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Analysis of cardiovascular system responses to forced vital capacity in COPD

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Análise das respostas do sistema cardiovascular ao teste de capacidade vital forçada na DPOC

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Abstract

Background: The forced vital capacity (FVC) test is routinely performed to evaluate pulmonary function in patients with chronic obstructive pulmonary disease (COPD). However, the influence of the FVC maneuver on the cardiovascular system of patients with COPD is poorly understood. **Objectives:** To analyze the behavior of heart rate (HR), blood pressure (BP) and heart rate variability (HRV) during the FVC test in COPD patients. **Methods:** Nineteen men with COPD (72±7 years, GOLD stage I=3, II=5, III=7 and IV=4 patients) performed the FVC test while having their HR monitored. HRV was assessed in time (rMSSD) and frequency domains (LF, HF and LF/HF) at rest, before and after the best FVC maneuver. BP was measured at rest, immediately before and at the end of the test, as well as 10 minutes after the end of the test. **Results:** At the beginning of the FVC maneuver, HR decreased (p<0.001) and then increased gradually until the end of the test (p<0.001). After the end of maneuver, HR continued to increase until it reached a peak (p<0.001), and then it fell quickly to below at-rest values (p<0.001) prior to returning to baseline. The BP and HRV indices did not change during the assessment. **Conclusion:** The FVC test influences the behavior of COPD patient HR without changing autonomic control or BP.

Keywords: chronic obstructive pulmonary disease; spirometry; vital capacity; heart rate; autonomic nervous system.

Resumo

Contextualização: O teste de capacidade vital forçada (CVF) é rotineiramente realizado na avaliação da função pulmonar de pacientes com doença pulmonar obstrutiva crônica (DPOC). Entretanto, permanece pouco compreendida a influência do teste de CVF sobre o sistema cardiovascular de pacientes com DPOC. **Objetivos:** Analisar o comportamento da frequência cardíaca (FC), pressão arterial (PA) e variabilidade da frequência cardíaca (VFC) no teste de CVF na DPOC. **Métodos:** Dezenove homens com DPOC (72 ± 7 anos, no estágio de gravidade GOLD I=3, II=5, III=7 e IV=4 pacientes) realizaram a manobra de CVF e tiveram sua FC monitorada durante todo o exame, e a VFC analisada nos domínios do tempo (rMSSD) e da frequência (BF, AF e BF/AF) durante o repouso, antes e após a melhor manobra de CVF. A PA foi analisada no repouso, imediatamente ao final da manobra de CVF e 10 minutos após o término de todos os testes. **Resultados:** Ao início da manobra de CVF, a FC reduziu (p<0,001) e, em seguida, aumentou progressivamente até o final do teste (p<0,001). Após término da manobra, a FC continuou a aumentar até atingir um pico (p<0,001) e depois caiu rapidamente a valores inferiores aos de repouso (p<0,001) e retornou ao seu valor basal. A PA e os índices da VFC não sofreram alterações nos períodos analisados. **Conclusão:** O teste de CVF influencia o comportamento da FC, sem alterar o seu controle autonômico, bem como a PA em pacientes com DPOC nos períodos analisados.

Palavras-chave: doença pulmonar obstrutiva crônica; espirometria; capacidade vital; frequência cardíaca; sistema nervoso autônomo.

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Introduction

Chronic obstructive pulmonary disease (COPD) is linked with high mortality and morbidity, is progressive and irreversible, and is characterized by obstruction of airflow[1]. Besides pulmonary involvement, cardiovascular events are commonly observed in this population[2], although the mechanisms responsible for these manifestations have not yet been fully elucidated. It is postulated that chronic systemic inflammation and/or cardiovascular autonomic neuropathy may be involved[3-6], since there is evidence that COPD patients present dysautonomia, sympathetic hyperactivity, reduced vagal tone and heart rate variability (HRV). These phenomena are highly associated with the appearance of arrhythmias and a risk of sudden death in this population[7-13].

An important method for diagnosing, classifying and following the progression of COPD is spirometry[1,14], which is considered the best means of assessing pulmonary function[15-17] and is routinely performed via the forced vital capacity (FVC) maneuver[18,19].

It is known that respiratory patterns exert great influence on the cardiovascular system[20,21] and that intrathoracic pressure, right atrium variations, changes in autonomic modulation and displacement of thoracic organs occur during forced expiratory maneuvers, which can induce the appearance of cardiac arrhythmias[5,22]. Much of the influence of breathing on the cardiovascular system occurs due to complex interaction with autonomic modulation of the cardiorespiratory system, which is generated by the close relationship between central neural control of these systems, the modulation of baroreceptors and chemoreceptors, changes in venous return and blood pressure (BP), and the activation of pulmonary and thoracic stretch receptors[23].

Due to cardiovascular involvement, the greater susceptibility of COPD patients to arrhythmic events, the significant influence of respiratory pattern on the cardiovascular system and the importance of spirometry in the clinical routine of these patients, the hypothesis was raised that the performance of forced respiratory maneuvers such as the FVC test influences cardiovascular system and autonomic cardiac control variables in this population. Thus, the aim of this study was to analyze heart rate (HR), blood pressure and heart rate variability in COPD patients undergoing FVC testing.

Methods

Study design

Cross-sectional observational study.

Subjects

A sample of 29 male patients with a clinical diagnosis of COPD who were undergoing treatment at the Center for Research and Care in Physical Therapy and Rehabilitation of the Universidade Estadual Paulista "Júlio Mesquita Filho" (UNESP), Presidente Prudente, SP, Brazil were selected.

The inclusion criteria were: COPD, a body mass index (BMI)<30 kg/m^2, the use of no medicine that might influence autonomic activity, no infections or inflammations of any kind, no metabolic disease or cardiopulmonary disorder that might interfere in cardiac autonomic control, and the ability to perform spirometry according to American Thoracic Society (ATS) criteria for acceptability and reproducibility[24]. Patients were required to have undergone outpatient medical treatment for at least the previous six months, to have been clinically stable for at least the previous 30 days and to have been using appropriate medication.

All procedures used in this study were approved by the Research Ethics Committee of the Faculdade de Ciências e Tecnologia (FCT), UNESP, Presidente Prudente, SP, Brazil (protocol nº 014/2005) and were in accordance with resolution 196/96 of The Ministry of Health. All volunteers were properly informed about the procedures and objectives of this study and, after having agreed, signed an informed consent form.

Method

In order to reduce the subjects' anxiety level during data collection sessions, the equipment was prepared and the environmental conditions controlled prior to their arrival, with a minimum of personnel circulating in the laboratory. All tests were carried out in the morning in order to avoid circadian influence, with the temperature maintained between 20 and 25ºC and the humidity between 50 and 60%.

Patients were instructed to avoid alcoholic beverages and stimulants such as coffee and tea, and to have had a light breakfast 2 hours before performing the protocol. Those who used maintenance medication (bronchodilators, mucolytics, anti-inflammatories, etc.) were also instructed to interrupt their use 12 hours before beginning the protocol.

On the assessment day, the volunteers met the researchers, were familiarized with the materials and were instructed again about the procedures to be performed. Anthropometric measurements were obtained following the methods of Lohman, Roche and Martorell[25]. Weight was measured on a digital balance (Plenna TIN 00139 MAXIM, São Paulo, Brazil) and height was measured with a stadiometer (ES 2020 - Sanny, São Paulo, Brazil). BMI was calculated according to the following formula: weight (kg)/height (m)^2.

Next, the transmitter belt was positioned over the patients' precordium region, and a Polar S810i heart rate receiver (Polar Electro, Kempele, Finland) was attached to the wrist. The patients then remained seated for 15 minutes in absolute rest, after which the FVC test was carried out. Between each test maneuver, the patients rested for at least 5 minutes after their HR had returned to baseline in order to stabilize it for the variability analysis.

Evaluation protocol

Spirometry

The FVC test was performed with a spirometer (MIR - Spirobank version 3.6, Rome, Italy) according to criteria established by the ATS[24], with predictive values based on Knudson et al.[26]. During the test, the volunteers were seated at 90º of hip flexion without posterior trunk support and with their arms relaxed and upright. Patients were instructed to perform two complete respiratory cycles at tidal volume followed by a deep inspiration until reaching total pulmonary capacity and then by an abrupt and continuous expiration until reaching residual volume. The test was carried out with a minimum of three and a maximum of eight repetitions.

Monitoring the cardiovascular system

Only the best curve of the pulmonary function test, which was chosen by the highest FVC value obtained among the reproducible curves, was used to analyze the behavior of the HR and HRV indices.

HR behavior was registered beat-by-beat during the entire experimental protocol with the Polar S810i frequency meter (Polar Electro, Kempele, Finland), which has been previously validated for capturing data for HRV analysis[27,28]. Data were collected at a sampling frequency of 1000 Hz and transferred to a computer through the Polar® interface via infrared signal. The QRS detection timing accuracy of the Polar® interface was set at 1 ms[29]. Data was recorded with Polar Precision Performance 3.0 software and displayed in a tachogram. The program identifies the QRS complexes, and the resulting signal is processed through a standard filter in the above-described equipment[30]. The RR intervals were manually edited, and areas with ectopic beats and artifacts were removed.

HRV analysis was performed on the following sections: a) the final 300s of the initial rest; b) 300s before the beginning of the best FVC test; and c) 300s after the return of HR to baseline value after the best FVC test. Only temporal series of more than 256 RR intervals were used for analysis[31].

The RR intervals were exported for analysis by HRV Analysis Software (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Finland)[32,33]. With this program, HRV

calculation was performed in the temporal and frequency domains. In the temporal domain, the rMSSD index was evaluated, which corresponds to the square root of the mean sum of the squared differences between adjacent normal RR intervals, registered in an time interval, divided by the number of RR intervals minus one, expressed in ms[34].

In the frequency domain, Fast Fourier transform (FFT) spectral analysis, a non-parametric method, was used. The spectral power was determined according to the Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology[31] as follows: a) high frequency (HF) was estimated between 0.15 and 0.40 Hz, b) low frequency (LF) was estimated between 0.04 and 0.15 Hz, and c) very low frequency (VLF) was estimated between 0.003 and 0.04 Hz. The LF/HF ratio was considered as a marker of sympatho-vagal balance[35]. The HF and BF values were given in absolute units (ms^2) and normalized units (un). The normalized unit was calculated as: HF or LF / (total spectral power - VLF) × 100.

BP was measured indirectly with an aneroid sphygmomanometer (Welch Allyn - Tycos, New York, USA) and a stethoscope (Littmann, Saint Paul, USA) immediately after the initial rest and 10 minutes after the completion of all FVC tests.

Statistical analysis

Data are expressed as mean and standard deviation. Normality was verified by the Kolmogorov-Smirnov test. Analysis of variance (ANOVA) for repeated measures with post-hoc Student-Newman-Keuls was used to compare data. The significance level was set at 5% for all tests. The program Sigma Stat 3.5 (SPSS Inc, USA) was used for statistical analysis.

The study power was calculated according to the number of analyzed volunteers and with a significance level of 5% (two tailed), thus guaranteeing a test power greater than 80% for detecting differences between variables.

Results

Of the 29 eligible patients, ten did not meet the inclusion criteria. With respect to the analyzed patients' comorbidities, two had a history of gout and two of sinusitis or typhoid fever. The anthropometric characteristics and pulmonary function of the 19 patients who concluded the study are expressed in Table 1.

To analyze the behavior of the cardiovascular system, the best FVC test was chosen because the comparison of HR and HRV index values revealed no differences between them, regardless of the number of tests performed (ANOVA, p≥0.05).

The predominant HR behavior during the FVC tests was initially a decrease (79%), followed by a progressive increase with oscillations (95%), and the highest value was reached after

the end of the maneuver (84%). The HR then decreased below the initial resting HR (58%) and later returned to baseline. One example of this behavior can be observed in Figure 1.

Table 2 shows the delta HR values obtained during the FVC maneuver in relation to initial HR. It was observed that at the beginning of the inspiratory phase of the FVC test, HR was reduced an average of 6.10±8.5 bpm (75.9±14.6 vs. 69.8±10.0 p<0.001) and then increased an average of 11.8±10.9 bpm until the end of the test, compared to the resting values (75.9±14.6 vs. 87.7±16.8; p<0.001).
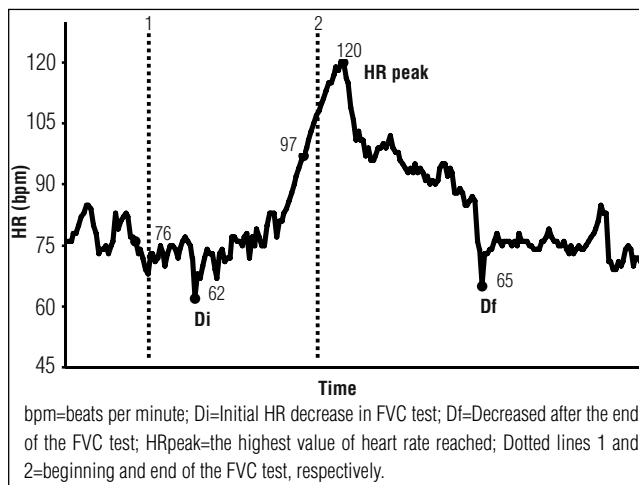

bpm=beats per minute; Di=Initial HR decrease in FVC test; Df=Decreased after the end of the FVC test; HRpeak=the highest value of heart rate reached; Dotted lines 1 and 2=beginning and end of the FVC test, respectively.

Figure 1. Example of heart rate (HR) behavior during FVC test in a COPD patient.

Table 1. Anthropometric characterization, pulmonary function and severity of 19 patients with COPD.

Anthropometric data	
Age (years)	72±8
Weight (kg)	62.4±15.4
Height (cm)	164.3±5.3
BMI (kg/m^2)	22.9±5.2
GOLD stage	
I / II / III / IV	3 / 5 / 7 / 4
Pulmonary Function	
FEV$_1$ (% of predicted value)	53.1±29.2
FVC (% of predicted value)	100.3±34.5
FEV$_1$/FVC	40.8±11.2

Data are expressed as mean ± standard deviation. BMI=body mass index; kg=kilogram; cm=centimeter; GOLD=Global Initiative for Obstructive Lung Disease; I=mild; II=moderate; III=severe; IV=very severe; FEV$_1$=forced expiratory volume in one second; FVC=forced vital capacity.

Even after the end of the FVC test, HR continued to increase an average of 21.3±13.9 bpm (75.9±14.6 vs. 97.2±21.8; p<0.001) and then reduce an average of 4.9±7.6 bpm (75.9±14.6 vs. 71.0±11.2, p <0.001) compared to resting values. The HR peak reached after the end of the FVC test was an average 9.5±8.3 bpm higher than obtained at the end of the test (87.7±16.8 vs. 97.2±21.8; p<0.001).

Despite an average increase of 6.3±20.1 mmHg (136.8±21.4 vs. 143.16±30.0) in systolic BP from the beginning to the end of the test and upon returning to baseline value after 10 minutes of rest (133.2±23.8 mmHg), there were no differences between the analyzed periods (p≥0.05). Diastolic BP remained unchanged during the periods analyzed (83.2±12.9 mmHg vs 85.3±13.9 mmHg vs 83.2±13.8 mmHg; p≥0.05).

The values of HRV indices can be observed in Table 3. There were no statistically significant differences in HRV indices in the temporal (rMSSD) or the frequency (LF, HF, and LF / HF ratio) domains between the analyzed periods (p≥0.05).

Discussion

The results of this study showed that the FVC test produced significant changes in COPD patient HR but did not change the BP or HRV index values during the analyzed periods.

The HR response to the FVC test was characterized by a reduction at the beginning of the inspiratory phase and by an increase at its end, with the HR peak being reached after the end of the test. The HR then decreased below resting HR values and subsequently returned to baseline value.

The initial reduction and subsequent increase in HR, which were observed in this study during the execution of the inspiratory phase of the FVC test, were similar to the pattern observed by Martins et al.[36] during the sustained inspiratory breath-holding maneuver.

It is postulated that the initial decrease in HR during the inspiratory phase of the test may be related, at least in part, to the activation of bronchopulmonary C-fibers. These fibers, when stimulated, produce reflex bradycardia and hypotension and may be related to the observed reduction in HR[37-39].

The subsequent progressive increase in HR may be attributed to the decrease in intrathoracic pressure that, consequently, produces a reduction in both the stroke volume of

Table 2. Values of heart rate delta obtained during the FVC maneuver in relation to initial heart rate.

	$\Delta HR_{QI} - HR_I$	$\Delta HR_F - HR_I$	$\Delta HR_P - HR_I$	$\Delta HR_{QF} - HR_I$
Mean±SD	-6.10±8.5	11.8±10.9	21.3±13.9	-4.9±7.6
Median	-2	10	17	-2
[CI95]	[-10.2 – -1.9]	[6.5 – 17.0]	[14.6 – 27.9]	[-8.6 – -1.2]
[Minimum – Maximum]	[-32 – 0]	[-10 – 38]	[3 – 60]	[-27 – 0]

SD=standard deviation; CI95=confidence interval of 95%; HR$_I$=initial heart rate (HR); HR$_{QI}$=initial HR decrease in FVC test; HR$_F$=HR at the end of the FVC test; HR$_P$=the highest HR value reached after finishing the FVC test; HR$_{QF}$=HR decreased after the end of the FVC test.

the left ventricle and in BP. This, in turn, would produce an increase in HR mediated by the activation of baroreceptors[40]. Another aspect to be considered is the stimulation of pulmonary stretch receptors induced by an increase in tidal volume during inspiration[41], which produces cardiac acceleration with subsequent tachycardia[38].

During the expiratory phase of the FVC test, the HR continued to increase gradually, which may be related to an increase in intrathoracic pressure and a decrease in venous return which, in turn, promotes changes in myocardial contractility, vasomotor tone and baroreflex control[42-44]. The reduction of vagal activity followed by the increase in sympathetic activity that occurs during expiration can also increase HR[42].

After the end of the FVC test, the HR continued to increase until it reached its highest value, which can be explained by the release of the expiratory effort[43,44]. During a sudden decrease in intrathoracic pressure, a large amount of blood is sequestered to the pulmonary vascular bed, which reduces the left ventricular filling and causes a rise in HR[44]. Moreover, the lower conduction velocity and the slow uptake and neutralization of noradrenaline by the sympathetic nervous system causes a gradual decay in the stimulus for increased HR, even after cessation of the expiratory effort[45].

The decrease in HR after the accomplishment of the FVC maneuver is similar to that observed by Marães et al.[43] after the release of strain during the Valsalva maneuver (phase IV), which they attributed to increased reflex vagal activity and inhibited sympathetic activity due to great stimulation of baroreceptors during the expiratory phase and which was followed by vasodilation and a reduction in HR to below baseline values[43].

Despite the influence of FVC maneuvers on HR fluctuations, the analysis of HRV indices showed no significant changes in the analyzed periods. This is similar to the results of Marães et al.[43], who analyzed HRV before and after the Valsalva maneuver in middle-aged individuals and observed no changes in the rMSSD index. The lack of change in HRV indices may be related to the short duration of the maneuver, the advanced age of the volunteers or the probable autonomic dysfunction present in these individuals. Paschoal, Petrelluzzi and Gonçalves[13] and Acharya et al.[46] observed that advancing age may reduce heart rate variability. Other studies have verified that COPD patients have depressed HRV when compared to healthy subjects matched by age and sex[7,8,47-49].

Furthermore, the FVC maneuver did not modify BP behavior during the analyzed periods. However, it should be pointed out that an indirect (auscultatory) method was used to measure BP, which, although reliable, did not allow measurement during the entire period of FVC performance, but only before and after the maneuver. Therefore, the possibility that

Table 3. HRV indices of COPD patients at rest, before and after the FVC maneuver.

	Rest	Before FVC	After FVC
Time domain			
rMSSD (ms)	17.6±11.3	22.5±18.5	23.4±30.4
Frequency domain			
LF (ms^2)	116.9±116.5	158.3±204.2	157.6±225.2
nu	72.3±14.9	66.9±16.4	70.8±13.7
HF (ms^2)	52.9±67.9	95.5±186.0	92.3±239.4
nu	27.7±14.9	33.1±16.4	29.2±13.7
LF/HF	4.0±3.4	3.6±4.3	3.6±3.2

rMSSD=square root of the mean of the squared differences between adjacent normal RR intervals recorded in a time interval, divided by the number of RR intervals minus one; HF=high frequency; LF=low frequency; nu=normalized unit; ms=milliseconds. (Repeated measures ANOVA with post-hoc Student-Newman-Keuls; p>0.05).

the test promoted changes in this variable during its execution should not be discarded.

The results of this study may benefit health professionals in the clinical setting, particularly physiotherapists, since according to COFFITO SECEX communication 123/9650 they are sufficiently qualified and specialized to perform spirometry.

Spirometry is considered the gold standard for diagnosing and evaluating COPD because it is the most reproducible, standardized and objective way of measuring airflow limitation[1]. Thus, understanding cardiovascular system responses to the FVC test, performed by spirometry, provides physical therapists with a better means of monitoring COPD patients during its performance.

A limitation of this study was the lack of a healthy control group, which might have clarified if the results were due solely to the FVC test or were influenced by the disease. Additionally, the inclusion of patients whose COPD severity varied widely could be considered another limiting factor, although most of our patients (63%) were classified according to GOLD as stage II and III. Some studies have indicated an association between low FEV1 and a high risk of cardiovascular disease[51,52], although Camillo et al.[53] observed no association between the degree of bronchial obstruction and the values of HRV indices.

Another aspect to be considered is the way that HR processes are analyzed during FVC. During the maneuver, the time necessary for completing the inspiratory and expiratory movements varies between subjects, which complicates the analysis of HR response over time, and thus it was decided only to describe what happened to it during the maneuver.

This study represents a description of cardiovascular system responses while performing the FVC maneuver, and the methodology allowed inferences to be made about the mechanisms involved in these responses. However, more studies investigating these mechanisms should be carried out.

The present results suggest that the FVC test significantly influences the HR behavior of COPD patients, but did not change autonomic modulation, according to HRV indices, or BP during the studied periods.

Acknowledgment

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