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Cardiorespiratory response of the Incremental Step Test in people with Chronic Obstructive Pulmonary Disease

Ana Leonor Paulino dos Santos Cardoso

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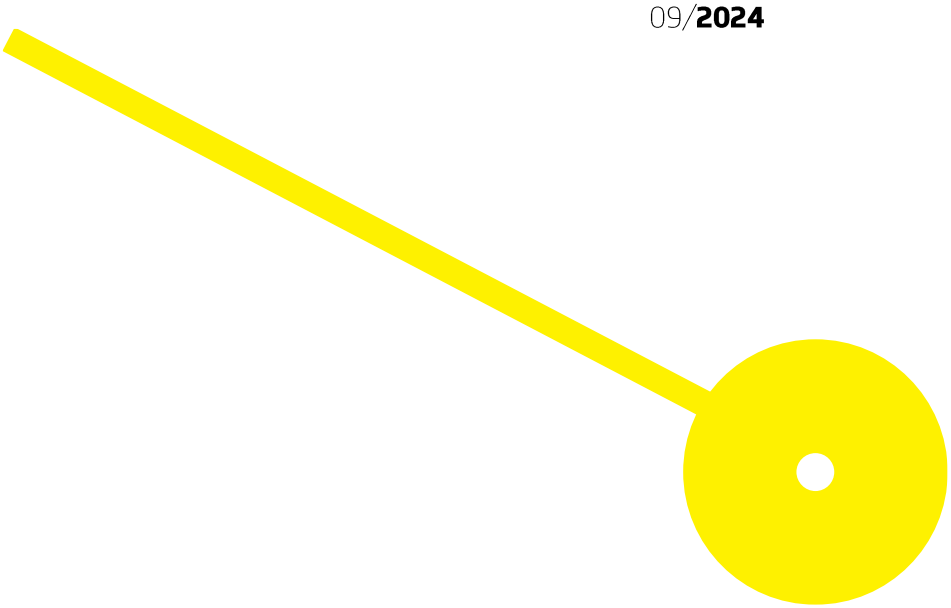

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Hospital Pulido Valente

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Resumo

Introdução: O Teste de Degrau Incremental (TDI) é uma ferramenta prática e barata na avaliação da capacidade de exercício em pessoas com Doença Pulmonar Obstrutiva Crónica (DPOC) e válida quando comparada com outros testes de campo, como o *Incremental Shuttle Walk Test*. Contudo, é fundamental comparar a resposta cardiorrespiratória do TDI, pela medição do VO_2 pico, com a do teste *gold standard*, a Prova de Esforço Cardiorrespiratória (PECR).

Objetivo: Avaliar a resposta cardiorrespiratória do TDI e compará-la com a PECR em indivíduos com DPOC.

Métodos: Realizou-se um estudo observacional analítico transversal em adultos com DPOC estável, recrutados no Hospital Pulido Valente, que realizaram a PECR e, até uma semana depois, o TDI duas vezes. Avaliou-se VO_2 pico, VCO_2, VE, RER, FC, FR e SpO_2 com um sistema portátil de análise de gases. A dispneia e a fadiga dos membros inferiores foram avaliadas através da Escala de Borg Modificada. A performance dos testes também foi avaliada. Testes de amostras emparelhadas (variáveis paramétricas), de Wilcoxon (variáveis não paramétricas), coeficientes de correlação de Pearson (variáveis normais) e Spearman (variáveis não normais) foram utilizados para a relação da resposta cardiorrespiratória entre os testes.

Resultados: Foram incluídos vinte adultos com DPOC (67. 8± 8. 62 anos; 12 homens; FEV1 = 56. 34± 15. 52 %). No esforço máximo, VO_2, VE, FR, FC e dispneia foram semelhantes entre os testes. VO_2 pico e a performance estão fortemente correlacionados nos dois testes (r= 0. 800, p< 0. 001 e p= 0. 816, p< 0. 001, respetivamente).

Conclusão: O TDI demonstrou uma resposta fisiológica máxima semelhante à PECR, sugerindo que deve ser considerado como máximo e limitado por sintomas em pessoas com DPOC.

Palavras-chave: Capacidade de Exercício Máxima; Testes de Campo; Prova de Esforço Cardiorrespiratória; VO_2 pico

Abstract

Introduction: Incremental Step Test (IST) is a feasible and inexpensive alternative to assess exercise capacity in people with Chronic Obstructive Pulmonary Disease (COPD) and valid when compared to other field tests, as the Incremental Shuttle Walk Test. However, it is necessary to compare the maximal cardiorespiratory response, through direct VO_2 peak measurement, during IST in comparison with Cardiopulmonary Exercise Testing (CPET).

Aim: Assess the cardiorespiratory response on IST and compare it with CPET in people with COPD.

Methods: A cross-sectional analytical observational study was conducted in adults with stable COPD, from Hospital Pulido Valente, they performed the CPET, followed by the IST twice within one week. VO_2 peak, VCO_2, VE, RER, HR, Bf and SpO_2 were monitored with a portable gas analysis system. Dyspnea and leg fatigue were assessed with Modified Borg Scale (mBorg) and performance was also assessed. Paired t-tests (parametric measures), Wilcoxon signed- rank sum tests (non-parametric measures) and Pearson (normal variables), Spearman (non-normal variables) correlation coefficients were used to evaluate within-group differences between tests.

Results: Twenty participants with COPD (67. 8± 8. 62 years; 12 men; FEV1 = 56. 34± 15. 52 %) were eligible. At peak effort, VO_2, VE, Bf, HR, and dyspnea were similar between tests. VO2 peak values and performance between tests were strongly correlated (r= 0. 800, p< 0.001 and p= 0. 816, p< 0. 001, respectively).

Conclusions: IST revealed a similar peak physiological response to CPET, suggesting that it should be considered as a maximal and symptom-limited test in people with COPD.

Keywords: Maximal Exercise Capacity, Cardiopulmonary Exercise Testing, VO_2 peak

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Table Index

Abbreviations

AT	Anaerobic Threshold
ATS	American Thoracic Society
BMI	Body Mass Index
BR	Breathing reserve
COPD	Chronic Obstructive Pulmonary Disease
CPET	Cardiopulmonary Exercise Testing
DGH	Directorate-General of Health
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in one second
FEV_1/FVC	Ratio Forced Expiratory Volume in one second/ Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HR	Heart Rate
IST	Incremental Step Test
mBorg	Modified Borg Dyspnoea Scale
mMRC	Modified Medical Research Council Scale
MVV	Maximal Voluntary Ventilation
OSAS	Obstructive Sleep Apnea Syndrome
$PaCO_2$	Carbon Dioxide Partial Pressure
PR	Pulmonary Rehabilitation
PROM	Patient- Reported Outcome Measures
RER	Respiratory Gas- Exchange Ratio
RPE	Rating Perception of Exertion
SpO_2	Peripheral Oxygen Saturation
VO_2peak	Peak Oxygen Uptake
VCO_2	Volume of Dioxide Carbon Production

1. Introduction

People with Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent and progressive airflow obstruction, dyspnea, and fatigue, which leads to reduced exercise capacity, with negative impact in maintaining their activities of daily living and their independence at home and/or outdoors(de Andrade et al., 2012). Thus, the assessment of exercise capacity is an important clinical measure of the functional status in people with COPD (Fletcher et al., 2013; Radtke et al., 2019; Tekerlek et al., 2020).

The gold standard test to assess the exercise capacity, through direct measurement of VO_2peak, is the Cardiopulmonary Exercise Testing (CPET) and it can be performed either in treadmill or in cycloergometer (Boutou et al., 2020; Garvey et al., 2016; Radtke et al., 2019). As a useful tool to recognize the physiological factors limiting the exercise, the CPET allows to quantify the pathology deficit, stablish therapeutic goals, assess the effects of an intervention, and provide prognostic data. This way, the CPET is very useful for the clinical decision, providing diagnostic and prognostic decisions, treatment selection and to assess the effects of a treatment and to follow-up (Radtke et al., 2019). Despite the degree of organ dysfunction assessment across multiple domains is superior (interrogating the cardiac, pulmonary, muscle, perception of dyspnea, and overall motivational function during exercise), the CPET is not always the privileged assessment method because of its high cost, sophisticated equipment and humans' resources needed. Thus, the field tests (e.g. the 6-minute Walk Test or the Incremental Shuttle Walk Test) are the most used alternatives, in people with COPD, but they not necessarily reflect the patient's ability to perform another type of exercise. It is possible that some patients do not complain of walking limitations but have limitations with stair climbing, as the latter is a more strenuous activity (Dal Corso et al., 2013; Stringer & Marciniuk, 2018). Nevertheless, the walking tests require big space, and it is not possible to set, in an objective way, the cause of the exercise limitation, because it has no measurements beyond heart rate and pulse oximetry (Boutou et al., 2020; Stringer & Marciniuk, 2018; Vilarinho et al., 2023). Maximal performance, inexpensive, simplicity and portability are the main advantages of incremental step tests over walking tests and stair-climbing tests, which facilitate the evaluation of exercise capacity in any environment (Dal Corso et al., 2013; de Andrade et al., 2012). Furthermore, the stepping skill requires little practice and represents a daily activity. The step tests with an externally paced profile proved to be more advantageous than the self-paced tests by providing a symptom-limited maximum response in people with COPD (Vilarinho et al., 2022).

The Incremental Step Test (IST) was developed for individuals with COPD to assess the cardiopulmonary capacity and based on the Incremental Shuttle Walk Test, because of its similarity to CPET in people with this disease (Vilarinho et al., 2022). The IST is composed of an incremental profile using a digital recording with a timed metronome step cadence and a twenty centimeters tall platform. The test consists of fifteen levels of step cadence, each of a one minute duration. The timed metronome sets the step cadence, which starts at ten steps per min and increases two steps per min every minute, with a step cadence maximum of thirty eight steps per min (level 15) (Vilarinho et al., 2023). The IST is already validated for the Portuguese adult population with COPD and the authors have found significant correlations between the number of steps in the IST and age and sex (Vilarinho et al., 2023).

The IST was developed to assess the cardiopulmonary capacity based on submaximal responses (Boutou et al., 2020; Vilarinho, Mendes, et al., 2021). This study aims to analyze whether IST can have a maximal cardiorespiratory response in people with COPD, similar to CPET, supporting its capacity to be considered a maximal and symptom-limited test. If confirmed, this will contribute to the application of a new alternative as the basis for individualized prescription of endurance training (step training) intensity in this population.

2. Methods

2.1. Study design and participants

A cross-sectional analytical observational study was designed to obtain measures of VO_2 peak on IST and CPET and to analyze the factors that may influence the performance in people with COPD in both tests, such as maximum heart rate, peripheral oxygen saturation (SpO_2), blood pressure, lung function (spirometry), symptoms (dyspnea and leg fatigue), anaerobic threshold (AT), respiratory gas- exchange ratio (RER), duration of the test and peak work rate (in Watts for the CPET and in number of steps for the IST). These outcomes were collected in a single assessment moment. The study was conducted between October 2023 and May 2024 and was defined following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

For this study were included adults, either male and female, with COPD, attending the Pulmonary Rehabilitation (PR) twice a week, at the Hospital Pulido Valente, in Lisbon. The participants were selected by the pneumologist and the physiotherapist and were considered eligible if they had an (1) established diagnosis of COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria – postbronchodilator Forced Expiratory Volume in the first second (FEV_1)/ Forced Vital Capacity ratio < 70% (GOLD 2023 REPORT, 2022), (2) were clinically stable over the past month (ie, no hospital admissions or exacerbations), (3) were undergoing pulmonary rehabilitation less than 3 weeks or being charged from the treatments for over 1 year. Participants were excluded in case of need of (1) supplementary oxygen during the effort, (2) presence of other significant pathologies (respiratory, cardiac, musculoskeletal or neuromuscular), (3) signs of cognitive impairment or significant risk of fall, (4) undergoing any other treatment besides usual care and (5) impossibility to meet the deadlines.

2.2. Ethical Considerations

Each participant was voluntary and was informed of the defined protocol and asked to sign the informed consent, with the necessary information about this study (name of the principal investigator, purpose of this study, data collection and its duration). After signing it, clinical data were collected (information about the pathology (GOLD criteria) and sociodemographic). The participants were free to leave the study at any moment, without any harm to the healthcare that was usually provided to them. It was clarified to each participant the potential and more frequent risks. In this case, the risks are mainly related to intense exercise practice because of the intensity

increase (on CPET and on IST), such as diaphoresis, peripheral desaturation, change in the dyspnoea and fatigue values, increase of heart rate and blood pressure, chest pain or leg cramps. The authors of this study were the only ones responsible for the data collection and its analysis. This study started after being accepted by the Ethical Committee of the Health Local Unit of Santa Maria, reference number 198, from December 2023 (Attachment 1).

3. Data Collection

The physiotherapist and the pneumologist had access to patients' information on the clinic software (Enterprise resource planning– EPR). After screening them, the physiotherapist selected those participants who were eligible according to the inclusion criteria and phoned them to voluntarily participate, firstly to perform the CPET and spirometry and, one week apart, the IST. Sociodemographic (age and sex) and clinical (medication, comorbidities, vital signs, peripheral oxygen saturation, body mass index, smoking status, lung function (spirometry), non-invasive ventilation) data were collected from all participants by the physiotherapist. On figure 1 it is represented the flow diagram of this study.

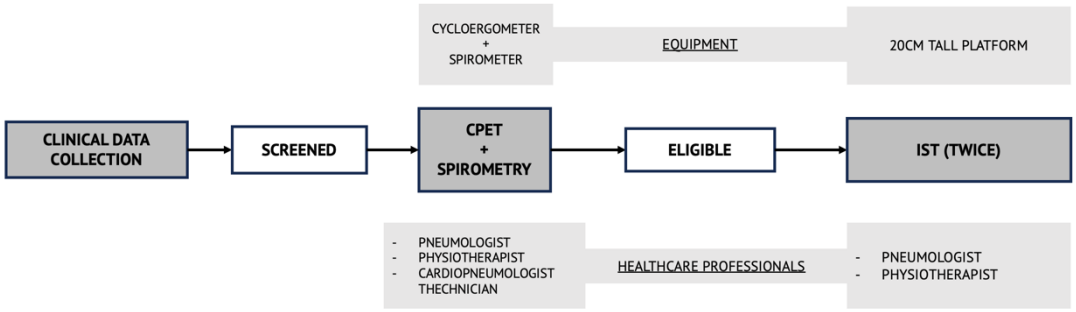

Figure 1– Flow diagram of study design. CPET: Cardiopulmonary Exercise Testing; IST: Incremental Step Test; FEV_1: Forced Expiratory Volume; FVC: Forced Vital Capacity

3.1. Patient-reported outcome measures (PROM)

According to GOLD criteria, the evaluation of respiratory symptoms is very important for the stratification of COPD severity, simultaneously with the assessment of the impact of those symptoms on quality of life, activities, and health status (GOLD 2023 REPORT, 2022). For this reason, the modified Medical Research Council (mMRC) scale, the COPD Assessment Test (CAT) questionnaire and the Modified Borg Dyspnea Scale (mBorg) were used(GOLD 2023 REPORT, 2022; Norma DGS DPOC, 2019).

3.1.1. Modified Medical Research Council

The mMRC scale is a 5 points (from 0 to 4) scale and measures breathlessness, according to its impact on daily activities. The lower the score the least impact breathlessness has on quality of life (GOLD 2023 REPORT, 2022; Jácome et al., 2019; Ribeiro et al., 2022) (Attachment 2).
Each participant filled this scale on the first contact with the physiotherapist.

3.1.2. COPD Assessment Test questionnaire

The CAT is an 8-item questionnaire that assesses health status and the impact of symptoms (cough, sputum, chest pain, breathlessness while climbing stairs, impact on daily activities, confidence on leaving home, sleep, and energy) on quality of life in patients with COPD. The score ranges from 0 to 40, the higher the score the greater the impact on patient's quality of life (GOLD 2023 REPORT, 2022; Norma DGS DPOC, 2019; Gupta et al., 2014)(Attachment 3).
Each participant filled this questionnaire on the first contact with the physiotherapist.

3.1.3. Modified Borg Dyspnea Scale

This scale is a 10 points (from 0 to 10) scale and measures the value of dyspnea and fatigue (Attachment 4) (GOLD 2023 REPORT, 2022; Jácome et al., 2019).
Dyspnea and fatigue values at rest and at peak effort (after either CPET or IST) were assessed.

3. 2. Lung function – Spirometry

Spirometry was assessed with a calibrated medical spirometer device (Vyntus SPIRO PC Spirometer from Vyaire Medical Inc company, Mettawa, Illinois, United States of America, and Vyaire Medical GmbH company, Hoechberg Germany) connected to Vyntus CPX, providing the analysis of the end of test criteria and the curves morphology to allow, in real time, setting the acceptability and reliability. The spirometry assesses the volume of air moved into or out of the lungs, in absolute value or according to time (volumes and flow, respectively), and compares these data with reference values (Oliveira et al., n.d.). It was needed the presence of a cardiopneumologist technician, a pneumologist and the physiotherapist.

3. 3. Cardiopulmonary Exercise Testing

For this test it was necessary the presence of a cardiopneumologist technician, a pneumologist and the physiotherapist. Before the CPET, each participant became aware of the project, the purpose of the study, and signed the informed consent (Attachment 5).

It was used the Vyntus CPX equipment, which includes automatic volume and gas calibration, digital volume transducer (through a facemask), ear oximeter, 12 derivations for the assessment and record of electrocardiographic trace, and, lastly, the cycloergometer model VIASPRINT 200 P, from Vyaire Medical Inc company, Mettawa, Illinois, United States of America, and Vyaire Medical GmbH company, Hoechberg Germany.

Thereafter, each participant performed the CPET on cycloergometer and was informed that it may finish at any time, by own choice, without any harm, however they were advised to achieve their very best effort to get more accurate data, which means effort was discontinued only in the event of limiting symptoms (chest pain, intolerable dyspnea, leg fatigue, diaphoresis and a pale or ashen appearance). The work-rate was continuously increased in a linear ramp pattern (10–15 Watts per minute) and was individually selected according to subject's regular physical activity, fitness, reported dyspnea in daily life and resting FEV_1 (Radtke et al., 2019). Each participant was monitored and watched by the medical team for the assessment of the vital sings: blood pressure (measured by an electric sphygmomanometer), heart rate and peripheral oxygen saturation (measured by ear oximeter), electrocardiograph trace (assessed by a 12- derivations electrocardiogram) and peak oxygen uptake (measured by face mask) (Radtke et al., 2019). The cardiopneumologist technician was also responsible to instruct and give feedback about the cadence (60 rotations per minute (rpm), approximately) (Glaab & Taube, 2022).The physiotherapist and the pneumologist supervised and monitored the vital signs (peripheral oxygen saturation, blood pressure and electrocardiograph trace) and measured the dyspnea and fatigue at rest and at peak effort, with mBorg scale. The stopping criteria was peripheral oxygen saturation $\leqslant$ 85%, requested by the participant, inability to maintain the cadence or presence of symptoms ("ATS/ACCP Statement on Cardiopulmonary Exercise Testing.," 2003).

Each participant was free to leave as soon as the heart rate and blood pressure reached the basal values (Radtke et al., 2019).

3.4. Incremental Step Test

For this test it was necessary the presence of the pneumologist and the physiotherapist. Before this test, each participant was asked to sign the informed consent (Attachment 6), where it was described the purpose and characteristics of the study. Each participant was informed about the risks related to maximal effort, which means effort was discontinued only in the event of limiting symptoms (chest pain, intolerable dyspnea, leg fatigue, diaphoresis and a pale or ashen appearance). Then, they were informed, once again, that this test may end at any time, by own choice, without any harm, however they were also motivated to achieve their very best effort to get more accurate data.

It was required, once again, the Vyntus CPX equipment and a 20cm height platform (90cm length, 35cm width), model Step of Cardio Training 500, Domyos.

Data at rest were collected such as peripheral oxygen saturation, blood pressure, heart rate and dyspnea and fatigue values, using the mBorg.

During this test, the pneumologist observed and assessed the vital sings: blood pressure (measured by an electric sphygmomanometer), heart rate and peripheral oxygen saturation (measured by ear oximeter), electrocardiograph trace (assessed by a 12– derivations electrocardiogram) and peak oxygen uptake (measured by face mask) (Radtke et al., 2019) .The physiotherapist watched the patient and kept count of the number of steps as the participant completes them, throughout the duration of the test. One step is considered when both feet step up and step down the platform. In case of imbalance, the use of a handrail was allowed if the participant intended to. The stopping criteria was inability to maintain the required step cadence for ten seconds, requested by the participant, peripheral oxygen saturation $\leq$ 85% or reported symptoms (chest pain, intolerable dyspnoea, leg cramps, diaphoresis and a pale or ashen appearance) (Vilarinho et al., 2023).

As soon as this test ended, the assessor recorded the total number of steps and the maximal step cadence performed, the dyspnea and fatigue values at peak effort, according to the last completed level, and duration of the test (Attachment 7).

4. Statistical analysis

Statistical analysis was performed using the SPSS Statistics software program, version 29.0. The level of significance was set at 0.05. Continuous variables were tested for normality using the Shapiro–Wilk test, because the sample size was inferior to 50 participants. For descriptive statistics, data were presented by mean ± standard deviation (for which normality was assumed), median and percentiles (for which normality was not assumed), minimum, maximum and frequencies (percentage).

Paired t-tests, for parametric measures, and Wilcoxon signed- rank sum tests, for non-parametric measures, were used to evaluate within-group differences between CPET and IST. We calculated the Pearson correlation coefficients to assess the relationship between VO_2 peak and other variables for which normality was assumed. For variables for which normality was not assumed, we calculated the Spearman correlation coefficient, as the correlation between the number of steps and work rate on IST and CPET. The strength of correlations was analyzed according to British Medical Journal guidelines: significant correlation coefficients of 0–0.19 were classified as very weak, 0.2–0.39 as weak, 0.4–0.59 as moderate, 0.6- 0.79 as strong and 0.8–1.0 as very strong (The British Medical Journal, n.d.).

Peripheral desaturation was considered when inferior to 85% and/or $\Delta SpO2 \geq 4\%$ ("ATS/ACCP Statement on Cardiopulmonary Exercise Testing.," 2003; Aviragee et al., 2017b).

5. Results

5.1. Participants' characteristics

In total, ninety individuals were screened from the PR at the Pulido Valente Hospital, but 57 individuals were excluded due to need of supplementary oxygen (14 participants), undergoing pulmonary rehabilitation longer than 3 weeks (19 participants), no COPD diagnosis (1 participant), significant risk of fall (2 participants) and/ or significant comorbidities (21 participants). On figure 2 is shown the flow diagram of participants through the study.

Therefore, twenty individuals participated in this study (12 males; minimum age 48 years and maximum age 81 years; body mass index 25.74 ± 1.03 kg/m^2). Half of the participants were classified as overweighted. All participants filled the mMRC scale and the CAT questionnaire, corresponding to 1 [1; 1.75] and 13.5± 6.72, respectively. Table 1 shows the participants' characteristics, but more detailed information is shown on Attachment 8.

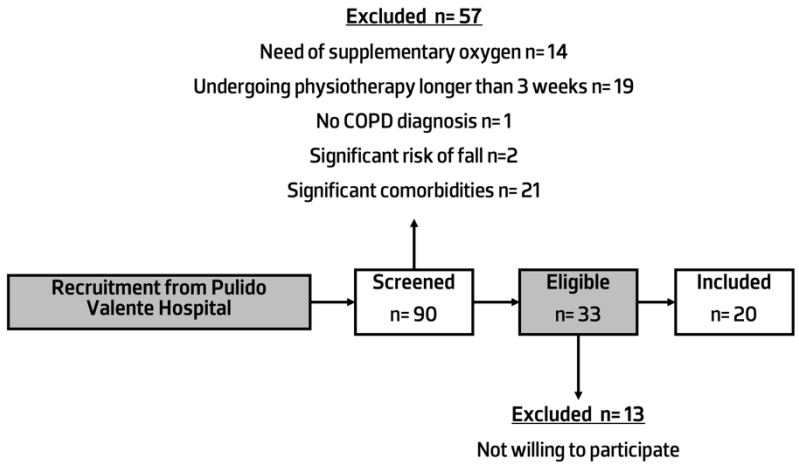

Figure 2– Flow diagram of participants throughout the study. COPD: Chronic Obstructive Pulmonary Disease

Table 1 – Participants' baseline characteristics

Variables	Total sample (n=20)
Age (years)	67.8 ± 8.6
Sex, male (%)	12 (60)
Body weight (kg)	69.79 ± 3.39
Height (m)	1.64 ± 0.02
BMI classification, n (%)	
Underweight	2 (10)

Normal weight	6 (30)
Pre-obesity	7 (35)
Obesity class I	3 (15)
Smoking status, n (%)	
Never	3 (15)
Current	4 (20)
Former	13 (65)
mMRC (total score), M [P25–P75]	1 [1; 1.75]
CAT (total score)	13.5 ± 6.72
FEV_1, (% predicted)	56.34 ± 15.52
FEV_1/ FVC, (%)	51.36 ± 11.28
GOLD Stages, n (%)	
GOLD I	2 (10)
GOLD II	12 (60)
GOLD III	5 (25)
GOLD IV	1 (5)
GOLD Group, n (%)	
A	9 (45)
B	7 (35)
E	4 (20)
Respiratory Comorbidities, n (%)	
Hypoxemic Respiratory Failure	2 (10)
Bronchiectasis	7 (35)
Asthma	4 (20)
Lung Adenocarcinoma	1 (5)
Comorbidities, n (%)	
Cardiac Disease	5 (25)
Arrythmia	1 (5)
Hypertension	8 (40)
Diabetes	1 (5)
Musculoskeletal Pathologies	5 (25)

Obstructive Sleep Apnea Syndrome	2 (10)
Long Term Oxygen Therapy, n (%)	0 (0)
Non-Invasive Ventilation, n (%)	3 (15)
Physical Activity, n (%)	
Sufficiently active	8 (40)
Insufficiently active	12 (60)

The values are expressed as mean ± standard deviation unless otherwise stated. Abbreviations: BMI – Body Mass Index; mMRC – modified Medical Research Council Dyspnea Scale; M – median; CAT – COPD Assessment Test; FEV_1 – forced expiratory volume in the first second; FVC – forced vital capacity.

All participants were able to successfully complete the IST (twice) and CPET without any adverse events. Both tests were stopped by the participant's demand when disproportionate symptoms were perceived to the effort.

5.2. Comparison and correlation between peak cardiorespiratory variables in IST and CPET

On table 2 are presented the peak cardiorespiratory response on IST and on CPET.

No significant differences were found between tests on the VO_2 peak.

The correlation between VO_2 peak on IST showed a significant positive and very strong correlation with the VO_2 peak on CPET ($\rho = 0.800$, $p < 0.001$).

The VCO_2, RER and BR were lower and significantly different on IST. The VE, B_f and HR were also lower, but no significant differences were found among tests.

The correlation between the VCO_2, on IST and on CPET, and the VE, on IST and on CPET, was strongly significant and positive ($\rho = 0.864$, $p<0.001$ and $\rho = 0.0837$, $p<0.001$, respectively). The correlation between B_f, on IST and on CPET, and HR, on IST and on CPET, was significantly positive and very strong ($\rho = 0.738$, $p<0.001$ and $\rho = 0.917$, $p<0.001$, respectively).

The comparison between difference saturation peak exercise and saturation at rest was greater on the IST than on CPET and significant differences were found among tests (showed on table 2). In fact, fifteen participants (75%) presented a negative difference on peripheral oxygen saturation on the IST while only half of the participants (50%) presented a negative difference on peripheral oxygen saturation on the CPET. Furthermore, on IST, three (15%) participants presented a peak exercise saturation below 88% and one (5%) participant presented 85% peak exercise saturation. On the CPET, the lowest peripheral oxygen saturation, at peak exercise, was 91%,

however the results showed that saturation at peak exercise was greater than 96% on seventeen (85%) participants.

5.3. Comparison and correlation between performance in IST and in CPET

No significant differences were found between performance among tests (showed on table 2).

The correlation between performance in IST showed a significant positive and very strong correlation with the performance in CPET ($r = 0.816$, $p < 0.001$).

Table 2 – Comparison of cardiorespiratory variables on IST and CPET

Variables	IST	CPET	p value
Duration	319.50 [202.25; 371.25]	390 [360; 433.5]	<0.001
Workrate (steps, watts)	60.50 [46; 81.50]	72 [43.50; 91]	0.073
Peak cardiorespiratory variables			
VO_2, mL/ Kg/ min	15.55 ± 3.36	14.65 ± 3.33	0.073
VCO_2, mL/ Kg/ min	14.90 ± 3.61	15.87 ± 3.71	0.035 *
RER	0.94 ± 0.09	1.07 ± 0.11	<0.001 *
VE, mL/ min	41.25 ± 11.56	44.15 ± 12.73	0.080
BR, %	91.41 [73.44; 101.1]	100.76 [78.44; 110.46]	0.010 *
B_f, bpm	34.60 ± 6.31	35.10 ± 6.32	0.630
HR, bpm/ min	122.25 ± 21.25	124.10 ± 22.82	0.376
Δ-SpO_2, %	-2.50 [-7; - 0.25)]	0.50 [-2; 1]	0.002 *

The values are expressed as mean ± standard deviation unless otherwise stated. Abbreviations: VO_2 – peak oxygen uptake; VCO_2 – carbon dioxide production; RER - respiratory exchange ratio; VE – pulmonary ventilation; BR – breathing reserve; B_f – breathing frequency; HR – maximal heart rate; Δ-SpO_2 – saturation peak exercise- saturation rest; Δ- Dyspnea – dyspnea peak exercise- dyspnea rest; Δ- Leg fatigue – leg fatigue peak exercise- leg fatigue rest

*A p value <0.05 was considered significant

5.4. Comparison and correlation between symptoms in IST and CPET

Table 3 shows the comparison between dyspnea at peak exercise and at rest and the comparison between leg fatigue at peak exercise and at rest on both tests.

5.4.1. Dyspnea

The difference between dyspnea at peak exercise and at rest was greater on IST than on the CPET but no significant differences were found among tests.

On IST, the participants have scored dyspnea up to very intense (score 7) and only 4 (20%) participants have scored it as less than moderate (scores 3 to 4). On CPET, five (25%) participants reported intense to very, very intense dyspnea (scores 5 to 9) and only one (5%) reported less than moderate dyspnea.

No significant correlations were found between difference on dyspnea at peak exercise and dyspnea at rest and the number of steps on IST ($\rho = -0.226$, $p = 0.338$). No significant correlations were found between difference on dyspnea at peak exercise and dyspnea at rest and the workload on CPET ($\rho = 0.262$, $p = 0.265$).

No significant correlations were found between dyspnea at peak exercise and VO_2 peak, on IST ($r = -0.237$, $p = 0.315$).

5.4.2.Leg Fatigue

The difference between leg fatigue at peak exercise and leg fatigue at rest was lower on IST than on CPET and showed to be significantly different on both tests ($p = 0.015$).

Participants have scored leg fatigue up to very intense (score 7) and only 3 (15%) participants have scored it less than moderate (scores 3 to 4), on IST. On CPET, participants have scored it up to very, very intense (score 9) and only two (10%) have scored it less than moderate.

No significant correlations were found between difference on leg fatigue peak exercise and leg fatigue at rest and the number of steps on IST ($\rho = 0.381$, $p = 0.098$). No significant correlations were found between difference on leg fatigue peak exercise and leg fatigue at rest and the workload on CPET ($\rho = -0.114$, $p = 0.633$)

No significant correlations were found between leg fatigue at peak exercise and VO_2 peak, on IST ($r = 0.283$, $p = 0.227$).

Table 3 – Comparison of symptoms on IST and CPET

Variables	IST	CPET	p value
Symptom scores			
Δ- Dyspnea	3.5 [2- 4]	3 [3- 4]	0.390
Δ- Leg fatigue	2.80 ± 3.05	4.65 ± 2.24	0.015*

The values are expressed as mean ± standard deviation unless otherwise stated. Abbreviations: VO_2 – peak oxygen uptake; Δ- Dyspnea – dyspnea peak exercise- dyspnea rest; Δ- Leg fatigue – leg fatigue peak exercise- leg fatigue rest

*A p value <0.05 was considered significant

5.5. VO_2 peak along IST and CPET

The VO_2 peak time courses during IST and CPET are depicted in Figure 4. Data from the first ten minutes, from all participants, were collected and analysed using simple linear regression. Either IST and CPET showed a positive correlation between VO_2 peak and time ($y= 1.4618x + 6.5157$; $R^2= 0.6423$ and $y= 0.8435x + 7.5693$; $R^2= 0.4635$, respectively). The same data is presented with median values in Figure 4 (Attachment 9). Data were collected from this period of time because it was the longest duration of effort/ maximal exercise either on IST and CPET, so it was the time frame to be analysed.

A

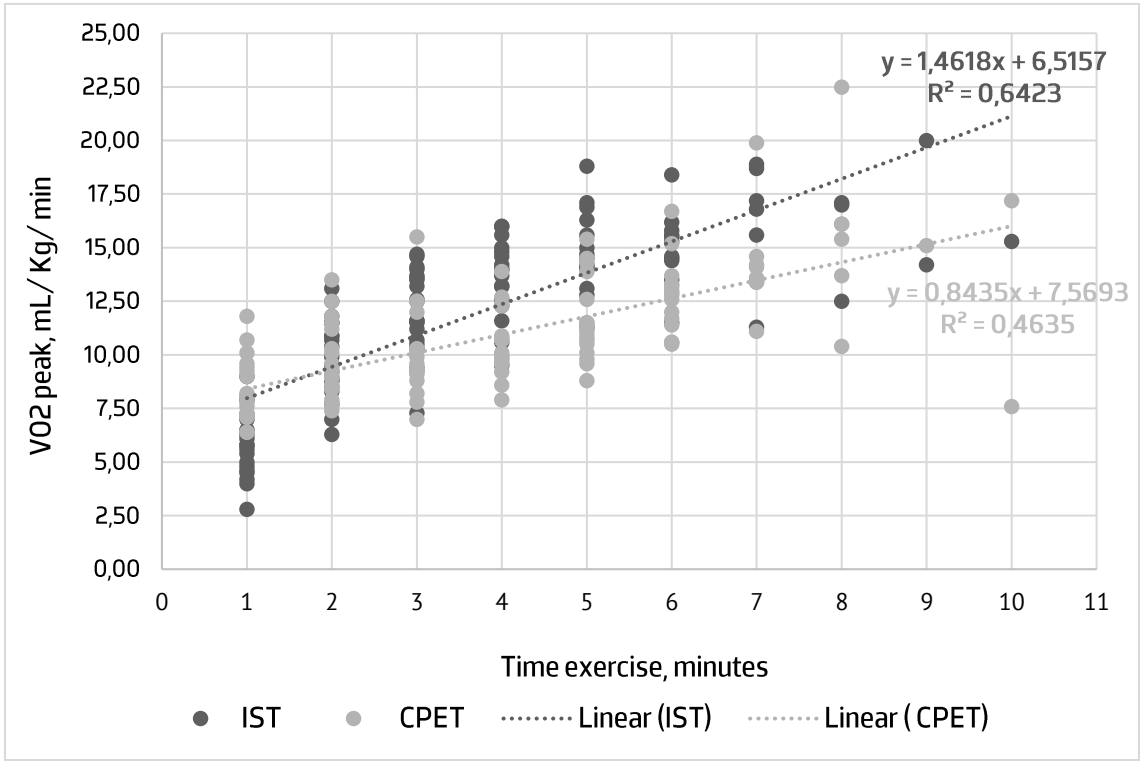

Figure 4- VO_2 peak time courses during IST (dark circle) and CPET (light circle). Data is expressed in absolute values.

5.6. Power of the study

The power of the study was assessed with G* Power 3.1 program. Firstly, we assessed the correlation between VO_2 peak measured on IST and on CPET, the power showed to be 0.807. Secondly, we assessed the VO_2 peak measured on IST and on CPET, as matched pairs, and the power showed to be 0.964. As both values are greater than 0.8, the correlation was significant.

6. Discussion

The novel findings of this study are: (i) the performance and time spent on IST is comparable to CPET in people with COPD; (ii) IST elicits a similar peak physiological response to CPET in people with COPD; (iii) VO_2 peak is related to performance on IST; (iv) FEV_1 (%) presents a negative influence on the performance on IST.

No adverse events were reported during this study, on both tests, which represents the potential safety of IST in people with COPD.

Our results suggest that the IST elicited a similar peak physiological response to CPET in people with moderate to severe COPD. We conclude this based on the VO_2 peak reached on both tests, which were strongly correlated, and no differences were found among tests. Moreover, in both tests, people with COPD reached ventilatory limitation based on the absence of ventilatory reserve.

The participants performed a similar workrate on both tests, with a significant positive and strong correlation between tests, demonstrating the identical physiological responses of this distinct modes of exercising (stepping vs. cycling).

As Holm et al reported, we also observed greater VO_2 peak values on the IST compared to the CPET, as standing exercise engages larger muscle mass, as the activation of arm and trunk muscles, compared to stationary cycling and may be a potential source of increased afferent input to the respiratory centers (Dal Corso et al., 2007; Holm et al., 2014; Pepin et al., 2005).

Respiratory gas- exchange ratio was significantly different between tests and superior on the CPET. It is well established that the RER increases with exercise intensity and duration, which was observed in this study (Rothschild et al., 2022).

One of the distinguishing features of many patients with moderate to severe COPD is a reduced breathing reserve (BR approaching or exceeding 100%), with a significant impact on exercise intolerance ("ATS/ACCP Statement on Cardiopulmonary Exercise Testing.," 2003). On both tests, the participants showed a reduced BR, but it was significantly different between tests, which might be explained by the VE values on each test. To determine the BR, it was used the ratio between VE at peak exercise and the estimated maximal voluntary ventilation (MVV= FEV_1 in liters x 35) (Gephine et al., 2020). The VE was inferior on IST when compared to VE on CPET, but no significant differences were found between tests. This demonstrates participants were able to be more efficient on IST because they presented greater oxygen uptake for a lower VE and for this reason the BR was lower on this test, which

may indicate these subjects presented expertise with the stepping. This study also showed where the greater the BR the worse the performance on the IST, proved by the negative correlation, however the correlation between the BR and the number of steps was very weak. So, we cannot determine reliably that BR may affect the number of steps in people with COPD. People with COPD exceeded the BR on IST as on CPET which implies IST is a maximal test.

Desaturation was detected either on the IST and the CPET but not superior to 4% (on the same test), however it was greater on the IST ($SpO2 < 88\%$). The fall in saturation can be explained by the pathophysiologic feature of COPD: gas exchange abnormalities which worsen during exercise. Destruction of lung parenchyma generates ventilation/ perfusion imbalance. In addition, COPD have an increased physiological dead space, due to peripheral airway obstruction and a reduced pulmonary vascular bed, that further worsen ventilation/ perfusion abnormalities. During exercise, there is worsening of gas exchange abnormalities and increasing ventilatory demand. Abnormalities in gas exchange in COPD, aging effect, muscle metabolism may lead to exercise hypoxemia and desaturation. But the demand placed by the exercise has influence on it. Stairclimbing requires an increased range of motion of lower limb joints and more intense muscular activity to generate larger forces that vertically translate the body's center of gravity, as the individual must work against gravity to ascend. Hence the demand of staircase climbing, the pathologic abnormalities of COPD and the aging effect all contribute to the increasing the ventilatory demand and early termination of exercise (Aviragee et al., 2017a; Dal Corso et al., 2013; Holm et al., 2014).

The results of this study showed no significant correlations between dyspnea and VO_2 peak, so we speculate dyspnea might be a limitation symptom to maximal exercise, more than leg fatigue in people with COPD.

The participants showed to be better tolerant to IST than to CPET, perceived by a lower leg fatigue at peak exercise on IST, even if no significant correlations were found, and a greater performance on this test, which may indicate the performance on IST is not dependent on the power of the lower limb. Exercise limitation in these patients is complex, multifactorial, and may be difficult to establish and to quantify. Abnormal symptoms perception, deconditioning, and peripheral muscle dysfunction are increasingly recognized to be important (co)contributors. It is well appreciated that muscle mass is an important factor limiting physical work. The functional consequences of such reduction are a loss of endurance, loss of strength, or both ("ATS/ACCP Statement on Cardiopulmonary Exercise Testing.," 2003).

During cycling, the ventilation response is believed to be regulated by an important contribution of nonaerobic metabolism, resulting from the predominant solicitation of the quadriceps muscle (Pepin et al., 2005). Besides, cycling is not a familiar activity to most of the participants whilst stairclimbing is a routinely activity and they may present better skills to fulfill the effort related to it.

Some participants reported difficulty in coordination in IST to keep up with the cadence, when the cadence got faster, which may have limited some participants to reach the maximal effort. Furthermore, the fact participants had to perform the IST with a gas analyzer (face mask) on, to measure the VO_2 peak, was reported to affect their performance. This might be explained because they could not see undoubtedly the step and could not feel confident to step up as the cadence got faster.

On CPET the participants consumed superior VO_2 peak at the very start (time =0 minutes) of the evaluation. This might be explained by the Fick equation, where the greater the HR, the greater the VO_2. On this test, there were several healthcare professionals watching/ monitoring the participant which may contribute to increase HR at rest (anxiety), leading to increase of VO_2 (Albouaini et al., 2007a).

The peak oxygen uptake was assessed overtime, for the first 10 times, on both tests. Both tests showed to have a positive response overtime, which indicates oxygen consumption increased overtime, as it was expected with increasing external work (Albouaini et al., 2007).

6.1. Strength and limitations

This study presents some strength and limitations. One strength of this study is the fact all the participants were diagnosed with moderate to severe COPD, according to GOLD criteria, and aged between 48 and 81 years. Moreover, it is interesting to point out that one of our subjects reached the last stage of the IST. This diversity improves the quality of the study.

According to COSMIN recommendations, a larger sample size is required for the criterion validity. However, based on the power of the study (>0.80), the results showed a positive, significant, and strong correlation between VO_2 peak on IST and on CPET, so this test can provide an alternative outcome measure in the assessment on people with COPD.

The present study did not include patients receiving Long Term Oxygen Therapy because they would be likely to need supplemental oxygen during exercise preventing the VO_2 measurement. Besides, it is shown that oxygen during exercise in COPD patients may impact

the time of exercise and intensity, positively, with less shortness of breath when using oxygen therapy (Branson, 2018; Stringer & Marciniuk, 2018). Hence, one of the exclusion criteria was the supplementary oxygen during the effort to standardize the sample.

7. Conclusion

This study demonstrated that IST produced a similar peak physiological response to CPET in people with COPD, supporting its capacity to be considered a maximal and symptom-limited test. Moreover, in both tests, people with COPD reached ventilatory limitation as evidenced by the absence of ventilatory reserve, suggesting aerobic fitness/ ventilatory capacity were limiting factors of IST performance.

In conclusion, our data show that cardiovascular and respiratory responses and performance during both IST and CPET were similar and strongly correlated at peak exercise.

Although the IST elicited maximum physiological response, this does not imply that it can replace the CPET, as the CPET has reference values established for both maximum exercise and dynamic responses, as well as the criteria for determining cardiovascular, ventilatory, and peripheral limitations. Hence, further studies are required to determine if IST may be an option for exercise prescription. Moreover, it should be studied the application of this study on other patients with different respiratory diseases, such as Asthma and Interstitial Lung Diseases, and in patients with supplementary oxygen during the effort.

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Supplementary Content

Attachment 1. Ethical Committee of the Health Local Unit of Santa Maria approval

CAML
CENTRO ACADÉMICO DE MEDICINA DE LISBOA

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Profª. Doutora Maria do Céu Patrão Neves
Profª. Doutora Patrícia Canhão

Exma. Senhora

Profª. Doutora Fátima Rodrigues

Coordenadora na Unidade de Reabilitação Respiratória - HPV

Centro Hospitalar Universitário Lisboa Norte, EPE

Lisboa, CHULN, 18 de Dezembro de 2023

Nossa Refª. Nº 198/23

Assunto: Estudo **"Validade de um novo teste incremental de Degrau para a população com doença pulmonar obstrutiva crónica (DPOC): comparação com a prova de esforço cardiorrespiratória"**

Pela presente se informa que o projeto citado em epígrafe obteve, na reunião ocorrida no dia 6 de Dezembro de 2023, parecer favorável da Comissão de Ética, considerando-se observados os imperativos que fundeiam as Boas práticas clínicas, os preceitos internacionalmente reconhecidos de qualidade ética e científica que devem ser respeitados na conceção e na realização dos estudos clínicos que envolvam a participação de seres humanos.

No uso das competências próprias constantes do disposto no Decreto-Lei. N.º 97/95 de 10 de Maio, e no exercício das suas funções em observância ao deliberado na Lei n.º 21/2014 de 16 de Abril, que aprova a lei da investigação clínica, na sua atual redação alterada pela Lei n.º 73/2015 de 27/07/15, complementada pelo Decreto-Lei n.º 80/2018 (DR n.º 198-2018, Série I de 2018/10/15) que reforça o papel das comissões de ética no contexto da instituição em que se integram, na sua missão de contribuir para o cumprimento de princípios da ética e da bioética, na prestação de cuidados de saúde e na realização de investigação clínica, e ainda em harmonia com os regulamentos internos do CHULN, os códigos deontológicos, as convenções, e as recomendações constantes das declarações e diretrizes internacionais, designadamente as Declarações de Helsínquia a de Tóquio, da Organização Mundial de Saúde e da União Europeia, a Comissão de Ética avaliou o projeto, que considera obedecer aos requisitos éticos fundamentais que devem ser respeitados, refletindo o primado da dignidade e da integridade humanas.

Encontra-se assegurado o direito à integridade moral e física do participante, cumpre as precauções essenciais, cujo desígnio visa minimizar eventuais danos para os seus direitos de personalidade, bem como o direito à privacidade e à proteção dos dados pessoais que lhe dizem respeito, respeitando os imperativos refletidos no Regulamento Geral sobre a Proteção de Dados (RGPD) entrado em vigor em 25 de Maio de 2016 e plenamente aplicável a partir de 25 de Maio de 2018, (Regulamento (UE) 2016/679 do Parlamento Europeu e do Conselho de 27/04/16), de 27 de abril, publicado no Jornal Oficial da União Europeia, no dia 4 de Maio de 2016, e na Lei n.º 58/2019, de 8 de Agosto

De acordo com os trâmites institucionais definidos, mais se informa, que o estudo em apreço integrará a lista mensal de estudos aprovados a ser presente ao Sr. Diretor Clínico, Prof. Doutor Rui Tato Marinho, para conhecimento

Com os melhores cumprimentos,

O Presidente da Comissão de Ética do CAML

Prof. Doutor João Forjaz de Lacerda

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Attachment 2. Modified Medical Research Council Scale

Medical Research Council Dyspnoea Questionnaire (MRCDQ)

Da seguinte tabela escolha a afirmação que melhor descreve a sua sensação de falta de ar.

GRAU 1

Sem problemas de falta de ar excepto em caso de exercício intenso.

"Só sinto falta de ar em caso de exercício físico intenso".

GRAU 2

Falta de fôlego em caso de pressa ou ao percorrer um piso ligeiramente inclinado.

"Fico com falta de ar ao apressar-me ou ao percorrer um piso ligeiramente inclinado".

GRAU 3

Andar mais devagar que as restantes pessoas devido a falta de fôlego, ou necessidade de parar para respirar quando ando no seu passo normal.

"Eu ando mais devagar que as restantes pessoas devido à falta de ar, ou tenho de parar para respirar quando ando no meu passo normal".

GRAU 4

Paragens para respirar de 100 em 100 metros ou após andar alguns minutos seguidos.

"Eu paro para respirar depois de andar 100 metros ou passado alguns minutos".

GRAU 5

Demasiado cansado ou sem fôlego para sair de casa, vestir ou despir.

"Estou sem fôlego para sair de casa".

Simão, P., & Almeida, P. (2009). Reabilitação Respiratória. Uma estratégia para a sua implementação (Comissão de Reabilitação Respiratória da SPP). Revista Portuguesa de Pneumologia , XV - Supl 1.

GIFCR

GRUPO DE INTERESSE EM FISIOTERAPIA CARDIO-RESPIRATÓRIA

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Attachment 3. COPD Assessment Test Questionnaire

Como está a sua DPOC (Doença Pulmonar Obstrutiva Crónica)? Faça o Teste de Avaliação da DPOC (COPD Assessment Test™– CAT)

Este questionário irá ajudá-lo a si e ao seu profissional de saúde a medir o impacto que a DPOC (Doença Pulmonar Obstrutiva Crónica) está a ter no seu bem estar e no seu quotidiano. As suas respostas e a pontuação do teste podem ser utilizadas por si e pelo seu profissional de saúde para ajudar a melhorar a gestão da sua DPOC e a obter o máximo benefício do tratamento.

Se deseja completar o questionário à mão, em papel, **clique aqui** e imprima o questionário.

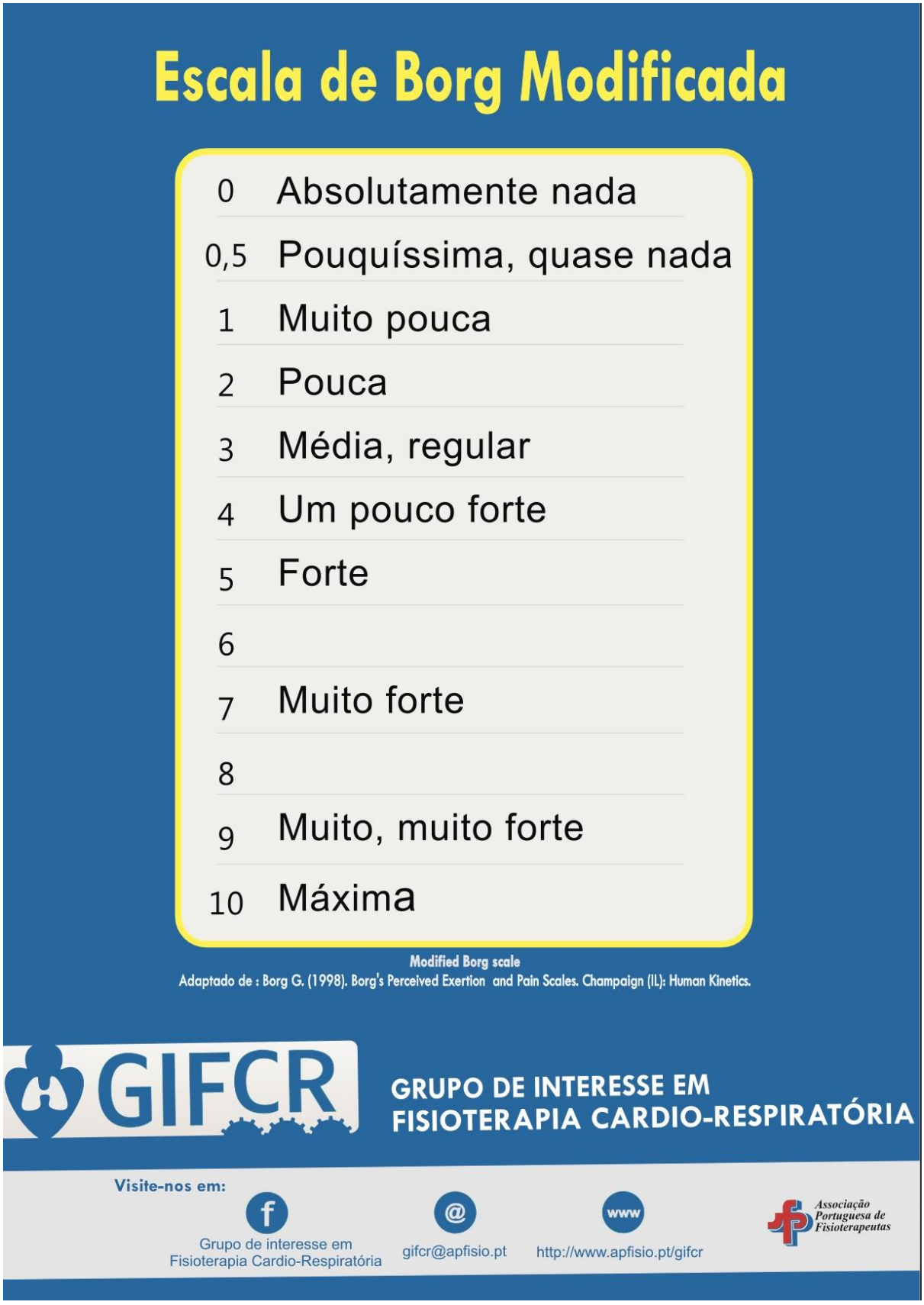
Para cada um dos itens a seguir, assinale com um (X) o quadrado que melhor o descreve presentemente. Certifique-se que selecciona apenas uma resposta para cada pergunta.

Por exemplo: Estou muito feliz (0) (X) (2) (3) (4) (5) Estou muito triste

								PONTUAÇÃO
Nunca tenho tosse	0	1	2	3	4	5	**Estou sempre a tossir**	
Não tenho nenhuma expectoração (catarro) no peito	0	1	2	3	4	5	**O meu peito está cheio de expectoração (catarro)**	
Não sinto nenhum aperto no peito	0	1	2	3	4	5	**Sinto um grande aperto no peito**	
Não sinto falta de ar ao subir uma ladeira ou um lance de escadas	0	1	2	3	4	5	**Quando subo uma ladeira ou um lance de escadas sinto bastante falta de ar**	
Não sinto nenhuma limitação nas minhas actividades em casa	0	1	2	3	4	5	**Sinto-me muito limitado nas minhas actividades em casa**	
Sinto-me confiante para sair de casa, apesar da minha doença pulmonar	0	1	2	3	4	5	**Não me sinto nada confiante para sair de casa, por causa da minha doença pulmonar**	
Durmo profundamente	0	1	2	3	4	5	**Não durmo profundamente devido à minha doença pulmonar**	
Tenho muita energia	0	1	2	3	4	5	**Não tenho nenhuma energia**	
							PONTUAÇÃO TOTAL	

Certifique-se de imprimir o seu questionário CAT antes de ter uma consulta com o seu profissional de

Attachment 4. Modified Borg Scale



Attachment 5. Written Informed Consent– CPET

Hospital
Pulido Valente

IDENTIFICAÇÃO
DO
DOENTE

Consentimento informado para internamento

Nome do doente_____
Fui informado(a) acerca da minha situação clínica e da necessidade de internamento.
Forma-me dadas informações sobre os tratamentos e os exames complementares (análises, radiografias, etc.) que se prevêem que tenha de fazer.

Falei com o (a) Dr (a)_____
Tive oportunidade de fazer perguntas. Recebi informação suficiente.

Dou ☐ Não dou ☐ o meu consentimento livre e informado para o internamento.

Dou ☐ Não dou ☐ o meu consentimento livre e informado para que os dados do meu processo clínico, referentes a este internamento, possam ser consultados e utilizados em estudos devidamente autorizados pela Comissão de Ética do hospital, desde que seja garantido sigilo quanto ao meu nome.

Lisboa, ____de_____de_____

Assinatura do Doente
Ou do seu representante legal

Assinatura do Médico
nº mecanográfico

Consentimento informado para procedimentos de diagnóstico e tratamento

Nome do doente_____
Fui informado(a) acerca da minha situação clínica e da necessidade de efectuar:
_____
_____
_____
Foram-me explicados os objectivos e os eventuais riscos e complicações deste procedimento.
Fui também informado(a) da possibilidade de adiamento deste procedimento por motivos imprevistos.

Falei com o (a) Dr (a)_____
Tive oportunidade de fazer perguntas. Recebi informação suficiente.

Dou ☐ Não dou ☐ o meu consentimento livre e informado para a realização do exame ou tratamento proposto.

Dou ☐ Não dou ☐ o meu consentimento livre e informado para que os dados do meu processo clínico, referentes a este procedimento, possam ser consultados e utilizados em estudos devidamente autorizados pela Comissão de Ética do Hospital, desde que seja garantido sigilo quanto ao meu nome.

Lisboa, ____de_____de_____

Assinatura do Doente
Ou do seu representante legal

Assinatura do Médico
nº mecanográfico

Alameda das Linhas de Torres, 117
1769-001 LISBOA
Tel: 217 548 000 – Fax: 217 548 215
www.chln.pt

Attachment 6. Written Informed Consent– IST

CENTRO HOSPITALAR LISBOA NORTE, EPE | HOSPITAL DE SANTA MARIA | Hospital Pulido Valente

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE
para Investigação Clínica

Parte Informativa

1. TÍTULO DO PROJECTO	Validade de um novo Teste Incremental de Degrau para a população com doença pulmonar obstrutiva crónica (DPOC): comparação com a prova de esforço cardiorrespiratória
2. DESCRIÇÃO DO PROJECTO, SUA NATUREZA E OBJETIVO Metodologia, nomeadamente identificação dos procedimentos do estudo, procedimentos invasivos, consultas e seus detalhes (p ex, número e duração).	Trata-se de um estudo observacional, a ser realizado para a Dissertação do Mestrado da investigadora principal, que tem como objetivo avaliar a sua capacidade cardiorrespiratória com recurso ao Teste Incremental de Degrau, comparando os dados obtidos com a prova de esforço cardiorrespiratória. No caso de aceitar participar neste estudo, a avaliação decorrerá em dois momentos: primeiramente, será submetido à prova de esforço cardiorrespiratória (em cicloergómetro) e, posteriormente, ao Teste Incremental de Degrau, com 1 semana de intervalo. Antes de cada prova será realizada uma gasometria e durante os investigadores estarão a monitorizar os seus sinais vitais, saturação de oxigénio, valor de dispneia (com recurso à Escala de Borg Modificada). A sua participação neste estudo poderá ser interrompida por si, a qualquer momento, sem nenhum prejuízo para os cuidados de saúde que lhes são prestados.
3. RISCOS GRAVES E RISCOS FREQUENTES Riscos ou incómodos previsíveis derivados do estudo	Os riscos associados a este estudo prendem-se com os efeitos inerentes ao exercício físico vigoroso, como é o caso da sudação, desaturação de oxigénio, dispneia, fadiga nos membros inferiores, aumento da frequência cardíaca e da tensão arterial.

4. BENEFÍCIOS Benefícios expectáveis, ou se tais benefícios não são expectáveis.	Espera-se com este estudo adquirir uma nova ferramenta de avaliação da aptidão cardiorrespiratória, alargando esta avaliação aos diversos contextos em que se encontra cada pessoa (desde a Unidade de Reabilitação Respiratória até ao próprio domicílio)
5. POSSÍVEIS ACONTECIMENTOS ADVERSOS (de todos os procedimentos do estudo).	Os possíveis efeitos adversos podem surgir com o aumento da intensidade do exercício, por acentuação dos sintomas percebidos por cada participante (dispneia e fadiga dos membros inferiores intoleráveis, desaturação de oxigénio, aumento significativo da tensão arterial e da frequência cardíaca)
6. APROVARAM O ESTUDO	Comissão de Ética do Centro Académico de Medicina de Lisboa Contato – 217805405

PARTE DECLARATIVA DO PROFISSIONAL

Confirmo que expliquei à pessoa abaixo indicada, de forma adequada e inteligível, os procedimentos que o estudo envolve.

Respondi a todas as questões que me foram colocadas e assegurei-me de que houve um período de reflexão suficiente para a tomada da decisão.

Expliquei o carácter Voluntario da participação; a recusa ou a retirada do consentimento e a possibilidade de pedir para interromper ou mesmo desistir de participar caso sinta necessidade ou vontade de o fazer, sem que daí advenha qualquer prejuízo no contexto da sua assistência clínica.

Informei que se encontra assegurada a privacidade dos dados pessoais coletados mediante a pseudonimização dos mesmos, garantida pela atribuição de um código cuja chave de descodificação é restrita ao Investigador Principal do projeto ou quem ele designar para o assistir e / ou em sua substituição, bem como se encontra acautelada a confidencialidade e a proteção dos dados pessoais de acordo com o Regulamento Geral sobre a Proteção de Dados (RGPD) entrado em vigor em 25 de Maio de 2016 e plenamente aplicável a partir de 25 de Maio de 2018, (Regulamento (UE) 2016/679 do Parlamento Europeu e do Conselho de 27/04/16), de 27 de abril, publicado no Jornal Oficial da União Europeia, no dia 4 de Maio de 2016, e na Lei n.º 58/2019, de 8 de Agosto.

Nome legível do investigador Principal _____

ASSINATURA

_____ **DATA:** _____ / _____ / _____

CONTACTO TELEFÓNICO _____ **E-mail** _____

À PESSOA/REPRESENTANTE

Por favor, leia com atenção todo o conteúdo deste documento. Não hesite em solicitar mais informações se não estiver completamente esclarecido/a. Verifique se todas as informações estão corretas. Se tudo estiver conforme, então assine este documento.

PARTE DECLARATIVA DA PESSOA QUE CONSENTE

Declaro ter compreendido os objetivos do que me foi proposto e explicado pelo profissional de saúde que assina este documento,

Foi-me dada oportunidade de fazer todas as perguntas sobre o assunto e para todas elas ter obtido resposta esclarecedora, ter-me sido garantido que não haverá prejuízo para os meus direitos assistenciais se eu recusar esta solicitação, e ter-me sido dado tempo suficiente para refletir sobre esta proposta.

AUTORIZO ☐ **NÃO AUTORIZO** ☐

Nome legível _____

Assinatura _____ **Data:** ____ / ____ / _____

SE NÃO FOR O PRÓPRIO A ASSINAR POR IDADE OU INCAPACIDADE (se o menor tiver discernimento deve também assinar em cima)

NOME: _____

Documento de Identificação Nº: _____ **Data ou validade** ____ / _____ /_____

Grau de parentesco ou tipo de representação:

_____

ASSINATURA _____

NOTA: Este documento é executado em duas vias – uma para o processo/estudo e outra para ficar na posse de quem consente.

Attachment 7. Incremental Step Test– Reporting Form

***Incremental Step Test* - Folha de registo**

Data: ___ / ___ / _____

Nome: _____

Data de Nascimento (dd/mm/aaaa): ___ / ___ / _____

Diagnóstico: _____

Oxigénio suplementar (fluxo, dispositivo, método de transporte): _____

Medicação tomada hoje (dose e quantas horas antes dos testes?): _____

_____

Observações: _____

***Incremental Step Test* – Primeira tentativa**

	Rep	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	11 min	12 min	13 min	14 min	15 min
FC																
TA																
%SpO_2																
Dispneia																
Fadiga																

Rep: repouso; FC: frequência cardíaca; TA: tensão arterial; SpO_2: saturação de oxigénio. Nota: a tensão arterial não deve de ser avaliada dada a dificuldade em avaliá-la durante o modo *stepping*.

Razões do término do teste:_____

Recuperação

FC: _____ %SpO_2: _____ Dispneia: _____ Fadiga: _____

Desempenho

Total número de *steps*: _____ Ritmo máximo: _____ Duração: _____

***Incremental Step Test* – Segunda tentativa**

	Rep	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	11 min	12 min	13 min	14 min	15 min
FC																
TA																
%SpO_2																
Dispneia																
Fadiga																

Rep: repouso; FC: frequência cardíaca; TA: tensão arterial; SpO_2: saturação de oxigénio. Nota: a tensão arterial não deve de ser avaliada dada a dificuldade em avaliá-la durante o modo *stepping*.

Razões do término do teste:_____

Recuperação

FC: _____ %SpO_2: _____ Dispneia: _____ Fadiga: _____

Desempenho

Total número de *steps*: _____ Ritmo máximo: _____ Duração: _____

Desempenho do melhor teste:

Total número de *steps*: _____ Ritmo máximo: _____ Duração: _____

Comentários: _____

_____

Attachment 8. Participants' baseline characteristics

Table 1 (continuation) – Participants' baseline characteristics (n=20)

Variables	Total Sample (n=20)
Unscheduled consultations (previous year), n (%)	3 (15)
Emergency department admission (previous year), n (%)	3 (15)
Hospitalizations, n (%)	3 (15)
Medication, n (%)	
SABA	4 (20)
LABA+LAMA	5 (25)
LABA+ICS	2 (10)
LAMA+LABA+ICS	13 (65)

Abbreviations: SABA – short-acting β2 agonist; LABA – long-acting β2 agonist; LAMA – long-acting muscarinic antagonist; ICS – inhaled corticosteroid

Attachment 9. VO_2 peak time courses during IST and CPET

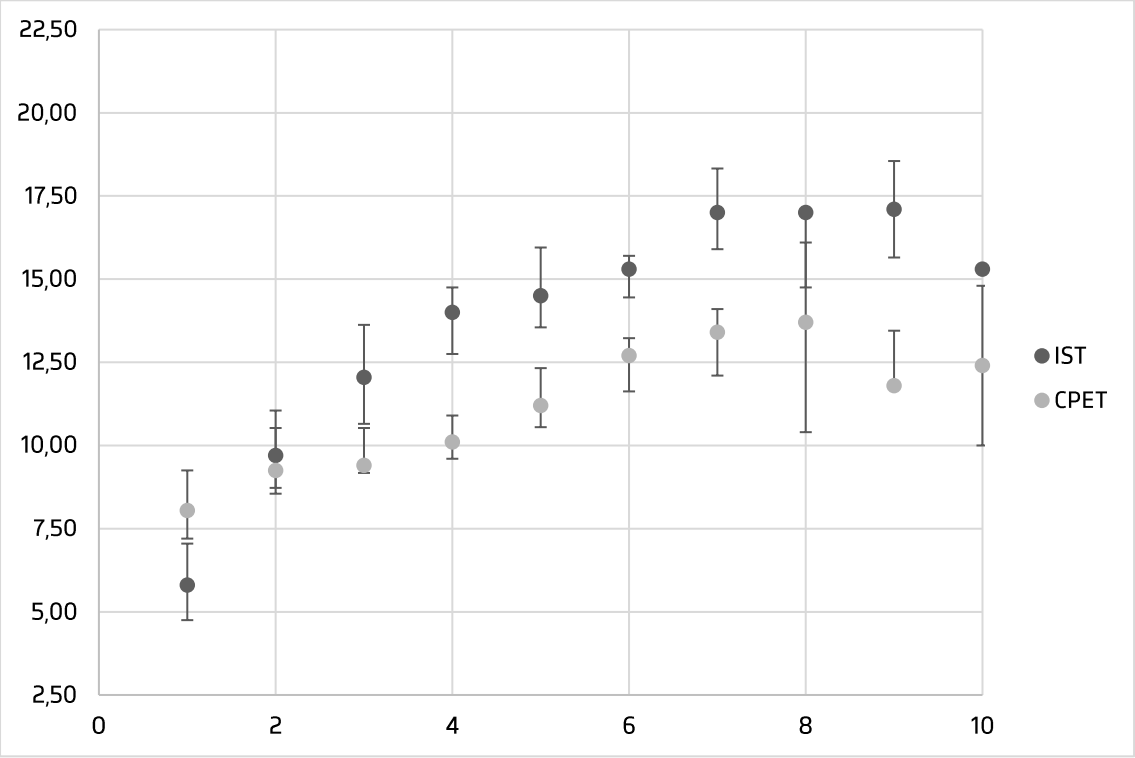


Figure 4 – VO_2 peak time courses during IST (blue circle) and CPET (orange circle). Data is expressed in median [P25–P75]

Attachment 10. Poster Presented at the European Respiratory Society Congress

I presented the following poster at the poster session on the past European Respiratory Society Congress, which took place in Vienna, Austria, from 7th to 11th September 2024.