



Inspiratory muscle glycemic threshold in COPD: functional and clinical associations in incremental testing

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ABSTRACT

It is known that COPD is multifactorial and reduces the function of several body systems; however, its impact on inspiratory muscle metabolism and its possible clinical implications and for inspiratory muscle training are still unclear. Furthermore, the use of the glycemic threshold (GT) of inspiratory muscles as a viable and clinically useful metabolic measure in COPD is not yet addressed in the literature. This study aimed to verify whether there is an association between the GT of inspiratory muscles with Borg, functional capacity (FC) and cardiovascular autonomic balance in COPD. Included patients with COPD under outpatient follow-up and evaluated them using incremental inspiratory muscle testing (IIMT), six-minute walk test (6MWT), and heart rate variability (HRV). The GT of inspiratory muscles was strongly associated with Borg in the IIMT. The strength endurance and aerobic capacity of inspiratory muscles demonstrated by the exhaustion point (EP) and delta GT/EP showed a strong inverse correlation with the cardiovascular autonomic balance demonstrated by the LF/HF ratio. Delta GT/EP also showed an inverse correlation with dyspnea by the mMRC scale and with the final Borg in the 6MWT. The study concluded that the GT and EP of the inspiratory muscles are strongly associated with Borg in individuals with COPD. Furthermore, the aerobic capacity of the inspiratory muscles was strongly associated with dyspnea on exertion and cardiovascular autonomic balance.

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a multifactorial disease that causes decreases in the function of several body systems, such as the cardiovascular and especially the respiratory systems, with an impact on dyspnea on exertion, reduced functional capacity, and quality of life [1].

Among the treatments proposed to improve COPD-related complications is Inspiratory Muscle Training (IMT) [2]. Studies have shown that IMT improves functional capacity and quality of life in individuals with heart failure [3,4]. However, results with individuals with COPD

are conflicting regarding the reduction of dyspnea on exertion, improvement in the ability to perform physical effort, and quality of life [1]. This divergence can be explained by the different forms of IMT prescription. Most studies are based on Maximum Inspiratory Pressure (MIP) to modulate the training load. This measurement is easy to apply clinically and produces objective results. However, its usefulness is limited to assessing static inspiratory muscle strength, which may limit the accurate diagnosis of inspiratory muscle function and consequently favour nonspecific IMT prescriptions. In this line of thought, we recently suggested that modulation of training load based on the Glycemic Threshold (GT) of the inspiratory muscles is more functional and

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presents better results than the traditional model based on the percentage of MIP for a population in the post-surgical period of myocardial revascularisation and valve replacement [5].

GT is one of the methods that can reliably replace the lactate curve for determining the anaerobic threshold (AT). This occurs because the flow of blood glucose to the skeletal muscle follows the metabolic demand imposed by muscle contractions, being mediated in physical exercise through the diffusion facilitated by the Glucose Transport Protein 4 [6], moved to the cell surface by complex molecular signaling, including Adenosine Monophosphate-Activated Protein Kinase [7], Ca²⁺ and Nitric Oxide Synthase (NOS) in the proximal part of the signaling cascade [7]. This process causes the blood glucose level to fall, activating the pancreatic α cells sensitive to its low level, which release the hormone glucagon and in turn breaks down hepatic glycogen, leading to an increase in blood glucose [8]. The GT therefore corresponds to the lowest glycemic point on the curve and is followed by a sometimes abrupt but normally linear increase after the GT [9].

However, determining GT from an Incremental Inspiratory Muscle Test (IIMT) [10] is laborious and requires time, skills, and specific training of professionals. An alternative to determine GT indirectly is to use Borg's subjective perception of effort (SPE). In a previous study with a young and healthy population, our group found a strong association between the GT point of the inspiratory muscles and Borg's SPE [11].

The reason for conducting this research is the possibility of using GT indirectly through Borg's RPE to determine the IIMT load in individuals with COPD. To propose this new prescription method, this study aims to verify in this population whether there is an association between GT of the inspiratory muscles and Borg's RPE, functional capacity (FC),

dyspnea on exertion and cardiovascular autonomic balance. The data from this exploratory study indicates whether there is a basis for conducting a study with a larger number of patients and subsequently for comparing the effects of IMT based on MIP and GT of the inspiratory muscles for this population.

2. Materials and methods

2.1. Design and sample

An exploratory observational study carried out at the pulmonology outpatient clinic of the Hospital Universitário of the Universidade Federal de Sergipe (HU/UFS), Brazil, in which adults of both sexes, sedentary or irregularly active, diagnosed with COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria - forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) <70 % post-bronchodilator [12], who did not use supplemental oxygen, without significant changes in resting electrocardiogram (ECG) recording or significant cardiovascular disease, such as symptomatic ischemic heart disease; neurological, such as neuromuscular dystrophies; musculoskeletal disease, signs of cognitive impairment or significant risk of falling; cancer, with or without chemotherapy treatment; diabetes mellitus and use of stimulants or anabolic steroids due to pre-disposition to metabolic changes, which could interfere with GT. The exclusion criterion adopted was the failure to sign the informed consent form and those who could not perform or correctly understand the execution of the tests. The sample selection and evaluation are illustrated in Fig. 1.

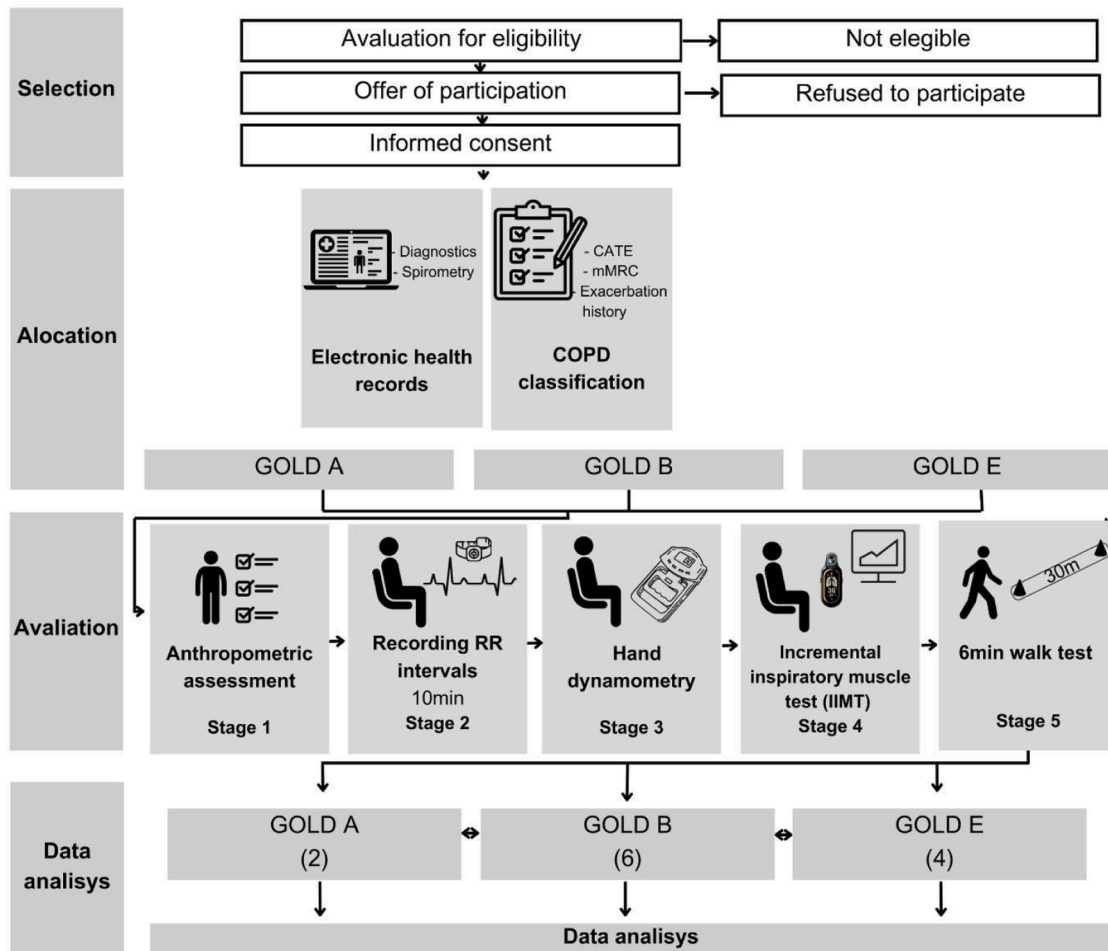


Fig. 1. Flow diagram of sample selection and evaluation.

2.2. Data collection

The modified Medical Research Council (mMRC) dyspnea scale [13] was applied to classify individuals functionally. This scale was chosen because it allows for objective and individual classification of dyspnea in daily activities. The COPD Assessment Test (CAT), Portuguese version [14], was applied to assess the severity of symptoms in daily life and the number of COPD exacerbations in the last year. Before performing the physical tests, blood pressure (BP) was measured with a Premium® tensiometer duly calibrated by the National Institute of Metrology (INMETRO) and a Bic® stethoscope, heart rate and oxygen saturation were measured with a Multilaser HC261® oximeter, followed by an anthropometric assessment with weight and height.

Height and weight were measured using a digital scale with a Welmi® stadiometer, performed with the subjects barefoot and their buttocks and shoulders supported on a vertical backrest. Total body mass was measured using a digital scale calibrated by Inmetro with its certificate. Body mass index (BMI) was calculated using mass and height measurements according to the Quetelet equation: mass (kg)/height (m²). The BMI cutoff point adopted was recommended by the V Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis of the Department of Atherosclerosis of the Sociedade Brasileira de Cardiologia (SBC) [15].

After the selection criteria described in the previous section were measured, the volunteer underwent recording of electrocardiographic RR intervals using a Polar H10® frequency meter connected to the Elite HRV® Android® APP via Bluetooth®. The recording was performed for 10 min with the volunteer seated in a chair with dorsal support for the spine and feet properly supported on the floor with 90° knee flexion and neutral ankle. The location was free of sound and visual stimuli. To assess heart rate variability (HRV), the RR intervals were sent to the e-mail via the Elite HRV® application log for later evaluation in the Kúbios HRV® Windows® software.

2.2.1. Incremental inspiratory muscle testing (IIMT)

The strength of the inspiratory muscles was tested using the POWERbreathe® K5, properly coupled to an HMEF barrier filter, connected to the BreatheLink® computer software, with the individual seated and

the spine erect. The method used by the device is the muscle pressure index (Sindex), expressed in cmH₂O. The volunteer was instructed to perform a slow expiration manoeuvre followed by a rapid and forced inspiration with the nose occluded by a nose clip. The manoeuvre was repeated 10 times consecutively, as proposed by Silva PE et al. [16]. The highest value was selected as the Sindex [16].

The resistance of the inspiratory muscles was assessed according to a protocol validated by our research group [10] through an IIMT performed on the POWERbreathe® K5, properly coupled to an HMEF barrier filter, connected to the BreatheLink® computer software. With a non-continuous incremental characteristic, this test consists of a maximum of 10 stages with a 2-minute interval between them. The test begins with 10 % of the Sindex value, increasing by 10 % at each level, and at the end of each stage, blood glucose, Borg, and HR measurements are performed. The equipment only imposes the determined load on the fourth inspiration for motor learning. Twenty incursions were performed at each level, with a 5-second ventilation cycle guided by a beep from the device. The test was interrupted at the load that the volunteer could not overcome or expressed inability to continue the test, which is called the exhaustion point (EP). Fig. 2 shows the step-by-step process for performing the IIMT.

2.2.2. Glycemic threshold (GT) assessment

The GT of the inspiratory muscles was tested by inspecting the blood glucose at the lowest point of the blood glucose curve in the IIMT, as described by our group in a previous study [11]. Blood samples were collected by puncturing one of the fingertips after asepsis with alcohol (70 %), using a disposable lancet for each stage and a procedure glove for each test. Blood glucose values were obtained by applying the blood to a test strip attached to the On-call plus® glucose monitor (expressed in mg/dL), obtaining the result immediately after contact with the blood on the test strip.

2.2.3. 6-Minute walk test (6MWT)

The 6MWT was performed following the American Thoracic Society/European Respiratory Society guidelines [17]; the test was performed only once within 60 min to 7 days of performing the 6MWT. The distance covered in the 6MWT was the main outcome, the recording of

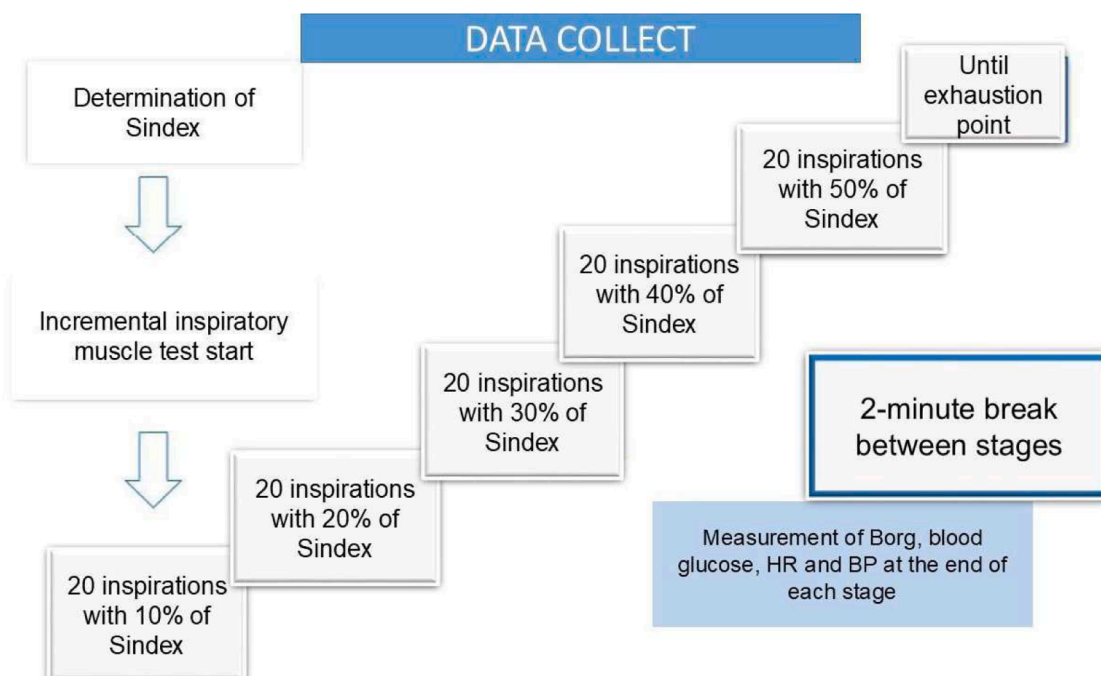


Fig. 2. Incremental inspiratory muscle testing (IIMT). (Adapted from: Oliveira FOO et al., [10].

electrocardiographic RR intervals using the Polar H10® and SpO2 (%) using the Multilaser HC261®, perception of dyspnea using the Borg scale were monitored at the beginning and end of the test.

2.2.4. Assessment of subjective perception of effort

The original Borg subjective effort scale was applied to quantify the intensity of effort in each IIMT load and during the 6MWT [18]. Borg is a scoring scale that ranges from 6 to 20, can be easily used, and is anchored by correlation with heart rate [18].

2.3. Study variables

Predictor variables: GT of inspiratory muscles; Borg of GT; EP of inspiratory muscles; Borg of EP; delta GT/EP as a predictor of anaerobic capacity of inspiratory muscles. Outcome variables: 6MWT, distance (m); 6MWT, % of predicted for sex, age, height and chronotropic response, according to the formula of Brito R et al. [19]; Borg final 6MWT, cardiovascular autonomic balance, measured by HRV: in the time domain: rMSSD for parasympathetic function; in the frequency domain: LF for sympathetic and vagal function (with sympathetic predominance); HF for vagal function; LF/HF ratio [20].

2.4. Statistical analysis plan

For descriptive analysis, the mean and standard deviation were used for parametric variables, and the median, with interquartile ranges for nonparametric variables, was confirmed after the D'Agostino normality test (k-samples). Categorical variables were presented in numbers and percentages.

The correlations between the IIMT, Borg, FC, and cardiovascular autonomic balance variables were verified by Pearson's linear correlation coefficient when parametric and by Spearman's correlation when nonparametric.

A p-value <0.05 was adopted as significant. IBM SPSS Statistics® version 29.0 and Graphpad Prism® 8.0.2 software were used for statistical analysis of the data. The number of participants was established by convenience sampling.

2.5. Ethical aspects

This research was assessed and approved by the research ethics committee of HUUFs, in compliance with Resolution 466/12 of the Conselho Nacional de Saúde (CNS), under CAAE number 63,397,422.9.0000.5546. The Free and Informed Consent Form (FICF) informed all participants about the research.

3. Results

Sociodemographic and anthropometric characteristics, lung function values and COPD staging, are described in Table 1.

After a multimodal analysis of the normality of each variable individually, the measures of central tendency and dispersion were chosen. Fig. 3 shows the overall behavior of median glycemia during the IIMT. A classic initial pattern of reduction in glycemia is observed, followed by an increase in the curve after 20 % of the Sindex.

Table 2 describes the values of the IIMT variables obtained by individualized visual inspection, 6MWT and HRV.

Table 3 presents the correlation analysis between the main variables of the IIMT, 6MWT, HRV, mMRC, Borg of rest, and Borg of IIMT. The GT of the inspiratory muscles was strongly associated with the Borg in the IIMT ($r = 0.84$) ($p < 0.01$). The EP and the delta GT/EP of the inspiratory muscles showed a strong inverse correlation with the LF/HF component ($r = -0.83$), ($p < 0.01$) and ($r = 0.71$), ($p < 0.01$), respectively, and with the resting Borg ($r = 0.75$), ($p < 0.01$) and ($r = 0.85$), ($p < 0.01$) respectively. The GT/EP delta also showed an inverse correlation with the mMRC ($r = -0.68$), ($p < 0.01$) and with the final Borg of the 6MWT

Table 1

Demographic and anthropometric characteristics, lung function, chronic obstructive pulmonary disease staging, and medications used by the study population ($n = 12$).

	Variables	
Demographic and anthropometric characteristics	Age (years)	62 ± 8.6
	Female, n (%)	7 (58)
	Height (m)	1.57 ± 0.86
	BMI (kg/m ²)	29 ± 10
	CAT	18 ± 7.6
	mMRC	1.9 ± 0.9
	Sindex (cmH ₂ O)	58 ± 8.2
Lung function	Rest Borg	8 ± 2.3
	FEV1, % predicted	46 ± 19.5
	FVC, % of predicted	58 ± 13.3
COPD Staging	GOLD A, n (%)	2 (17)
	GOLD B, n (%)	6 (50)
	GOLD E, n (%)	4 (33)
	GOLD stage I, n (%)	1 (8)
	GOLD stage II, n (%)	3 (25)
	GOLD stage III, n (%)	5 (42)
	GOLD stage IV, n (%)	3 (25)
Main drugs in use	LABA, n (%)	8 (67)
	SABA, n (%)	5 (42)
	LAMA, n (%)	12 (100)
	Inhaled corticosteroid, n (%)	3 (25)
	Azithromycin, n (%)	4 (33)

CAT - COPD Assessment Test; FVC - Forced vital capacity; COPD - Chronic Obstructive Pulmonary Disease; GOLD - Global Initiative for Chronic Obstructive Pulmonary Disease; BMI - body mass index; LABA - Long-Acting Beta2-Adrenergic Agonists; LAMA - Long-Acting Muscarinic Antagonists; SABA - Short-acting beta2-adrenergic agonists; Sindex - inspiratory muscle strength index; FEV1 - forced expiratory volume in the first second.

($r = -0.83$), ($p < 0.05$), but not with the distance covered in the 6MWT ($p = 0.99$).

It can be observed in Fig. 4 the distribution and correlation between the IIMT variables with the Borg of GT and rest Borg, inspiratory muscle strength by Sindex, 6MWT variables, self-reported dyspnea by mMRC, and cardiovascular autonomic balance by the LF/HF ratio.

4. Discussion

We tested whether there is an association between IIMT variables and functional capacity, SPE, and cardiovascular autonomic balance in individuals with COPD. Although there was no correlation between the distance covered in the 6MWT and the TMII variables, the final SPE of the 6MWT was strongly correlated with the strength resistance of the inspiratory muscles, the EP. In addition, the data show a strong correlation between the GT and EP of the IIMT with the subjective perception of effort and the LF/HF ratio. On the other hand, there was no relationship between isokinetic inspiratory muscle strength, measured by Sindex, and any of the IIMT or functional capacity variables.

Despite being an exploratory study with a small number of individuals, the association of SPE with IIMT variables is a trend pointed out in previous studies with other populations [11,21]. This result suggests that SPE measured by the Borg scale can be an excellent predictor of load for training inspiratory muscles when using the GT of the IIMT, both for healthy and young populations and for elderly individuals with COPD. Given these data, the question arises: from a functional point of view, wouldn't it be more appropriate to use the GT load rather than only the maximum inspiratory muscle strength to prescribe IMT?

If we look at the traditional IMT prescriptions for individuals with COPD, we will see that the studies use loads ranging from 30 to 85 % of MIP [1]. Considering that most studies start training with 30 to 40 % of MIP, we could infer that they would use loads close to the EP load obtained in the IIMT. This is because, considering the population of the

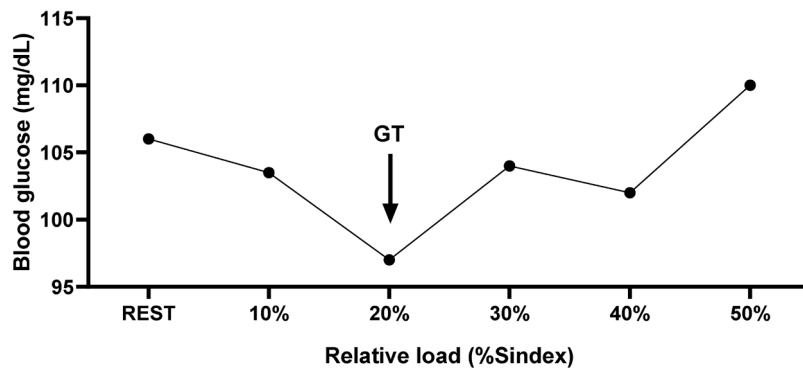


Fig. 3. Median blood glucose behavior during incremental inspiratory muscle testing (IIMT). Glycemic Threshold [GT].

Table 2

Values of the IIMT, 6MWT, and HRV variables.

	Variables	Mean ± SD	CI 95 %
IIMT	GT, relative load (% Sindex)	25 ± 11.6	18 - 32
	GT, absolute head (cmH2O)	14 ± 6.3	10 - 18
	Borg of LG	13 ± 3.9	11 - 16
	EP, relative load (%Sindex)	50 ± 16.5	40 - 60
	EP, absolute head (cmH2O)	28 ± 10	22 - 35
	Borg of EP	19 ± 1.2	18 - 20
	Delta GT/EP, relative load (%)	25 ± 19.3	13 - 37
6-Minute Walk Test	6MWT, distance (m)	473 ± 21	458 - 489
	6MWT distance, % of predicted	89 ± 3.7	87 - 92
	6MWT, Borg final	15 ± 3.4	13 - 18
Heart rate variability	RMSSD	16 ± 5.4	13 - 20
	LF	51 ± 21	38 - 67
	HF	37 ± 22	22 - 53
	LF/HF	1.6 (0.95 - 3.60)	0.6 - 4.7

@ - Variable described in the median; SD – Standard deviation; GT – glycemic threshold; EP – point of exhaustion; IIMT – Incremental inspiratory muscle test; Sindex – inspiratory muscle strength index; 6MWT – 6-minute walk test; rMSSD - square root of the mean of the square of the differences between adjacent normal RR intervals; LF – low frequency; HF – high frequency.

present study, 40 % of the Sindex obtained represents an absolute load of 24 cmH2O, which corresponds to approximately 86 % of the absolute EP load (28 cmH2O) and a load 60 % above the GT load (14 cmH2O), Table 2. We could ask ourselves whether the fact that the studies used MIP and not Sindex in their majority influences the result. However, taking as a basis the study by Silva et al. [22], carried out in a population with heart failure, we would say no since, in this study, there was clear parity between MIP and Sindex. Therefore, another question we can raise is whether the inconsistent IMT results reported in research on patients with COPD [1] for improving dyspnea, functional exercise capacity, and quality of life are linked to the use of inadequate loads (mentioned above).

The diaphragm is a muscle that essentially has resistance (Type I) and resistance strength (Type IIA) fibres in its composition, which gives it high resistance capacity and resistance strength [23]. When working with loads much higher than those of the GT, it is possible that both the biomechanics of movement (greater use of accessory muscles) and the functional characteristics of the inspiratory muscles are not adequately trained, which consequently does not reflect gains in functional capacity, quality of life and dyspnea. In previous studies using inspiratory training loads in the GT, we observed satisfactory improvement in quality of life [24] and functional capacity [11,24]. The most accurate answer to this question will come after conducting a clinical trial using control groups, with IMT based on MIP and IMT based on the GT. In

Table 3

Correlations between variables of incremental inspiratory muscle testing, 6-minute walk test, heart rate variability, modified Medical Research Council scale, and rest Borg.

Variables		GT (% Sindex)	EP (% Sindex)	Delta GT/EP	6MWT, % of predicted
Borg IIMT	r-value	0.84	0.40	–	–
	p-value*	<0.01	0.19	–	–
Sindex	r-value	–0.49	–0.04	0.26	0.20
	p-value*	0.10	0.90	0.40	0.56
6MWT, % of predicted	r-value	–0.25	–0.18	–0.002	–
	p-value*	0.47	0.61	0.99	–
6MWT, Borg final	r-value	0.60	–0.54	–0.83	–0.11
	p-value*	0.06	0.10	<0.01	0.76
RMSSD	r-value	–0.26	0.39	0.51	–0.22
	p-value*	0.43	0.23	0.10	0.56
LF/HF	r-value#	<0.01	–0.83	–0.71	0.33
	p-value#	0.98	<0.01	0.01	0.38
mMRC	r-value	0.43	–0.49	–0.68	–0.22
	p-value*	0.47	0.10	0.01	0.56
Rest Borg	r-value	0.34	–0.75	–0.85	–0.05
	p-value*	0.26	<0.01	<0.01	0.88

GT – glycemic threshold; EP – point of exhaustion; Sindex – inspiratory muscle strength index; 6MWT – 6-minute walk test; mMRC - modified Medical Research Council scale; rMSSD - root mean square of the square of the differences between adjacent normal RR intervals. LF – low frequency; HF – high frequency.

* Pearson's linear correlation coefficient.

Spearmam correlation test.

addition to this line of reasoning, we observed that most studies evolved the percentage load of the IMT throughout the rehabilitation period. In [5] what we proposed for determining the IMT load, we maintained the same Borg, evolving only the absolute load and not the percentage of MIP [5,24].

Analysing the other findings of this exploratory study, we reported no association between the IIMT variables and the distance walked in the 6MWT, but rather with Borg's SPE at the end of the 6MWT. These findings suggest that the condition of the inspiratory muscles in the TMII may not influence the walking distance during 6 min but may

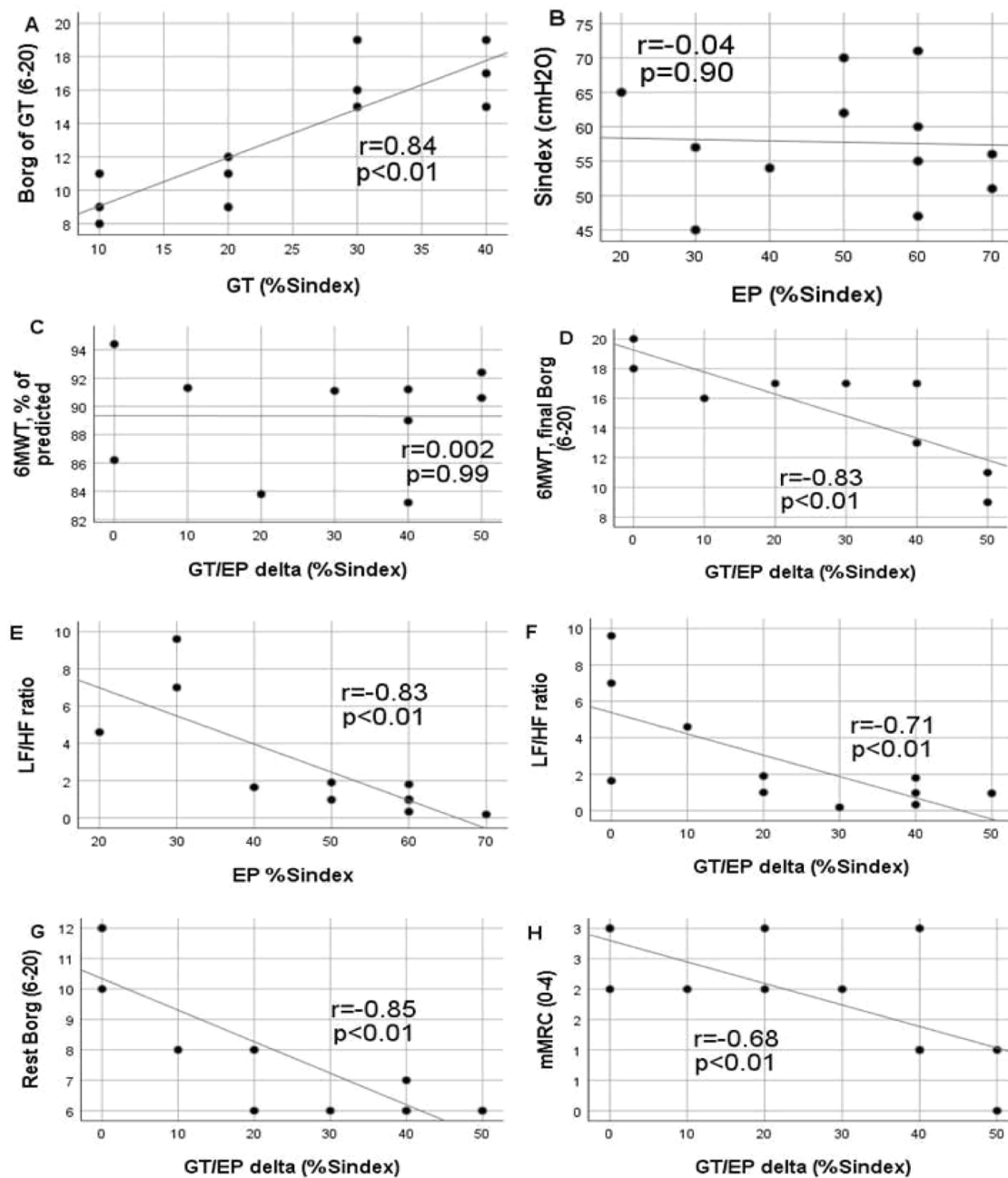


Fig. 4. Correlation between the variables of the Incremental Inspiratory Muscle Test with the subjective perception of Borg effort, autonomic control (LF/HF ratio), 6-minute walk test variables, inspiratory muscle strength and self-reported dyspnea by mMRC.

significantly affect dyspnea at the end of this period of effort. Another point that reinforces this hypothesis is the correlation between the mMRC scale and the delta GT/EP, which leads us to the hypothesis that the lower the functional aerobic reserve of the inspiratory muscles (delta GT/EP), the greater the severity of dyspnea in exertional activities in daily life, a function measured by the mMRC. This confirms the inference that training the inspiratory muscles at the GT load is more efficient than at loads closer to the EP since the conditioning of the muscle fibre at the GT stimulates specific favourable metabolic responses that can significantly improve the aerobic capacity of the inspiratory muscles [25]. It is plausible that this IMT approach would be contradictory since, in individuals with COPD, there is a mutation of Type IIA and IIX fibres to Type I fibres [26]. Therefore, we could argue that training the inspiratory muscles at loads higher than those of GT would be more indicated. However, when we shed more light on the findings of the

studies that demonstrated this conversion (Type II to I fibres) [26], we observe that in addition to this mutation, there is also a decrease in the capacity of Type I fibres, that is, they become less functional (efficient). Therefore, working at GT load could provide better adaptability to both Type I and Type IIA fibres, and the evolution of this capacity may be reflected in the ability to perform the submaximal exercise and the perception of effort.

Another important point to be discussed is the biomechanics of ventilation. Satoake M et al. [27] showed that the increase in self-reported dyspnea by Borg during the 6MWT in individuals with COPD appears to be related to dynamic hyperinflation. Understanding dyanapsis [28,29] helps to clarify this mechanism. Physiologically, during exercise, ventilatory mechanics are regulated so precisely that the work performed by the respiratory muscles is minimised [29]. However, since expiratory flow is limited, inspiratory reserve volume

must be increased to increase flow during exercise and even at rest. High volume causes the diaphragmatic fibres to be pushed to maximum shortening, thus increasing the muscle's biomechanical disadvantage and oxygen consumption [27]. Furthermore, excessive diaphragmatic stretching stimulates a reflex response mediated by the muscle spindle and type III and IV afferent nerve fibres [30] to the cerebral cortex, generating a high subjective perception of effort and reducing respiratory efficiency [31,32]. Therefore, it is plausible to deduce that IMT performed with high loads or above the GT of the inspiratory muscles can promote positive feedback of this mechanism and limit the gains that IMT could confer to this population.

When observing the graphs in Fig. 4 (E and F), we note a strong association between the Sindex and the delta GT/EP and the LF/HF ratio at rest. Likely, a reduction in the parasympathetic domain and an increase in the sympathetic tone at rest may mitigate the sympathetic reserve during exertion and, consequently, blood flow to the diaphragm [33]. The combination of reduced oxygen supply with decreased biomechanical effectiveness of respiratory muscle function may be the determining factor in the dyspnea reported by this population during activities of daily living. This aspect reinforces the idea that IMT should be performed with lower loads (GT load) that minimise the decrease in biomechanical performance rather than with higher loads (close to EP), as most studies report.

Our results are broad and should be interpreted cautiously to avoid hasty conclusions. The main limitation of the extrapolation and confirmation of the results is that this is an exploratory study with few individuals and a cross-sectional analysis. Another point is that we did not balance the sample between the sexes and could not perform any analysis based on COPD staging. Furthermore, the fact that this is the first study to evaluate the GT of the inspiratory muscles with the IIMT method in individuals with COPD limited the inferences and the better elucidation of our results with the current literature.

The main clinical inference of this study is the possibility of using the GT of the inspiratory muscles to prescribe IMT. This may be a determining factor for the assertiveness of IMT in individuals with COPD. In addition, the possibility of using Borg reduces clinical costs and makes the practice more accessible and noninvasive. The findings of this study are similar to what we found in healthy and irregularly active individuals [11], regarding the correlation between the GT of the inspiratory muscles and Borg. The mean Borg score of GT was also similar, which reinforces the sensitivity of Borg in predicting the training load of the inspiratory muscles, making it possible to prescribe IMT even without prior manovacuometry assessment. In addition, other advantages, such as the practicality of applying Borg and its low financial cost, make this method clinically accessible. To test the above hypotheses, randomized clinical trials will be needed to evaluate the effect of IMT in people with COPD using the GT of the inspiratory muscles as a parameter.

5. Conclusions

Our results indicate that the glycemic threshold (GT) and the point of exhaustion (EP) of the inspiratory muscles are strongly associated with the subjective perception of effort in individuals with chronic obstructive pulmonary disease. In addition, the inspiratory muscles' aerobic capacity (delta GT/EP) was strongly associated with dyspnea on exertion and cardiovascular autonomic balance.

Funding

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Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Hospital

Universitário of Universidade Federal de Sergipe (HUUFS), São Cristóvão, SE, Brazil in compliance with Resolution 466/12 of the National Health Council, under CAAE number: 63397422.9.0000.5546 on december 5, 2022.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Abbreviations

The following abbreviations are used in this manuscript:

IIMT	Incremental inspiratory muscle testing
COPD	Chronic obstructive pulmonary disease
GT	Glycemic threshold
FC	Functional capacity
6MWT	Six-minute walk test
EP	Exhaustion point
mMRC	modified Medical Research Council
CAT	COPD Assessment Test
BP	Blood pressure
BMI	Body mass index
Sindex	Muscle pressure index
IMT	Inspirator muscle training
HR	Heart rate
HRV	Heart rate variability
LF	Low frequency
HF	High frequency
rMSSD	square root of the mean of the square of the differences between adjacent normal RR intervals
GOLD	Global Initiative for Chronic Obstructive Pulmonary Disease
FVC	Forced vital capacity

CRedit authorship contribution statement

Wasly S. Silva: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Felipe J. Aïdar:** Writing – review & editing, Writing – original draft, Software, Investigation, Data curation. **Georgian Badicu:** Writing – review & editing, Writing – original draft, Visualization, Supervision. **Juliana D. Andrade:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation. **Patricia F. Sá:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources. **José B. Neto:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Luca Paolo Ardigo:** Writing – review & editing, Writing – original draft, Visualization. **Jefferson Petto:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision.

Declaration of competing interest

The authors declare no conflicts of interest.

Data availability

Data will be made available on request.

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