory muscle function of patients. In this table, the mean $P_{0.1}$ of patients was significantly lower than the reference figures (0.46 Kpa vs. 0.72 Kpa).

The mean PImax was also lower than the standard measure (3.9 Kpa vs. 8 Kpa). Other respiratory drive indices such as $P_{0.1}/P_{0.1}$ max (29.2% vs. 5%) and $P_{0.1}$/Pi max (16.95% vs. 3%) showed a significant increase.

The mean tension-time index for respiratory muscles in our under study patients was 0.11± 0.14 which was lower than the fatigue threshold. However, maximum tension-time index was significantly higher than the fatigue threshold (0.56). Table 4 demonstrates the correlation between the anthropometric data of the understudy patients with the severity of airway obstruction and their respiratory muscle function.

Table 4. The statistical correlation between the anthropometric data and spirometric findings.

	AGE(year)	*WEIGHT(Kg)*	*HEIGHT(cm)*	*BMI(kg/m²)*
FEV1	-0.357	0.447**	-0.72	0.496*
PImax	-0.127	0.246	0.143	0.210

There was a significant correlation between the patients' weight ($p<0.05$) and their BMI ($p<0.01$) with FEV1. Table 5 demonstrates the correlation between FEV1 and PImax with other spirometric and respiratory findings. Significant correlations were found between FEV1 and PImax, $P_{0.1}/P_{0.1}max$ ($p<0.01$), Ti/Ttot, $P_{0.1}$ and $P_{0.1}$/PImax. No significant correlation was found between FEV1 and TTI but a significant relationship was found between PImax and TTI ($p<0.01$). Also, there was a significant correlation between Ti/TV, $P_{0.1}$ and FEV1 ($p<0.05$).

Table 5. Statistical correlation between the severity of airway obstruction, spirometric findings and respiratory muscle function

	FEV1(L/S)	*PI-max(Kpa)*
FEV1	-	0.510**
VT/Ti	0.6	0.085
Ti/Ttot	0.375*	0.211
$P_{0.1}$	-0.411*	-0.226
$P_{0.1}$-mean	-0.408*	-0.302
$P_{0.1}$-max	0.286	0.597+
$P_{0.1}/P_{0.1}max$	-0.537**	-0.437*
$P_{0.1}$/PImax	-0.446*	-0.533**
$P_{0.1}$*Ti/VT	-0.371*	-0.202
TTI	-0.079	-0.0607+

*Correlation is significant at the 0.05 level (2-tailed)

**Correlation is significant at the 0.01 level (2-tailed)

+Correlation is significant at the 0.001 level (2-tailed)

DISCUSSION

In this study, stable COPD patients with no exacerbation of symptoms were studied. Table 1 demonstrates the mean anthropometric information of patients. Considering the BMI, 6 patients had significant weight loss.

Heunks in his study discussed the weight loss and the related malnutrition in patients with moderate to severe COPD (11). According to Nishimura et al., several factors are responsible for muscular fatigue among which changes in BMI can be named. Assessment of BMI alterations is important in recognizing the causes of muscular fatigue (12). However, BMI of our under study patients was within the normal limit.

Based on this study and that of Yan et al, gender played no role in the obtained results (13).

Table 2 demonstrates the spirometric indices of under study patients. Evaluation of patients' FEV1 showed a significant decrease (the mean FEV1=63.3%, FEV1/FVC=57.66%). Also, a significant difference was observed between FEV1 and FEV1/FVC ratio in patients. In a study by Hayot et al, patients had very low FEV1 values (14).

Hyperinflation indices including RV and RV/TLC were also high in our patients. In this study, the mean RV was 225±82% and the mean RV/TLC was 195±34%. Hayot (14) obtained the same results in his study. The mean ventilatory data showed different values. Although the values for VT, VT/Vi and Ti/ Ttot were slightly different than the standard values, the value for Ti was significantly lower than the standard value (0.89 vs. 1.33) indicating the decreased inspiratory time in under study patients.

Table 3 shows the data regarding the respiratory drive and respiratory muscle function. Values of $P_{0.1}$ were higher than normal whereas the values of PImax were lower than normal range. Therefore, the proportion of $P_{0.1}$/PImax is shown to be significantly high. The mean ratio of PI/PImax was calculated to be 0.27. In Hayot's study, this rate was reported to be 0.21 which was almost similar to ours. In our study, the mean inspiratory muscle tension-time index was calculated to be 0.11indicating a significant increase but only in 3 cases it exceeded the fatigue threshold of 0.15. In Hayot's study, the mean TTI was 0.08 (14). In a study by Vassilakopouls on COPD patients under mechanical ventilation, those with TTI=0.108 were able to wean from the ventilator (15) whereas, patients with TTI=0.162 could not tolerate the weaning.

Table 4 demonstrates the Pearson's correlation coefficient between FEV1, PImax, age, weight, height and BMI of patients. According to this table, patients' FEV1 had a significant correlation with their weight (P<0.01) and BMI (P<0.05). PImax had no significant correlation with anthropometric findings. This finding was in contrast with Hayot's findings. In his study, PImax was significantly correlated with the weight of COPD patients (14).

Table 5 evaluates the Pearson's correlation coefficient between spirometric findings and respiratory drive with FEV1 and PImax (and the correlation of these two with each other). PImax was significantly correlated with FEV1. It indicates the excess chronic pressure on the respiratory muscles and diaphragm in COPD patients. Martinez et al. obtained similar results in his study on COPD patients (8). Table 5 also demonstrates some information regarding the correlation between FEV1 and pulmonary and neuromuscular function.

Respiratory drive characterized by $P_{0.1}$ (and the related formulas such as $P_{0.1}/P_{0.1}$max and Ti/VT) had a significant correlation with FEV1 but no significant correlation was found between $P_{0.1}$max and FEV1. On the other hand, inspiratory time and related criteria had different correlations with FEV1. Also, Ti/Ttot had a significant correlation with FEV1; whereas, VT/Ti had no correlation with FEV1. It may be a strategy taken by the respiratory muscles in order to reduce the mechanical work load via decreasing the Ti/Ttot in cases with severe obstruction of the airways. It is noteworthy that TTI had no significant correlation with FEV1 whereas components of its formula (such as Ti/Ttot and PImax) each had a significant correlation with FEV1. Also, in studies by Hayot (14), Ramonatxo (16), Bellemare and Grassino (17, 18), a significant correlation was reported between the severity of obstruction (FEV1, FRC and FRC/TLC) and TTI. Our finding in this regard was not in accord with that of previous studies. Table 5 shows the correlation between PImax, spirometric findings and respiratory muscle function. According to this table, VT/Ti, Ti/Ttot, and $P_{0.1}$ showed no significant correlation with PImax. On the other hand, PImax had a significant correlation with FEV1 ($p<0.05$), $P_{0.1}$max ($p<0.001$), $P_{0.1}/P_{0.1}$max ($p<0.05$) and $P_{0.1}$/PImax ($p<0.001$). Also, there was a significant correlation between PImax and TTI in COPD patients ($p<0.001$). This is justifiable since the PImax is incorporated in the TTI formula. The regression curves for variables with significant correlations with each other (and also the regression curve for the correlation between FEV1 and TTI) are demonstrated in the appendix.

CONCLUSION

In this study, significant correlations were found between the severity of airway obstruction (FEV1), hyperinflation of the lungs (RV, RV/TL), function of respiratory muscles (PImax/PI), and inspiratory time TI/Ttot. Also, a significant correlation was seen between PImax and tension-time index (TTI).

REFERENCES

1. Rochester DF. The respiratory muscles in COPD. State of the art. ***Chest*** 1984; 85 (6 Suppl): 47S- 50S.
2. Donahoe M, Rogers RM, Wilson DO, Pennock BE. Oxygen consumption of the respiratory muscles in normal and in malnourished patients with chronic obstructive pulmonary disease. ***Am Rev Respir Dis*** 1989; 140 (2): 385- 91.
3. Koppers RJ, Vos PJ, Boot CR, Folgering HT. Exercise performance improves in patients with COPD due to respiratory muscle endurance training. ***Chest*** 2006; 129 (4): 886- 92.
4. Loring SH, Garcia-Jacques M, Malhotra A. Pulmonary characteristics in COPD and mechanisms of increased work of breathing. ***J Appl Physiol*** 2009; 107 (1): 309- 14.
5. De Troyer A, Wilson TA. Effect of acute inflation on the mechanics of the inspiratory muscles. ***J Appl Physiol*** 2009; 107 (1): 315- 23.
6. Burrows B, Strauss RH, Niden AH. Chronic Obstructive Lung Disease. 3. Interrlatonships of Pulmonary Function Data. ***Am Rev Respir Dis*** 1965; 91: 861-8.
7. Rochester DF. The diaphragm in COPD. Better than expected, but not good enough. ***N Engl J Med*** 1991; 325 (13): 961- 2.
8. Martinez FJ, Couser JI, Celli BR. Factors influencing ventilatory muscle recruitment in patients with chronic airflow obstruction. ***Am Rev Respir Dis*** 1990; 142 (2): 276- 82.
9. Gayan-Ramirez G, Palecek F, Chen Y, Janssens S, Decramer M. Inotropic effects of aminophylline on canine

diaphragm are enhanced by hyperinflation. ***J Appl Physiol*** 1994; 76 (1): 39- 44.

10. Mador MJ, Deniz O, Aggarwal A, Shaffer M, Kufel TJ, Spengler CM. Effect of respiratory muscle endurance training in patients with COPD undergoing pulmonary rehabilitation. ***Chest*** 2005; 128 (3): 1216- 24.
11. Heunks LM, Dekhuijzen PN. Respiratory muscle function and free radicals: from cell to COPD. ***Thorax*** 2000; 55 (8): 704- 16.
12. Nishimura Y, Tsutsumi M, Nakata H, Tsunenari T, Maeda H, Yokoyama M. Relationship between respiratory muscle strength and lean body mass in men with COPD. ***Chest*** 1995; 107 (5): 1232- 6.
13. Yan S, Kaminski D, Sliwinski P. Inspiratory muscle mechanics of patients with chronic obstructive pulmonary disease during incremental exercise. ***Am J Respir Crit Care Med*** 1997; 156 (3 Pt 1): 807- 13.
14. Hayot M, Perrigault PF, Gautier-Dechaud V, Capdevila X, Milic-Emili J, Prefaut C, et al. Tension-time index of inspiratory muscles in COPD patients: role of airway obstruction. ***Respir Med*** 1998; 92 (6): 828- 35.
15. Vassilakopoulos T, Zakynthinos S, Roussos C. The tension-time index and the frequency/tidal volume ratio are the major pathophysiologic determinants of weaning failure and success. ***Am J Respir Crit Care Med*** 1998; 158 (2): 378- 85.
16. Ramonatxo M, Boulard P, Préfaut C. Validation of a noninvasive tension-time index of inspiratory muscles. ***J Appl Physiol*** 1995; 78 (2): 646- 53.
17. Bellemare F, Grassino A. Force reserve and timing of contraction on human diaphragm fatigue. ***J Appl Physiol*** 1982; 53:1190-5.
18. Bellemare F, Grassino A. Force reserve of the diaphragm in patients with chronic obstructive pulmonary disease. ***J Appl Physiol*** 1983; 55 (1 Pt 1): 8- 15.