A Retrospective Analysis of Nutritional Parameters in Chronic Obstructive Pulmonary Disease between Sexes

Ugur Gonlugur¹,* and Tanseli E. Gonlugur²

¹Department of Chest Diseases, School of Medicine, Cumhuriyet University, 58140, Sivas, Turkey
²Department of Chest Diseases, Sivas State Hospital, 58040, Sivas, Turkey

Received 6 October, 2006; Accepted 2 April, 2007

Summary  The aim of this study was to reveal the relationships between nutritional parameters and pulmonary functions in patients with chronic obstructive pulmonary disease (COPD) in both sexes. Spirometric, laboratory, and demographic data of 450 consecutive patients were analysed retrospectively. Males had significantly greater pack-years of smoking, more severe airway obstruction, and lower body mass index (BMI). In non-smokers, BMI was significantly lower in men independent of age and pulmonary functions. Creatine kinase levels showed no correlation with any pulmonary function parameters. Serum albumin levels correlated better than BMI with pulmonary functions. In conclusion, females with COPD were maintained weight better than men.

Key Words: gender differences, lung diseases, obstructive, malnutrition, biomass

Introduction

Body weight and body mass index (BMI) are independent risk factors for mortality in chronic obstructive pulmonary disease (COPD) patients [1, 2]. It is still unclear why patients with COPD become undernourished as the disease progress. We researched the relationships between possible nutritional parameters (haemoglobin levels, serum albumin, blood urea nitrogen, creatinine, cholesterol, triglycerides, creatine kinase—a myocyte-derived enzyme) and lung functions in COPD.

Materials and Methods

Spirometric, laboratory, and demographic data of 450 consecutive patients (348 men and 102 women), aged 39 to 84 years, were analysed retrospectively. All the patients had COPD, according to the GOLD consensus report [3] and chronic airflow limitation, defined as measured forced expiratory volume in one second (FEV1)/forced vital capacity (FVC)<70 percent. Exclusion criteria were malignancy, tuberculosis, bronchiectasis, surgical operation within 6 months, severe endocrine, hepatic, or renal disorders. The best and technically acceptable spirometric data, height and weight data, and smoking habits of each patient were noted. Patients were considered to be underweight if their BMI was <20 kg.m⁻². FVC, FEV1, FEV1/FVC, maximum mid-expiratory flow (MMEF), and peak expiratory flow rate (PEF) levels were recorded as pulmonary function parameters. All spirometric values obtained were related to a reference value and expressed as a percentage of the predicted value [4]. Serum albumin, blood urea nitrogen (BUN), creatinine, cholesterol, triglycerides, creatine kinase, haemoglobin levels and pulmonary function test results were recorded when the patients were in a stable period. A non-COPD group consisted of the patients who had not airway obstruction (FEV1/FVC>70%).

All statistical analyses were performed with SPSS version 10.0 (SPSS Inc, Chicago, IL). Data were analysed using independent-samples t test, and Pearson’s correlation test, and Spearman Rank correlation test if the population was
non-parametric. If correlation coefficient was less than 0.3, the results were considered as non-significant. A 2-tailed \( p \) value less than 0.05 was considered significant.

The study was approved by the Ethical Committee of the School of Medicine, Cumhuriyet University (2005-2/2).

**Results**

All data are presented as means ± SE. The mean age years of 102 females (22.7%) and 348 males (77.3%) were 62.9 ± 0.8 and 61.4 ± 0.5 respectively \( (p>0.05) \). A non-COPD group, consisted of 103 males (77.4%) and 30 females, was gender- and age-matched. Demographic, spirometric, and biochemical parameters of two groups were presented in Table 1. The patients who had airway obstruction had significantly greater pack-years of smoking, blood urea nitrogen and serum creatinine levels but lower BMI.

When compared to female patients with COPD, males had significantly greater pack-years of smoking, haemoglobin levels, more severe airway obstruction but lower BMI (Table 2). The prevalence of a BMI less than 20 kg.m\(^{-2}\) was 9.6% among the 450 outpatients studied, 13.9% in severe COPD \( (\text{FEV1}<50\% \text{ of reference}) \) and 4.0% in mild to moderate COPD. Only one of the women with severe disease had BMI<20 kg.m\(^{-2}\).

There was a negative correlation between BMI and pack-years of smoking \( (r: 0.24, p<0.01) \) but not in non-COPD group. The decreasing effect of smoking on BMI was valid only in COPD group \( (\text{Odds ratio:} \ 1.41, 95\% \text{ confidence intervals:} \ 1.22-1.63) \). For the relationships between BMI and pulmonary functions, the correlation coefficients were 0.21 for FVC, 0.26 for FEV1, and 0.32 for FEV1/FVC in COPD group.

In non-smokers, BMI was significantly lower in men independent of age and pulmonary functions (Table 3). In the entire COPD group \( (\text{Table 4}) \) and in non-smokers \( (\text{Table 5}) \), BMI was not related any of pulmonary functions. However, serum albumin showed a good correlation with pulmonary functions. Multiple linear regression analysis revealed that serum albumin level was the best predictor of FEV1 \( (\beta = 12.307, p<0.001) \). Creatine kinase levels showed no correlation any of the pulmonary function parameters \( \text{(data not shown)} \).

**Discussion**

Table 1 showed that the patients with COPD had significantly greater pack-years of smoking but lower BMI. The relationship between BMI and smoking was restricted only in COPD group. This finding suggests that the lower BMI is due to the loss of lung functions. The higher correlation coefficients between BMI and lung functions than those between BMI and smoking also support this idea. Table 2 demonstrated that males had more severe loss of pulmonary parenchyma because they had greater load of smoking than females. Consequently, the males had lower BMI than those of women.

Serum albumin level decreased with declining in pulmonary function in our study. Schols et al. [5] reported that serum albumin levels are positively associated with exercise

| Parameters                  | COPD group \( (n=450) \) | Non-COPD group \( (n=133) \) | \( p \) level |
|-----------------------------|---------------------------|-----------------------------|---------------|
| Age                         | 61.9 ± 0.4                | 60.9 ± 0.7                  | 0.28          |
| FVC (%)                     | 69.3 ± 1.0                | 88.7 ± 1.3                  | <0.01         |
| FEV1 (%)                    | 48.9 ± 0.9                | 96.0 ± 1.4                  | <0.01         |
| FEV1/FVC (%)                | 55.3 ± 0.4                | 78.7 ± 0.6                  | <0.01         |
| MMEF (%)                    | 21.9 ± 0.5                | 89.3 ± 2.7                  | <0.01         |
| PEF (%)                     | 39.2 ± 0.7                | 85.3 ± 1.7                  | <0.01         |
| BMI (kg.m\(^{-2}\))         | 26.1 ± 0.2                | 28.5 ± 0.4                  | <0.01         |
| Haemoglobin (g.dL\(^{-1}\)) | 14.8 ± 0.1                | 15.0 ± 0.2                  | 0.29          |
| Serum albumin (g.L\(^{-1}\))| 37.7 ± 0.4                | 38.2 ± 0.6                  | 0.46          |
| Blood urea nitrogen (mg/dl) | 21.9 ± 0.9                | 16.9 ± 0.6                  | <0.01         |
| Serum creatinine (mg/dl)    | 1.33 ± 0.03               | 1.00 ± 0.03                 | <0.01         |
| Serum creatine kinase (U/L) | 77.2 ± 4.0                | 96.4 ± 9.3                  | 0.06          |
| Serum cholesterol (mg/dl)   | 174.5 ± 7.7               | 179.9 ± 6.3                 | 0.59          |
| Serum triglycerides (mg/dl) | 136.7 ± 12.1              | 121.0 ± 7.3                 | 0.27          |
| Smoking history (Pack-years)| 33.4 ± 2.2                | 23.3 ± 3.2                  | 0.01          |

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, MMEF: maximum mid-expiratory flow, PEF: peak expiratory flow, BMI: body mass index
performance, Katsura et al. [6] found that low serum albumin can be a risk factor for poor outcome in COPD. We found that serum albumin levels correlated better with pulmonary functions than BMI. This finding suggests that systemic catabolic process in COPD affects serum albumin concentration more than BMI. Additionally, Table 3 showed that BMI was significantly lower in male than in female in non-smokers subset. Males were more susceptible to weight loss and protein degradation despite the anabolic effects of testosterone. One explanation for these findings is ethnicity. For example, German women had a lower BMI than Turkish ones [7]. Other explanation can be higher leptin levels in women [8]. Another explanation is the different aetiology of COPD. In our study, females had a history of tobacco use of less than 5.5 pack-years. However, the minimum requirement

| Table 2. Comparison of pulmonary functions and nutritional parameters in two genders |
|-----------------------------------------------|
| Parameters                  | Males \( n = 348 \) | Females \( n = 102 \) | \( p \) level |
| FVC (%)                     | \( 70.0 \pm 1.1 \)  | \( 77.8 \pm 2.2 \)  | <0.01 |
| FEV1 (%)                    | \( 46.8 \pm 1.0 \)  | \( 56.9 \pm 1.8 \)  | <0.01 |
| FEV1/FVC (%)                | \( 54.2 \pm 0.5 \)  | \( 59.7 \pm 0.7 \)  | <0.01 |
| MMEF (%)                    | \( 22.0 \pm 0.6 \)  | \( 22.1 \pm 0.9 \)  | 0.92  |
| PEF (%)                     | \( 38.9 \pm 0.9 \)  | \( 41.2 \pm 1.4 \)  | 0.17  |
| BMI (kg.m\(^{-2}\))         | \( 24.8 \pm 0.2 \)  | \( 30.5 \pm 0.6 \)  | <0.01 |
| Haemoglobin (g.dL\(^{-1}\)) | \( 15.0 \pm 0.2 \)  | \( 13.9 \pm 0.3 \)  | <0.01 |
| Serum albumin (g.L\(^{-1}\))| \( 37.3 \pm 0.4 \)  | \( 37.8 \pm 0.7 \)  | 0.52  |
| Blood urea nitrogen (mg/dl) | \( 22.6 \pm 1.0 \)  | \( 19.7 \pm 1.3 \)  | 0.09  |
| Serum creatinine (mg/dl)    | \( 1.33 \pm 0.03 \) | \( 1.31 \pm 0.02 \) | 0.88  |
| Serum creatine kinase (U/L) | \( 79.7 \pm 5.5 \)  | \( 66.1 \pm 5.8 \)  | 0.09  |
| Serum cholesterol (mg/dl)   | \( 167.6 \pm 8.8 \) | \( 187.5 \pm 14.9 \)| 0.26  |
| Serum triglycerides (mg/dl) | \( 127.3 \pm 11.4 \)| \( 154.3 \pm 27.5 \)| 0.38  |
| Smoking history (Pack-years)| \( 40.5 \pm 2.3 \)  | \( 5.3 \pm 3.2 \)   | <0.01 |

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, MMEF: maximum mid-expiratory flow, PEF: peak expiratory flow, BMI: body mass index

| Table 3. Nutritional markers and pulmonary functions in non-smoker patients with COPD |
|-----------------------------------------------|
| Parameters                  | Males \( (n = 24) \) | Females \( (n = 41) \) |
| Age (years)                 | \( 60.6 \pm 2.2 \)  | \( 63.3 \pm 1.4 \)  |
| FVC (%)                     | \( 65.8 \pm 4.4 \)  | \( 71.1 \pm 3.5 \)  |
| FEV1 (%)                    | \( 47.4 \pm 3.5 \)  | \( 49.9 \pm 2.9 \)  |
| FEV1/FVC (%)                | \( 57.2 \pm 1.9 \)  | \( 57.3 \pm 1.2 \)  |
| MMEF (%)                    | \( 23.1 \pm 2.5 \)  | \( 18.9 \pm 1.4 \)  |
| PEF (%)                     | \( 40.6 \pm 3.4 \)  | \( 37.0 \pm 2.0 \)  |
| BMI (kg.m\(^{-2}\))         | \( 25.7 \pm 0.7 \)  | \( 30.1 \pm 0.9^* \) |
| Haemoglobin (g.dL\(^{-1}\)) | \( 15.1 \pm 0.3 \)  | \( 13.9 \pm 0.6 \)  |
| Serum albumin (g.L\(^{-1}\))| \( 39.8 \pm 0.9 \)  | \( 37.7 \pm 0.8 \)  |
| Blood urea nitrogen (mg/dl) | \( 18.3 \pm 1.4 \)  | \( 22.0 \pm 2.0 \)  |
| Serum creatinine (mg/dl)    | \( 1.22 \pm 0.09 \) | \( 1.52 \pm 0.03 \) |
| Serum creatine kinase (U/L) | \( 80.9 \pm 1.4 \)  | \( 66.2 \pm 6.2 \)  |
| Serum cholesterol (mg/dl)   | \( 171.5 \pm 5.5 \) | \( 177.2 \pm 27.9 \)|
| Serum triglycerides (mg/dl) | \( 129.5 \pm 8.5 \) | \( 109.9 \pm 16.5 \)|

* \( p < 0.01 \)

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, MMEF: maximum mid-expiratory flow, PEF: peak expiratory flow

| Table 4. Correlation coefficients between nutritional markers and lung functions in both sexes (Pearson’s correlation) |
|-----------------------------------------------|
| Parameters                  | FVC (%) | FEV1 (%) | FEV1/FVC (%) | MMEF (%) | PEF (%) |
| Serum albumin (g.L\(^{-1}\)) | Males    | —        | 0.38        | 0.38     | 0.37     |
|                             | Females  | —        | —           | —        | 0.38     |

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, MMEF: maximum mid-expiratory flow, PEF: peak expiratory flow

| Table 5. Correlation coefficients between nutritional markers and pulmonary functions in non-smokers (Spearman’s correlation) |
|-----------------------------------------------|
| Parameters                  | FVC (%) | FEV1 (%) | FEV1/FVC (%) | MMEF (%) | PEF (%) |
| Serum albumin (g.L\(^{-1}\)) | Males    | 0.54     | 0.49        | —        | 0.51     |
|                             | Females  | —        | 0.36        | 0.44     | 0.37     |

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, MMEF: maximum mid-expiratory flow, PEF: peak expiratory flow
is 10 pack-years for the development of COPD in most clinical trials [9]. Ekici et al. [10] demonstrated that biomass fuel exposure could cause chronic airway obstruction in our region. Possibly COPD due to biomass exposure can lead to different systemic effects than tobacco-induced COPD. This result, however, await confirmation in a large prospective study.

The effect of malnutrition on pulmonary function is mediated in part by its effect on respiratory muscles. Arora and Rochester [11] showed that nutritional depletion reduced respiratory muscle strength in patients without lung disease. On the other hand, skeletal muscle weakness is frequently observed in patients with COPD, and is associated with wasting of extremity fat-free mass [12]. Depletion of fat-free mass, indicating loss of muscle mass, plays a pivotal role in exercise tolerance [13]. In this study, we assessed serum creatine kinase levels to evaluate myocyte dysfunction. However, we did not find a correlation between this muscle-derived parameter and pulmonary functions because serum creatine kinase is not a specific marker for malnutrition.

In conclusion, nutritional depletion is associated with impaired pulmonary functions in COPD. When compared to controls, rising levels of BUN and serum creatinine suggest a protein catabolism in patients with COPD. This catabolic process appeared to be active only in male patients. Serum albumin concentration is more accurate parameter than BMI for assessing pulmonary dysfunction due to catabolic process in COPD. Weight maintenance in females may be due to a different aetiology of COPD.

Acknowledgments

No portion of this work supported by a foundation. The first author had primary responsibility for the study design. The patients’ data were collected with second author. Both of them had drafted the manuscript.

References

[1] Schols, A.M., Slangen, J., Volovics, L., and Wouters, E.F.: Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med., 157, 1791–1797, 1998.

[2] Landbo, C., Prescott, E., Lange, P., Vestbo, J., and Almdal, T.P.: Prognostic value of nutritional status in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med., 160, 1856–1861, 1999.

[3] Global Strategy for the diagnosis, management and prevention of COPD, NHLBI/WHO Workshop Report. Global initiative for COPD. National Institutes of Health, 2001.

[4] Quanjer, P.H., Tammeling, G.J., Cotes, J.E., Pedersen, O.F., Peslin, R., and Yernault, J.C.: Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, European community for steel and coal. Official statement of the European respiratory society. Eur. Respir. J., 16 Suppl, 5–40, 1993.

[5] Schols, A.M., Mostert, R., Soeters, P.B., Greve, L.H., and Wouters, E.F.: Nutritional state and exercise performance in patients with chronic obstructive lung disease. Thorax, 44, 937–941, 1989.

[6] Katsura, H., Ogata, M., and Kida, K.: Factors determining outcome in elderly patients with severe COPD on long-term domiciliary oxygen therapy. Monaldi Arch. Chest Dis., 56, 195–201, 2001.

[7] Hergence, G., Schulte, H., Assmann, G., and von Eckardstein, A.: Associations of obesity markers, insulin, and sex hormones with HDL-cholesterol levels in Turkish and German individuals. Atherosclerosis, 145, 147–156, 1999.

[8] Hellstrom, L., Wahrenberg, H., Hruska, K., Reynisdottir, S., and Arner, P.: Mechanisms behind gender differences in circulating leptin levels. J. Int. Med., 247, 457–462, 2000.

[9] Miravitlles, M., Fernandez, I., Guerrero, T., and Murio, C.: Development and results of a screening program for COPD in primary care. The PADC Project (Program for the Increase in the Diagnosis of COPD in Primary Care). Arch. Bronconeumol., 36, 500–505, 2000.

[10] Ekici, A., Ekici, M., Kurtipek, E., Akin, A., Arslan, M., Kara, T., Apaydin, Z., and Demir, S.: Obstructive airway diseases in women exposed to biomass smoke. Environ. Res., 99, 93–98, 2005.

[11] Arora, N.S. and Rochester, D.F.: Respiratory muscle strength and maximal voluntary ventilation in undernourished patients. Am. Rev. Respir. Dis., 126, 5–8, 1982.

[12] Engelen, M.P., Schols, A.M., Does, J.D., and Wouters, E.F.: Skeletal muscle weakness is associated with wasting of extremity fat-free mass but not with airflow obstruction in patients with chronic obstructive pulmonary disease. Am. J. Clin. Nutr., 71, 733–738, 2000.

[13] Wouters, E.F.: Nutrition and metabolism in COPD. Chest, 117, 274s–280s, 2000.