CLINICAL SCIENCE

Neurophysiological Aspects and their relationship to clinical and functional impairment in patients with Chronic Obstructive Pulmonary Disease

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OBJECTIVE: The purpose was to assess functional (balance L–L and A–P displacement, sit-to-stand test (SST) and Tinetti scale – balance and gait) and neurophysiological aspects (patellar and Achilles reflex and strength) relating these responses to the BODE Index.

INTRODUCTION: The neurophysiological alterations found in patients with chronic obstructive pulmonary disease (COPD) are associated with the severity of the disease. There is also involvement of peripheral muscle which, in combination with neurophysiological impairment, may further compromise the functional activity of these patients.

METHODS: A cross-sectional study design was used. Twenty-two patients with moderate to very severe COPD (>60 years) and 16 age-matched healthy volunteers served as the control group (CG). The subjects performed spirometry and several measures of static and dynamic balance, monosynaptic reflexes, peripheral muscle strength, SST and the 6-minute walk test.

RESULTS: The individuals with COPD had a reduced reflex response, 36.77 ± 3.23 ($p<0.05$) and 43.54 ± 6.60 ($p<0.05$), achieved a lower number repetitions on the SST 19.27 ± 3.88 ($p<0.05$), exhibited lesser peripheral muscle strength on the femoral quadriceps muscle, 24.98 ± 6.88 ($p<0.05$) and exhibited deficits in functional balance and gait on the Tinetti scale, 26.86 ± 1.69 ($p<0.05$), compared with the CG. The BODE Index demonstrated correlations with balance assessment (determined by the Tinetti scale), $r = 0.59$ ($p<0.05$) and the sit-to-stand test, $r = 0.78$ ($p<0.05$).

CONCLUSIONS: The individuals with COPD had functional and neurophysiological alterations in comparison with the control group. The BODE Index was correlated with the Tinetti scale and the SST. Both are functional tests, easy to administer, low cost and feasible, especially the SST. These results suggest a worse prognosis; however, more studies are needed to identify the causes of these changes and the repercussions that could result in their activities of daily living.

KEYWORDS: Chronic obstructive pulmonary disease; Neurophysiological aspects; BODE Index; EMG; Prognosis.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by obstruction in airflow;[1] however, COPD is a systemic illness. Lung impairment is only one of the symptoms, and mechanisms such as oxidative stress and inflammation may be involved in the development of the systemic effects. The skeletal musculature is affected, and there are alterations regarding the type of fiber and muscle mass, enzymatic metabolism and capillarization of blood vessels.[2–5]

Other abnormalities are seen in these patients and are related to neurophysiological aspects. Electromyography (EMG) is useful in the detection of abnormal electrical activity in muscles, in which a substantial reduction in the speed of the reflex response may correspond to a nerve conduction pathology, such as a peripheral neuropathy.[6,7]

Neurophysiological alterations, such as nerve conduction (monosynaptic reflex test) and strength, have been correlated with smoking, the severity of the disease, hypoxemia, age, hypercapnia and peak expiratory flow.[8] However, these aspects have not been compared with functional capacity and other predictors, such as the BODE Index (four factors are addressed: 1. Body mass index (BMI), calculated from the formula weight/height (kg/m^2); 2. Airflow obstruction, assessed from the FEV_1 (% predicted post-bronchodilator use) by means of spirometry; 3. Dyspnea scale, Modified Medical Research Council (MMRC) Dyspnea scale; 4. 6-minute walk test (6MWT), assessment of functional capacity as recommended by the American Thoracic Society (ATS)), described as a survival prognosis score for patients with COPD.[9]

The presence of neurophysiological alterations was first described by Appenzeller et al. in 1968.[10] Kayacan et al. found neurophysiological alterations in 93.8% of patients with COPD.[11] Jann et al. found a slight reduction in both nerve conduction speed and the range of action potential of the motor unit in chronic respiratory failure, thereby suggesting the occurrence of peripheral neuropathy.[12]

Functional alterations can be observed through simple tests such as the 6MWT, sit-to-stand test (SST) and others that measure balance, such as the Tinetti scale (balance and gait scale) and pressure plate (L–L and A–P displacement) and muscle strength.

The somatosensorial, visual and vestibular systems undergo changes during aging and may subsequently offer reduced or inappropriate feedback to the posture control centers. The association of these changes and illnesses such as COPD makes elderly individuals more susceptible to balance alterations.[13]

Butcher et al. investigated balance, mobility and coordination in patients with COPD and found significantly lower scores in the oxygen-dependent group. The authors point out that balance and coordination are important elements in the majority of activities of daily living and that the American College of Sports Medicine recommends the assessment and treatment of balance in patients with COPD.[14] Another study found a reduction in muscle strength, mobility and coordination in hypoxemic patients at rest.[15]

Peripheral muscle strength has been studied in the realm of pulmonary rehabilitation. However, O'Shea et al. suggest that further investigations should be carried out on the impact of strength on functional performance in individuals with COPD as well as the results of an increase in strength regarding an improvement in functional activity, including the measurement of balance.[16]

Other examinations have sought the same efficacy as the walk test, but in a smaller space, thereby facilitating their execution. One such examination is the SST. Ozalevli et al. compared both tests and concluded that the SST determines the functional condition of patients with moderate to severe COPD as well as the 6MWT, while offering lesser hemodynamic stress.[17]

We hypothesized that patients with COPD show a slowing of the monosynaptic reflexes and functional alterations compared with healthy individuals of similar age and that this may be associated with a worse prognosis assessed by the BODE Index.

The purpose of the present study was to assess static (pressure plate) and dynamic balance (Tinetti scale), monosynaptic reflexes, peripheral muscle strength and the SST, comparing elderly individuals with COPD with healthy elderly individuals, then to correlate these responses with a prognosis index of mortality, the BODE Index.

MATERIALS AND METHODS

Sample

After the statistical calculation of the sample, triage was performed of the patients with COPD at the Pneumology Clinic of the Santa Casa de Misericórdia de São Paulo (Brazil), from which 22 patients over 60 years of age with moderate to very severe COPD (FEV_1 ≤50% of predicted post-bronchodilator use) were selected.[18] The inclusion criteria were clinical stability for at least 4 weeks prior to the study and not having participated in any pulmonary rehabilitation program in the previous year. The second group of 16 healthy, but sedentary elderly individuals made up the control group (CG). All participants should be currently non-smokers and not have other associated comorbidities such as asthma and neurological diseases.

The study received approval from the ethics committee (no. 133742/2007) in Sao Paulo, Brazil. All participants were informed as to the objectives and procedures of the study and agreed to participate by signing terms of informed consent.

Procedure/protocol

Supplementary oxygen was used during the walk test if the patient exhibited a drop in $SatO_2$ >4% of the baseline value[19] or an accentuated drop with clinical signs indicating the use of supplementary oxygen.

Spirometry

Post-bronchodilator spirometry was performed according to ATS standards[20] at the Pulmonary Function Laboratory prior to the other evaluations. The relative predicted values were calculated considering the values described by Knudson et al.[21]

BODE Index evaluation

This index has scores ranging from 0 (best) to 10 (worst) and has a correlation with survival in COPD.[9,19] The following four factors are addressed: 1. Body mass index (BMI), calculated from the formula weight/height^2 (kg/m^2); 2. Airflow obstruction, assessed from the FEV_1 (% predicted post-bronchodilator use) by means of spirometry;[20,21] 3. Dyspnea scale, Modified Medical Research Council (MMRC) Dyspnea scale;[22] 4. 6-minute walk test (6MWT), assessment of functional capacity as recommended by the ATS.[23]

Evaluation tests for neurophysiological aspects

Electromyographic evaluation. An electromyograph (EMG System, Brazil, CS 800 AF) was used. The components of the signal acquisition system were connected to a signal conditioner module, in which the analogue signals amplified totaled a final gain of 1000. The signals were filtered through a bandpass filter from 10 Hz to 500 Hz. The four pairs of active, bipolar, differential surface electrodes with common rejection mode ratio of 80 dB were placed on the motor point of the Retus femoris (patellar reflex), Vastus lateralis, Tibialis anterior and Soleus (Achilles reflex), following the recommendations of the Project SENIAM.[24] The electromyographic signal was collected in two distinct situations – monosynaptic reflex and peripheral muscle strength (load cell).

Monosynaptic reflex test. This was performed using a neurological examination hammer adapted with a switch in the percussion area for the patellar and Achilles reflexes.[25]

Evaluation of peripheral muscle strength. With the patient seated, the knee was extended under resistance at maximal strength capacity – peak isometric contraction force of the right quadriceps was collected by means of the load cell in kg/force.[26]

Evaluation of static balance. The pressure plate (TeKScan; MatScan model; 0.50 × 0.60 cm) was used to analyze oscillations in pressure points in relation to speed as well as anterior–posterior and lateral–lateral displacement. After calibrating the system, each patient was instructed to remain in a static position on the platform, for 60 s with the head aligned, maintaining the distance between the feet similar to the distance between the shoulders.[27] While the patient remained in the orthostatic position for 60 s, data were collected at the center of pressure (COP is the point on a body where the total sum of a pressure field acts, causing a force and no moment about that point), and projected on the pressure platform.

Tinetti Scale – gait and balance. The Tinetti Scale was used for the assessment of gait as well as static and dynamic balance. This scale consists of 16 tasks, such as Sitting balance (without touching), Lift, Attempts to rise, Orthostatic balance, Rotate 360˚, Sit and Initiation of gait, Stride length and height, Step symmetry, Continuity of the steps, Posture during gait, analyzed through observations by the examiner (maximum of 28 points – being ''0'' with hesitation, ''1'' without a hesitation, and some items with a score of ''2'' points for better performance and without hesitation). Patients who achieved a score below 19 points are considered to be at high risk of falls.[28]

Sit-to-Stand test. A standard chair (height 46 cm) without armrests was used for this test. The patient was instructed to begin the movement, standing up from and sitting down on the chair with no support from the hands, repeating the procedure as many times as possible within a 1-min period at a patient-defined pace at which the participant felt safe and comfortable. The number of repetitions was recorded.[17]

Statistical analysis

Statistical analysis was performed using a specific software package (SPSS, version 16.0 for Windows). It was determined that 14 patients were required to yield 80% power ($\alpha = -0.05$) to detect a difference clinically important between the groups using a standard deviation of the latency time of monosynaptic reflexes, sit-to-stand test and strength. The Kolmogorov–Smirnov test was used, and normal distribution was determined for all data. As all data were parametric, the Student's t-test was used for the comparison of means between the COPD and CG. Person's correlation coefficient was used to determine the degree of association between two variables in the COPD group; $p<0.05$ was considered statistically significant.

RESULTS

Thirty-eight individuals participated in the study, distributed among two distinct groups: COPD (n = 22) and CG (n = 16) (Table 1). The groups were similar, with no statistically significant differences regarding age, weight and height ($p>0.05$). The BODE Index (total score) was not determined for the healthy individuals (Table 1). It can be seen in Table 1 that the CG had a mild degree of dyspnea, probably because they were elderly and sedentary.

Table 1 - Demographic characteristics, BODE Index and variables that make up the BODE Index (FEV_1, 6MWT, dyspnea and BMI) of the participants.

	COPD n = 22	CG n = 16
Male/female gender (n)	19/3	9/7
Age (years)	70 (±6.66)	68 (±6.56)
Weight (kg)	67.22 (± 2.41)	77.16 (±18.86)
Height (m)	1.62 (±0.06)	1.59 (±0.09)
BODE – total score	3.66 (±1.57)	–
BODE – variables:		
FEV_1 (% of predicted)	39.88 (±8.69)	130 (±28.78)*
6MWT (m)	415.04 (±94.01)	491.90 (±49.52)*
Dyspnea (MMRC)	2.18 (±0.90)	0.54 (±0.68)*
BMI (kg/m^2)	25.32 (±3.54)	30.08 (±6.00)*

FEV_1 = force expiratory volume in the 1st second; 6MWT = six-minute walk test; MMRC = modified Medical Research Council Dyspnea scale; BMI = body mass index.
Values are given as means and standard deviations.
*Student's t-test ($p<0.05$).

Evaluation of functional and neurophysiological aspects

Regarding the functional and neurophysiological aspects, there were statistically significant differences ($p<0.05$) between the groups regarding the majority of variables analyzed (Table 2). Thus, the CG differed significantly from the COPD group with a lower latency time regarding patellar and Achilles reflexes, better performance on the SST, with a greater number of repetitions, a greater value for peripheral muscle strength and Tinetti balance and gait scale.

Figures 1 and 2 illustrate statistically significant strong and moderate negative associations ($p<0.05$) for the Tinetti Scale and SST respectively. Correlations were weak for the other variables (Table 3).

DISCUSSION

The primary objective of the present study was to determine possible functional and neurophysiological alterations caused by COPD. As expected based on previous studies, individuals with COPD achieved worse results in comparison with the control group regarding the speed of patellar and Achilles nerve conduction, number of repetitions on the SST, peripheral muscle strength and also on the Tinetti scale.[8,11,12,17,18,29]

Butcher et al. state that differences encountered in balance, coordination and mobility between groups were related to the severity of the disease.[14] In the present study, no statistically significant differences were found between the groups regarding the platform – on which balance was assessed through by means of A–P and L–L displacement.

Table 2 - Means and respective standard deviations regarding neurophysiological and functional parameters.

	COPD n = 22	CG n = 16
Patellar reflex (ms)	36.77 (±3.23)	22.90 (±6.41)*
Achilles reflex (ms)	43.54 (±6.60)	19.74 (±6.99)*
L–L displacement (cm)	1.89 (±0.78)	1.81 (±0.76)
A–P displacement (cm)	3.07(±1.36)	2.75 (±0.58)
SST	19.27 (±3.88)	23.40 (±3.74)*
Strength mm (kg/f)	24.98 (±6.88)	33.00 (±5.52)*
Tinetti	26.86 (±1.69)	27.81 (±0.40)*

L–L = lateral–lateral; A–P = anterior–posterior; SST = sit-to-stand test (number of repetitions); Strength mm = muscle strength of quadriceps; Tinetti = Tinetti balance and gait scale.
*Student's t-test ($p<0.05$).

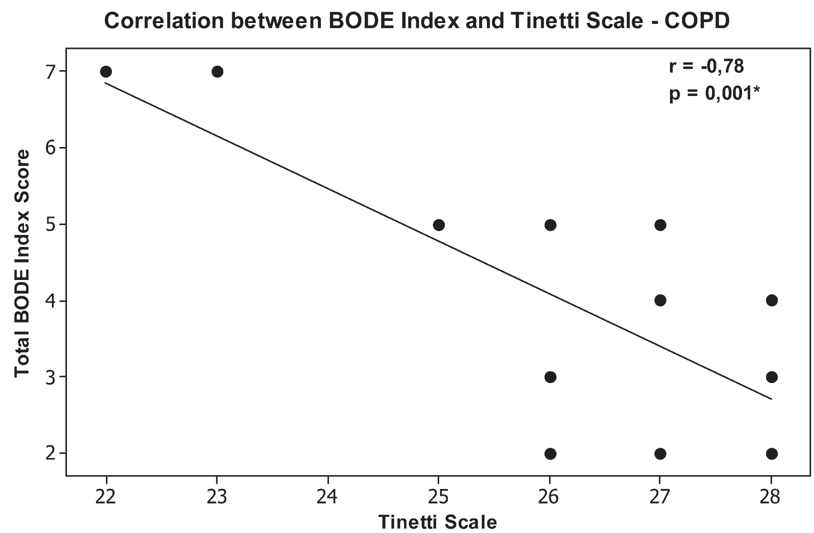

Figure 1 - Correlation between BODE Index and Tinetti Scale in the COPD group (*$p<0.05$).

Statistically significant differences were observed only on the Tinetti Scale also was associated with the BODE Index.

The latency time in the patellar and Achilles reflexes was statistically different between the CG and the COPD group. The speed of nerve conduction may be impaired by diseases secondary to the skeletal muscle, such as COPD.[6] Appenzeller et al. associated these alterations with COPD in malnourished patients.[10]

Kayacan et al. found neurophysiological alterations in 93.8% of patients with COPD, but reported that this high incidence may have been due to the severity of hypoxemia in the group studied in comparison with other studies in which the incidence ranged from 28% to 87%.[11] In the study, the authors concluded that smoking, airflow obstruction due to COPD and duration of the disease result in changes in gasometric values (hypoexemia, hypercapnia, respiratory acidosis), which can slow down the conduction speed of peripheral nerves and cause neurophysiological alterations in patients with COPD.

Agrawall et al. analyzed conduction speed, amplitude and latency of motor and sensory nerves.[9] The authors obtained a 16.7% prevalence of sensory impairment and associated the neuropathy with smoking, severity and duration of the disease.

We did not find any study that correlated alterations in nerve conduction speed in COPD with other variables, such as functional tests. In the present study, there was a weak correlation between latency time in the patellar and Achilles reflexes with the BODE Index. The correlation graphs for these variables demonstrate considerable variability in the sample (coefficient of variability 10.93–37.43%), in which individuals with the same BODE Index score had different reflex latency times.

The SST was one of the evaluations performed for the analysis of functional aspects. Ozalevli et al. compared the SST with the 6MWT and found that the SST determined functional capacity as well as the 6MWT, while offering less hemodynamic stress for patients with COPD.[17]

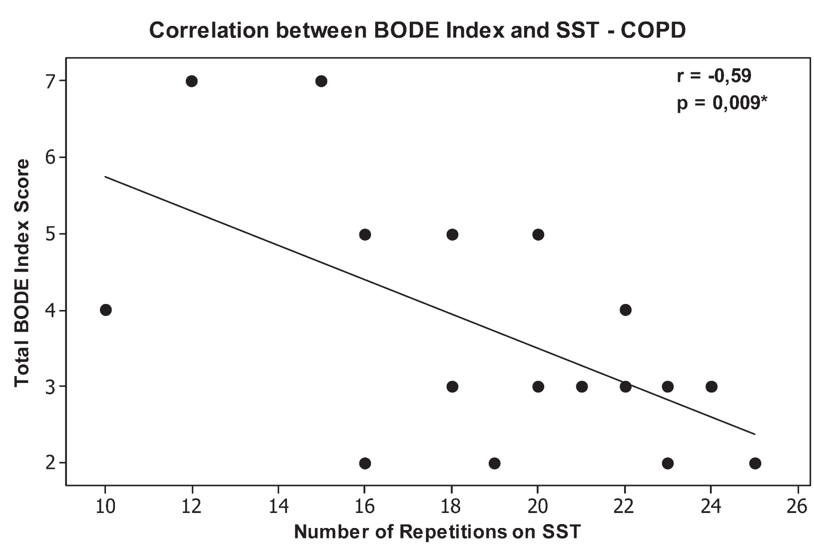

Figure 2 - Correlation between BODE Index and SST in the COPD group (*$p<0.05$).

Table 3 - Correlation between BODE score and neurophysiological and functional variables in the COPD group.

	Total BODE score (n = 22)
	r
Patellar reflex (ms)	0.03
Achilles reflex (ms)	0.22
L–L displacement (cm)	0.06
A–P displacement (cm)	0.11
SST	−0.59*
Strength mm (kg/f)	−0.26
Tinetti	−0.78*

r = Pearson's correlation coefficient; L–L = lateral–lateral; A–P = anterior–posterior.
*$p<0.05$.

Furthermore, the authors found that the test was correlated with both dyspnea and peripheral muscle strength, and not with FEV_1. We suggest that the SST can reflect a worse prognosis for individuals with COPD because of its statistically significant association with the BODE Index.

The peripheral muscle strength did differ between the COPD group and the CG. Peripheral muscle strength is compromised as a result of a reduction in the quadriceps cross-sectional area as well as a reduction in both types of muscle fibers, and has been indicated as the main predictor of mortality in COPD.[30] This suggests a significant impact of peripheral muscle structure and function on the general health status of patients with COPD.[19,29]

LIMITATIONS OF THE STUDY

Probably a larger sample could demonstrate differences regarding static balance assessed through the platform and show relatively stronger associations of neurophysiological variables with the BODE Index.

CONCLUSION

The individuals with COPD had functional and neurophysiological alterations in comparison with the control group. The BODE Index was correlated with the Tinetti scale and the SST. Both are functional tests, easy to administer, low cost and feasible, especially the SST. These results suggest a worse prognosis; however, more studies are needed to identify the causes of these changes and the repercussions that could result in their activities of daily living.

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