This journal is the official publication of Bangladesh Society of Physiologists (BSP)
Web URL: www.banglajol.info/index.php/JBSP

Abstracted /indexed in Index Copernicus, Director of Open Access Journal, HINARI Index Medicus for South East Asia Region, Google Scholar, 12OR, infobse index, Open J gate, Cite factor, Scientific indexing services

pISSN-1983-1213; e-ISSN-2219-7508

Article

Received: 3rd February 2022
Accepted: 5th May 2022
DOI: https://doi.org/10.3329/jbsp.v17i1.63211

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Cite this article:
Tasnim SF, Begum S, Sultana S, Islam SR. Effect of physical exercise on non-linear parameters of heart rate variability in Chronic Obstructive pulmonary disease. J Bangladesh Soc Physiol 2022;17(1):6-13.

Effect of physical exercise on non-linear parameters of heart rate variability in Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is associated with autonomic nerve dysfunction. Nonlinear methods of heart rate variability (HRV) analysis have been gaining interest as a method of detecting changes in cardiac autonomic nerve function. Regular practice of physical exercise may cause improvement of this impaired autonomic nerve function. **Objectives:** To assess the effect of physical exercise on nonlinear measures of HRV analysis in male patients with COPD. **Methods:** This prospective interventional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka in 2018 on 60 diagnosed male COPD patients aged 40-75 years with disease duration of at least 5 years selected from the Department of Respiratory Medicine, BSMMU, Dhaka. Thirty patients underwent physical exercise (walking for 30 minute and pursed lip and diaphragmatic breathing 10 minuts)for 3 months in addition to standard treatment. Thirty (30) patients received only standard treatment for 3 months. For comparison, 30 age matched apparently healthy males were also enrolled. HRV data of all patients were recorded before and after 3 months of follow up. HRV data of healthy controls were recorded once at baseline. For assessing autonomic dysfunction, nonlinear parameters of HRV were recorded by Power Lab 8/35. For statistical analysis, paired sample t-test and independent sample

t-test were done as applicable. **Results:** SD1, SD2 and SD1/SD2 were found significantly lower in COPD patients compared to healthy controls at baseline. After 3 months of physical exercise, significant increment of these parameters occurred with a trend of improvement in cardiac autonomic nerve function in these patients. **Conclusion:** This study concluded that physical exercise can improve cardiac autonomic nerve dysfunction function in COPD patients.

Keywords: HRV, COVD, Physical Exercise, SD1, SD2

Introdction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of chronic morbidity and mortality and is the third leading cause of death worldwide, causing around 3.23 million deaths annually.[1] It is a highly prevalent and grossly underdiagnosed public health problem in Bangladesh affecting 4.32% of the population.[2]

Chronic Obstructive Pulmonary Disease is a disease state characterized by chronic airflow limitation that is not fully reversible & is associated with significant systemic manifestations[3], such as involvement of the cardiovascular system.

COPD is associated with a 2-4 fold increased risk of death from cardiovascular disease.[4] Previous studies reported autonomic dysfunction in COPD characterized by increased sympathetic and decreased parasympathetic activity, increasing risk of arrhythmias and sudden cardiac death.[5]

Several authors used HRV analysis to establish the presence of autonomic dysfunction in patients with COPD[7,8]. Of the various HRV parameters, nonlinear methods represent a potentially effective tool and Poincaré analysis is the most commonly used nonlinear measure.[8,9] In a Poincaré plot, two adjacent RR interval represent one point in the plot. The first RR interval is plotted in X axis and the next is plotted in the Y axis. By constructing an ellipse over the discrete distribution of Poincaré data, the HRV can be quantitatively analyzed.[10] Mostly, three indices are measured from these plots: the standard deviation of short-term R-R interval variability (minor axis of the cloud, SD1) representing parasympathetic activity, the standard deviation of the long-term R-R interval variability (major axis of the cloud, SD2) representing sympathetic activity & the axes ratio (SD1/SD2) representing sympathovagal balance.[10-12]

Regular physical exercise has been shown to positively modulate autonomic function both in healthy individuals and in those suffering from various clinical conditions including those with cardiac disease.[13-15]

Since respiratory muscle dysfunction plays an important role in exercise limitation for COPD patients, inspiratory muscle training is included in some pulmonary rehabilitation programs. Pursed lip breathing and diaphragmatic breathing are such techniques which increase parasympathetic activity.[16]

Several previous studies investigated the effect of physical exercise on lung function status and exercise tolerance in COPD patients.[16-19] Currently, however, only a few studies investigated the impact of such interventions on HRV in COPD patients. Of the available research, the HRV measures being tested are mainly the linear ones. Therefore, this study was designed

to investigate the effects of 3 months of a comprehensive exercise regimen (moderate physical exercise by walking along with breathing exercises in a domiciliary/home-based setting) on nonlinear measures of HRV in COPD patients. In addition, the results of this study may be used to create consciousness among physicians and patients that exercise performance in COPD patients not only improves lung function but also is beneficial for cardiovascular health.

Methods

Study design, setting and participants

This prospective interventional study was carried out in the year 2018 at the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka to observe the effect of physical exercise on cardiac autonomic nerve function by assessing nonlinear measures of HRV obtained by Poincare plot analysis.

In this study, 60 male diagnosed stable, Stage II or III COPD patients with duration of disease at least 5 years aged between 40 to 75 years participated. These patients were randomized equally into two groups of 30, one of which received standard pharmacologic therapy for COPD and the other half underwent physical exercise in addition to receiving medication. In addition, 30 age-sex matched healthy controls were also enrolled.

Patients were selected from the Department of Respiratory Medicine at BSMMU and controls were selected from among the general population.

All patients were studied at baseline and after 3 months of receiving only medication or a combination of medication and exercise. In addition, age-sex matched healthy controls were also studied.

Exclusion criteria

Patients were excluded from the study with history of exercise programs in the past year, unstable COPD, cardiovascular disease, renal disease, cerebrovascular disease, thyroid disorder, psychiatric disorders, musculoskeletal disorders as well as those on drugs that alter autonomic function.

Data collection procedure

On enrolment into the study, an informed written consent was taken from each subject. In preparation for the HRV test, subjects were given some instructions to follow the night before. They were advised to finish their meal by 9 pm, to remain free from any type of stress and not to take any sedatives or hypnotics.

On the morning of the test day, they were asked to have a light breakfast without tea or coffee and then attend the Autonomic Nerve Function Laboratory in the Department of Physiology, BSMMU at a time from 8-10 am.

A thorough physical examination was done including the recording of pulse, blood pressure, height, weight. BMI was also calculated. The subject was allowed to take rest for 15-20 minutes in a noise and temperature controlled laboratory environment. During this period, he was not even allowed to talk, eat or drink, to perform any physical or mental exertion or even to sleep.

ECG was recorded on lead II for 5 minutes by data acquisition device PowerLab 8/35 (AD Instruments, Australia).RR interval of ECG recordings were analysed by LabChart software which generated Poincare plot measures.

Intervention

The exercise regimen was explained to the subject at length; they were asked to walk at submaximal speed for 30 minutes, once daily for 3 months. Breathing exercises such as pursed lip and diaphragmatic breathing were also prescribed for 10 minutes each, once daily for 3 months. Breathing exercises were taught by a demonstration sessions. Each session lasted 20 minutes and was repeated until their performance

was deemed satisfactory. In addition, subjects were told to feel free to visit the Department of Physiology for further sessions, if they needed any.

Patients were monitored by occasional home visits and communication was also established 3-5 times per week via telephone for treatment compliance. Patients were advised to come for follow up after 3 months in the same lab in the same department.

Statistical analysis

Data was expressed as Mean ± SE and percentage. Statistical analysis was done by Paired sample 't' test and independent sample 't' test using SPSS version 16 and Microsoft Excel 2010. P value of < 0.05 was considered as being statistically significant.

Results

In this study, all COPD patients were similar to healthy control by age, waist hip ratio and MUAC. BMI was significantly lower in COPD patients than healthy controls. In addition, all these parameters were similar in exercise and non-exercise COPD patients (Table I).

Also in this study, at baseline, mean heart rate (HR), SBP and DBP were significantly higher ($p<0.05$) in COPD patients than those of healthy controls (Table II).

The nonlinear parameters SD1 and SD2 ($p<0.001$) and SD1/SD2 ($p<0.5$) were found significantly lower in COPD patients of both groups compared to control. No significant differences were observed in the above mentioned parameters between the two COPD groups (non-exercise and exercise) at baseline (Table II).

After three months, on follow up, COPD patients not performing exercise and receiving only medication did not show significant changes in the afore mentioned parameters as compared to their baseline values. On the other hand, after three months, those COPD patients performing exercise along with medication, values of mean HR ($p<0.01$), SBP ($p<0.01$), DBP ($p<0.001$) significantly decreased while nonlinear parameters such as SD1 ($p<0.01$), SD2 ($p<0.01$) and SD1/SD2 ($p<0.5$) significantly increased (Table III).

Again, post intervention values of all these parameters showed significant decrease in exercise COPD group compared to their non-exercise counterparts. After 3 months on follow-up, SD1 and SD2, despite increasing, were still significantly less than control. On the other hand, post intervention SD1/SD2 increased and reached closer to control value (Table IV).

Table I: Age, BMI, Waist hip ratio and MUAC of all group (N=82)

Parameters	Control (n=30)	Non exercise COPD (n=26)	Exercise COPD (n=26)
Age (years)	57.30±1.61	59.69±1.36	59.38±1.74
BMI (Kg/m^2)	22.74±0.56	21±0.51*	21.15±0.49*
Waist-hip ratio	0.94±0.005	0.95±0.009	0.95±0.011
MUAC (cm)	26.97±0.36	25.85±0.55	26.27±0.58

Data were expressed as mean± SE. Statistical analysis was done by independent sample t test. BMI=Body mass index, MUAC= Mid upper arm circumference. *p<0.05 (*non exercise and exercise COPD baseline vs Control baseline).

Table II: Baseline Mean heart rate, blood pressure and nonlinear measures in different groups (n=82)

Parameters	Control (n=30)	Non exercise COPD (n=26)	Exercise COPD (n=26)
Mean HR(b/min)	72.76±1.79	81.24±1.98**	79.13±2.66*
SBP(mm Hg)	115.5±1.18	120.6±1.58*	121.81±1.73*
DBP(mm Hg)	76.7±0.96	80.0±1.21*	80.58±1.25*
SD1	22.47±2.11	9.33±0.85***	8.2±0.64***
SD2	42.09±1.79	24.32±1.39***	22.1±1.55***
SD1/SD2	0.49±0.03	0.39±0.03*	0.39±0.02*

Data were expressed as mean ± SE. Statistical analysis was done by independent sample t test. HR-Heart rate, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, SD1-Standard deviation of short term RR interval variability, SD2-Standard deviation of long term RR interval variability, SD1/SD2 ratio= Ratio of short term and long term. RR interval variability. *p<0.05, **p<0.01, ***p<0.001 (*non exercise and exercise COPD baseline vs Control baseline).

Table III: Pre and post intervention values of mean HR and blood pressure and nonlinear measures in different groups (n=82)

Parameters	Non exercise COPD (n=26)		Exercise COPD (n=26)	
	Pre	Post	Pre	Post
Mean HR(b/min)	81.24±1.98	79.94±2.02	79.13±2.66	72.34±2.25**
SBP(mm Hg)	120.6±1.58	120.6±1.55	121.81±1.73	116.2±1.25**
DBP(mm Hg)	80.0±1.21	79.92±1.28	80.58±1.25	74.23±0.86***
SD1	9.33±0.85	10.68±0.96	8.2±0.64	14.85±2.15**
SD2	24.32±1.39	27.73±1.52	22.1±1.55	30.06±2.76**
SD1/SD2	0.39±0.03	0.39±0.04	0.39±0.02	0.48±0.04*

Data were expressed as mean ± SE. Statistical analysis was done by paired sample t test. SBP= Systolic blood pressure, DBP= Diastolic blood pressure, SD1= Standard deviation of short term RR interval variability, SD2=Standard deviation of long term RR interval variability, SD1/SD2 ratio= Ratio of short term and long term RR interval variability. ***p<0.001,**p<0.01, *p<0.05 (Post Exercise vs Pre Exercise).

Table IV: Post follow up values of mean HR, blood pressure and nonlinear measures in different groups (n=82)

Parameters	Control (n=30)	Non exercise COPD (n=26)	Exercise COPD (n=26)
Mean HR(b/min)	72.76±1.79	79.94±2.02	72.34±2.25*
SBP(mm Hg)	115.5±1.18	120.6±1.55	116.2±1.25*
DBP(mm Hg)	76.7±0.96	79.92±1.28	74.23±0.86***
SD1	22.47±2.11	10.68±0.96	14.85±2.15#
SD2	42.09±1.79	27.73±1.52	30.06±2.76###
SD1/SD2	0.49±0.03	0.39±0.04	0.48±0.04

Data were expressed as mean ± SE. Statistical analysis was done by independent sample t test. SBP= Systolic blood pressure, DBP= Diastolic blood pressure, SD1= Standard deviation of short term RR interval variability, SD2= Standard deviation of long term RR interval variability, SD1/SD2 ratio= Ratio of short term and long term RR interval variability. **p<0.01,*p<0.05 (*Exercise vs non Exercise); ###p<0.001 (#Exercise vs Control).

Discussion

Data of this study showed lower BMI in COPD patients compared to healthy control but similar BMI in both patient groups. Lower BMI in COPD patients were also reported by several studies, though their difference was not significant. Lower BMI of COPD patients might be related to muscle wasting and subsequent weight loss resulting from disuse, hypoxemia, malnutrition, oxidative stress and systemic inflammation.[20]

In this study, significantly higher resting pulse rate, SBP and DBP in patient groups agrees with other investigators reporting similar observations.[19,21] In COPD, the raised resting HR is an expression of the presence of sympathetic overactivity.[19] The raised BP in COPD is attributed to increased arterial stiffness irrespective of smoking history.[21]

After performance of the comprehensive exercise regimen for 3 months, the significant decrement of resting HR, SBP and DBP in the COPD group suggests improvement of cardiac autonomic nerve function (CANF) in these group of patients. In contrast, there was no improvement in CANF in patient group not performing exercise as seen by a non-significant change in HR, SBP and DBP. To conclude, it can be said that a combination exercise regimen is an effective means to improve CANF, but the improvement was not enough to restore parasympathetic activity to levels enough to attain normal CANF as the post intervention HR, SBP, DBP of exercise group is still not close to the control values.

In the current study, significantly lower values of SD1, SD2 and SD1/SD2 in the patient groups at baseline is suggestive of impaired autonomic modulation in COPD. Such findings were also found in other studies.[22]

Moreover, after 3 months of performing prescribed exercise regimen, there was a significant improvement of these parameters in COPD patients suggesting a shift towards an autonomic balance that is beneficial.[2,3]

On the other hand, no significant change was found in the aforementioned parameters in patients not performing PE suggesting continued impaired autonomic function in the absence of intervention.

Even though values of SD1 and SD2 improved after 3 months, the increase was not enough to reach close to healthy control values, but SD1/SD2 values reached close to control. This finding indicated that PE for 3 months may restore sympathovagal balance.

The improvement in sympathovagal balance found in this study may be the result of the combined beneficial effects of both physical as well as breathing exercises. Physical exercise induced improvement in sympathovagal balance may be linked to the fact that exercise remodels cardiorespiratory centers, and thereby reduces sympathetic and enhances parasympathetic (vagal) outflow.[24] Breathing exercises also cause improvement in sympathovagal balance by increasing vagal tone.[16,25-26]

Conclusion

Based on the results of this study it can be concluded that physical exercise along with breathing exercises may improve impaired autonomic function in COPD patients by increasing parasympathetic while decreasing sympathetic activity with the autonomic balance favouring parasympathetic dominance in such patients. So, a combination of walking and breathing exercise are effective measures to minimize the risk of cardiovascular disease in COPD patients.

Conflict of interest- None

Ethical approval-This study was approved by Institutional Review Board of BSMMU

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