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PULMONARY REHABILITATION PROGRAM'S EFFICACY ON FLUCTUATIONS IN HEART RATE VARIABILITY AND PHYSICAL PERFORMANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Fluctuations in autonomic control tend to be examined in COPD patients through utilizing heart rate variability (HRV) in treatment. Our objective ended up being towards examines the existence of autonomic dysfunction and to evaluate the impact of a rehabilitation application. R-R intervals had been assessed for six minutes in 36 people (16 female; 20 male) earlier and after an inpatient pulmonary rehabilitation application which incorporated thirty minutes of respiratory training, chest wall mobilization, understanding managed breathing methods, inhalation, expectoration as well as personalized training. Ectopic beats had been eradicated.

Variables used: minimal pulse (p.min), average pulse (p.avg), maximal pulse (p.max), maximum-minimum pulse variation (p.max-p.min). Long-term continuous RR intervals (stda), standard deviation of instantaneous beat-to-beat variability (stdb), the number of pairs of adjacent NN intervals varying through more than fifty ms divided by the overall number of all NN intervals (pNN50).

Spectral evaluation supplied the low-frequency/high-frequency ratio (LF/HF). HRV revealed reduced p.max-p.min (15.78 ± 9.2 bpm), depressed dynamics (stda: 39.63 ± 33.5; stdb: 22.72 ± 35.84) with sympathetic overload (pNN50:3.17 ± 5.24, LF/HF: 169.52 ± 208.83), heavy parasympathetic modulation (pNN50:5.51 ± 5.59, LF/HF: 27.28 ± 13.12) in severe COPD patients. Rehabilitation resulted at decreased p.min-p.max (12.5 ± 9.01 bpm), over-depressed dynamics (stda: 34.56 ± 35.97; stdb: 20.88 ± 41.5) strong sympathetic overload (pNN50:3.33 ± 6.76, LF/HF: 252.01 ± 351.16). Patients revealed irregular physiological reaction in resting autonomic regulation. The rehabilitation lead in enhancement in general status, autonomic balance.

Keywords: *Heart rate variability; chronic obstructive pulmonary disease; pulmonary rehabilitation; cardiovascular function; sympathetic and parasympathetic nervous system.*

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INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is actually a complicated as well as heterogeneous medical disorder discovered in 6-8% of the populace. COPD patients feel practical and structural variations of the respiratory system that profoundly affect cardiovascular function. A number of aspects, such as abnormal autonomic control of cardiopulmonary function, might lead towards the enhancement of arrhythmias in these types of patients. Persistence of autonomic balance might become prominent in comprehending the pathophysiology of COPD and may be helpful clinically in the treatment of patients with COPD. The application of heart rate variability (HRV) to evaluate the danger of abrupt cardiac death and diabetic neuropathy is very well known (B, M and J, 2018).

The sympathetic and parasympathetic (autonomic) nervous systems innervate the heart and regulate the heart rate (HR). As illustrated in Figure 1 the HRV represents a physiological phenomenon that may be monitored and analyzed to determine the state of the nervous system that controls the heart. HRV data can be collected in relatively simple devices such as modern wrist computers. Although autonomic control of the cardiovascular system is also affected by baroreceptors, chemoreceptors, muscle afferents, local tissue metabolism, and circulating hormones (Figure 2). Critical adjustments are continually made to the cardiovascular system to meet the diverse demands of the musculature and heart (Bédard et al., 2016).

These dynamic adjustments in cardiac and peripheral vascular control, including their regulation by the autonomic nervous system (ANS), occur in part as a response to rapid alterations in heart rate and blood pressure. Though there are some reports on alterations in time-domain and frequency-domain heart rate variability in COPD patients, the information on HRV in patients with COPD has so far been conflicting.

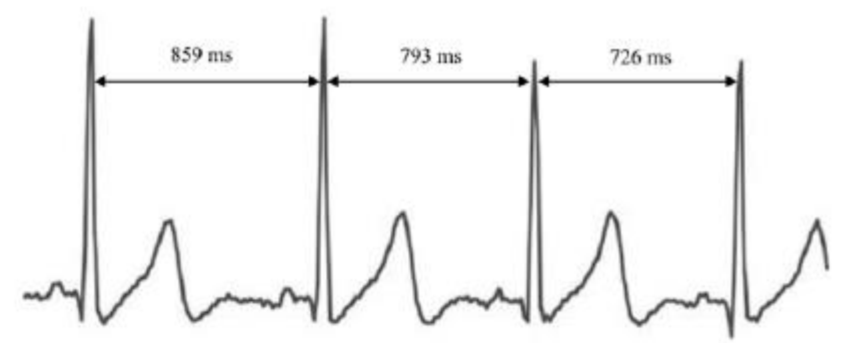

Figure 1: R-R variants of R-R distance for calculation of heart rate variability (HRV).

Source: (Bédard et al., 2016)

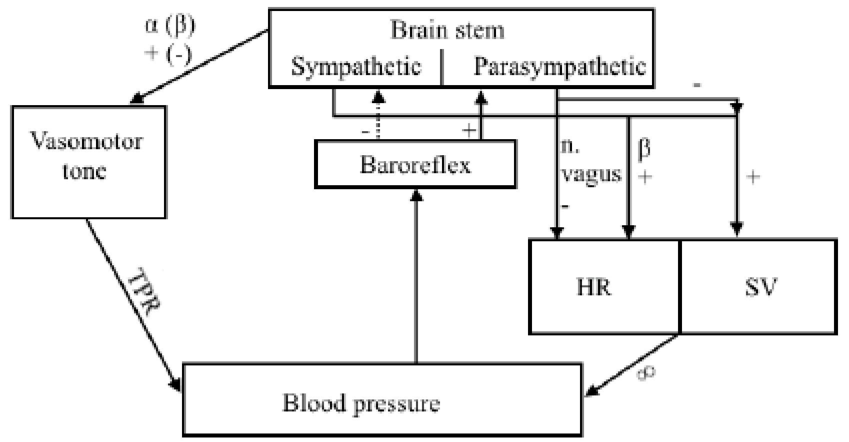

Figure 2: This model of HRV control illustrates independent actions of the vagal, α- and β- sympathetic system. The actions of these systems can be assessed by measuring heart rate variability, blood pressure variability, and the baroreflex mechanism. The parasympathetic nervous system is responsible for the bradycardia accompanying baroreceptor stimulation, and for the tachycardia accompanying baroreceptor deactivation, with the sympathetic nervous system also playing a minor role.

Source: (Bédard et al., 2016)

The basic objective of the study was to examine the autonomic dysfunction presence in patients with COPD by HRV and to analyze the impact of a four-week rehabilitation program.

MATERIALS AND METHODS:

Study subjects

In this study, 36 patients with COPD (age: 65.4 ±7.4 years (51-78); BMI: 26 ±5 kg/m2, male: female: 20:16) participated in this study. All of the patients provided written consent for the study in the Department of Pulmonary Rehabilitation. It was an observational study using the general management of the patient; it was a non-interventional study. Patients' characteristics are presented in Table 1.

Characteristics (n=36)	
Age (years)	65.47 ± 7.39
Male: female	20:16
BMI (kg/m^2)	27.99 ± 6.98
FEV$_1$ (%pred)	45.43 ± 20.2
Hypertension	32:36
Diabetes	11:30
Atherosclerosis	27:36
Pulmonary hypertension	9:36
BMI: body mass index; FEV$_1$: forced expiratory volume in the first second	

Table 1: Patients' characteristics.

Pulmonary function

As per the ATS/ERS specifications all patients underwent a postbronchodilator pulmonary function testing (Vmax 229 and Autobox 6200, Sensormedics), including spirometry measurements. COPD patients inhaled 400 µg salbutamol 20 minutes before testing.

Measurements

The 6 minutes walking distance was monitored at the corridor of our department. Before, during and after walking, oxygen saturation and heart rate were measured, and a modified Borg-scale was evaluated. The speed of walking was as fast as possible. The

6MWD was made according to the international guideline (Bédard et al., 2016).

Chest wall expansion:
CWE (Chest wall expansion) means the difference of chest circumferences between deep inspiration and expiration. It is measured at the level of processus xypho ideus.

Maximal inspiratory pressure:
While analyzing the "Maximal Inspiratory Pressure" in this study we used a special digital instrument. Power Breathe K1. The calculation of diaphragmatic force was based on the patients' height, weight, age and sex (very poor, poor, average, fair, good, very good). Patients were asked to inhale suddenly with maximal force after a maximal exhalation (Bédard et al., 2016).

Breathe holding time:
BHT or Breath holding time (BHT) displays the severity of COPD. After a maximal inhalation the subjects were asked to hold the breath as long as possible with closed nose and mouth without inhalation.

Parameters of HRV measurements
The most frequently utilized HRV variables in ANS assessment tend to be the frequency-domain, time-domain, and Poincare plot parameters. Whilst the nomenclature of the various dimensions is complicated, they express different means in order to search at the variability and distribution of the heart rate over time. The following time domain variables had been used: minimal pulse (p.min), average pulse (p.avg), maximal pulse (p.max) of the 6 minutes resting measurements, and maximum minimum pulse difference (p.max-p.min). For HRV analysis in the frequency domain; we used standard deviation of the long-term continuous RR intervals (stda), standard deviation of instantaneous beat-to-beat variability (stdb), and the number of pairs of adjacent NN intervals differing by more than 50 ms divided by the total number of all NN intervals (pNN50). Spectral analysis provided the low-frequency/high-frequency ratio (LF/HF) (Corbo et al., 2016).

Statistical analysis
Characteristics of patient, HRV analysis, lungs function, resting and exercise functional variables were compared by a paired *t*-test, a nonparametric sign test and a Wilcoxon test. Significance was accepted at the $p<0.05$ level. The distribution around the mean was expressed as ± SD in tables.

RESULTS:
Quality of life and functionality variables are presented before and after the rehabilitation program in Table 2. Pulmonary function did not show enhancement after the rehabilitation period (Table 2). Prominent alterations were detected in MIP, CWE, BHT, GS, 6MWD, CAT, mMRC (Table 2). The clinically prominent difference was accepted at $p<0.05$ level (Table 2). Eleven patients had severe arrhythmias (8 males. 3 females). And the ectopic beats were left out of the analysis. After the four-week rehabilitation, the ectopic beats ceased in all but 4 patients (3 males. 1 female).

Parameter	Before Treatment	After Treatment	p-value
FEV_1 (l)	44.00 ± 17.00	45.48 ± 17.05	n.s.
FVC (l)	73.59 ± 17.04	76.00 ± 13.84	n.s.
mMRC	1.97 ± 0.61	1.55 ± 0.56	<0.01
MIP (cm H_2O)	60.38 ± 16.74	69.17 ± 15.34	<0.001
CWE (cm)	3.31 ± 1.72	4.86 ± 2.17	<0.001
BHT (sec)	28.45 ± 9.94	35.69 ± 12.85	<0.001
GS (kg)	26.60 ± 9.92	28.89 ± 10.01	<0.001
6MWD (m)	347.45 ± 89.96	403.62 ± 112.07	<0.001
CAT	15.86 ± 8.07	10.24 ± 6.16	<0.001
FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; mMRC: modified Medical Research Council Dyspnoea Scale; MIP: maximal inspiratory pressure; CWE: chest wall expansion; BHT: breath holding time; GS: grip strength; 6MWD: 6-minute walking distance; CAT: COPD assessment test			

Table 2: Functional and quality of life marker parameters.

(Source: Corbo et al., 2016)

The minimal, average and maximal pulse decreased, as did maximum minimum pulse difference. These alterations represented only a marginal enhancement but prominent increment was shown in min-max pulse difference (Table 3).

Parameter	Before Treatment	After Treatment	p-value
p. min (bpm)	68.86 ± 15.53	66.53 ± 13.52	n.s.
p. avg (bpm)	76.11 ± 14.26	73.06 ± 13.04	n.s.
p. max (bpm)	84.5 ± 14.22	79.31 ± 13.46	n.s.
p. max- p. min (bpm)	15.78 ± 9.2	12.5 ± 9.01	<0.05
Stda	39.63 ± 33.5	34.56 ± 35.97	<0.05
Stdb	22.72 ± 35.84	20.88 ± 41.5	n.s.
pNN50 (%)	3.17 ± 5.24	3.33 ± 6.76	n.s.
LF/HF	169.52 ± 208.83	252.01 ± 351.16	n.s.
p. min: minimal pulse; p. avg: average pulse; p. max: maximal pulse; p. max- p. min: maximal-minimal pulse difference; stda: standard deviation of the long-term continuous RR intervals; stdb: standard deviation of instantaneous beat-to-beat variability; pNN50: the number of pairs of adjacent NN intervals differing by more than 50 ms divided by the total number of all NN intervals; LF/HF: spectral analysis of the low-frequency/high-frequency ratio			

Table 3: HRV results.

(Source: Corbo et al., 2016)

The standard deviation of the long-term continuous RR intervals and the standard deviation of instantaneous beat-to-beat variability have not shown a clear, prominent enhancement. Considering alterations on an individual level, these parameters show a narrowing tendency (Table 3). The decreasing trend in HRV was confirmed with the data found in our research on COPD patients (Table 3). We would like to underline that 12 patients were in a very severe parasympathetic overload. On average the four-week treatment resulted in no prominent enhancement in stda and stdb, but the ratio shifted into a sympathetic autonomic modulation. As a result of the four-week rehabilitation program, the number of pairs of adjacent NN intervals differing by more than 50 ms divided by the total number of all NN intervals and the spectral analysis of the low-frequency/high-frequency ratio represented enhancement, although these alterations did not achieve clinical significance (Table 3). These results show that four weeks of rehabilitation had a favorable impact on autonomic function and overall wellbeing.

DISCUSSION:

Pulmonary rehabilitation program resulted in a clear decrease in HRV data with a shift into sympathetic autonomic modulation. As a result of the rehabilitation program in our research, we did not find any correlation between HRV and functional markers. Although decreasing HRV is related to increased morbidity and mortality, we believe that the alterations in HRV were caused by higher sympathetic stimulation, contributing to improved health-related quality of life, autonomic function and overall wellbeing (Corbo et al., 2016).

Beat-to-beat variability in heart rate is a well-known phenomenon. Breathing, digestion, thermoregulation, but even breathing aritmia, extrusion, applying cold to the face, alterations in body position and stress all lead to alterations in the length of time between heartbeats; the heart rate variability (HRV) analysis measures these alterations. HRV has been used as a tool to analyze the behavior of the autonomic nervous system on the heart and to compare possible differences between healthy and unhealthy people. Decrease in HRV is related to increased morbidity and mortality. Other studies indicate that there are alterations in HRV in a list of cardiorespiratory disorders. COPD is associated with vascular remodeling that modifies the pulmonary circulation; this pathological mechanism is usually caused by hypoxia generated by the disease (Corbo et al., 2016).

Reis, et al. (2014) aimed to evaluate the influence of respiratory muscle strength on the magnitude of respiratory sinus arrhythmia. They assumed that respiratory muscle weakness negatively influences HRV during respiratory maneuvers in COPD. This study had a very similar protocol to ours: ECG signal and the instantaneous HR were obtained at rest in the supine position for 15 minutes while volunteers went through a respiratory sinus arrhythmia maneuver in the same position in the following order: For one

minute at rest with spontaneous breathing; for four minutes while performing the respiratory sinus arrhythmia maneuver; and for one minute at rest with spontaneous breathing (Diamantis et al., 2017).
As in our study, COPD patients represented evidence of impaired autonomic modulation of heart rate at rest and during respiratory sinus arrhythmia maneuver. Both COPD and congestive heart failure (CHF) patients show alterations in autonomic modulation of heart rate at rest and during respiratory sinusal arrhythmia maneuver (RSA-M) compared with apparently healthy individuals. COPD patients represented a reduction in sympathetic activity compared to the control group at rest. In our study we found similar results at the start of the four-week rehabilitation program: Lower min-max pulse difference, depressed Poincare plot proportion and LF/HF ratio (Diamantis et al., 2017).

The patients demonstrated reduced sympathetic activity; in 12 patients we found heavy parasympathetic overload. These findings indicate a possible relationship between regulatory alterations of the autonomic centers and the sensitivity of chemoreceptors or respiratory pattern characterized by periodic oscillations in COPD patients.

In another clinical study, it is found that decreased stda (SD1) and stdb (SD2) in COPD patients group while the stda/stdb ratio were similar between healthy and COPD patient groups. These findings are in line with ours and also suggest a reduced HRV in patients with COPD. The reduced stda index indicates a reduction in the activity of these individuals. Compared with healthy subjects he found a collapse in the values of stdb too in patients with COPD. This indicates an overall reduction in the autonomic modulation of these individuals, which suggests global autonomic damage in COPD. Our findings show similar tendencies; both stda and stdb show loss of variability, reduced vagal control and autonomic modulation. These effects are chronic as pulmonary rehabilitation program has not resulted in clinically prominent alterations in stda and stdb (Diamantis et al., 2017).

Researchers analyzed that HRV after two exercise programs in 40 COPD patients. Two groups were created: A high-intensity, endurance exercise group and low-intensity calisthenics, breathing exercise group. The three months of high-intensity exercise training proved to have an important role in post-training cardiac autonomic function enhancement in patients with COPD. This underlines the importance of further investigation of the sustained long-term effects of our four weeks rehabilitation program.

HRV is an important tool for assessing the autonomic nervous system (ANS), which has an important role in maintaining homeostasis. It is a clear predictor of the internal functions of the body, whether they are normal or pathological conditions. The correct usage can lead to characterization, evaluation and identification of problems in human development, growth and health (Gallucci et al., 2016).

CONCLUSION:

The statistics accumulated in this examine display the significance of HRV as a low-fee approach for early prognosis of cardiovascular diseases, deranged autonomic modulation, and loss of HRV concomitant with lung diseases on account that those illnesses tend to coexist, influencing the morbidity and mortality of those patients. It is well-known that COPD sufferers generally tend to have a declined HRV and, therefore, a deterioration of symptoms. Our study tried to reveal the importance and complexity of the pulmonary rehabilitation application, because it facilitates to minimize the outcomes that COPD can also have in patients.

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