Inspiratory muscle performance relative to the anaerobic threshold in patients with COPD

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ABSTRACT: Rehabilitation programmes in chronic obstructive pulmonary disease (COPD) require exercise training above the anaerobic threshold. However, not all COPD patients develop metabolic acidosis during exercise. The hypothesis of this study was that non-exercise variables, characterizing the mechanical load on the inspiratory muscles during breathing at rest, can be used to reliably predict which patients with COPD are not able to develop metabolic acidosis during exercise.

Thirty participants with COPD performed a symptom-limited cycle ergometer test. The oesophageal pressure/time index (PTIoes: the product of pressure magnitude and duration), the mean rate of pressure development during inspiration (Poes/T_I), and the mean airway resistance (Raw)/maximal oesophageal pressure (Poes$_{max}$) ratio served as indices for the mechanical load on the inspiratory muscles. The oxygen uptake ($\dot{V}o_2$) at which plasma standard bicarbonate was seen to decrease from its baseline value was taken as the anaerboic threshold (AT).

Mean Raw was significantly higher in those patients in whom the AT could not be detected. No other lung function parameters measured at rest allowed the accurate selection of those patients who did or did not develop exercise metabolic acidosis. On the other hand, Raw/Poes$_{max}$, PTIoes and Poes/T_I were significantly different in the two patient groups. Additionally, whereas in the patient group with identifiable AT exercise hyperpnoea produced a non-linear increase of Poes/T_I with respect to PTIoes above the AT, in the patient group without identifiable AT there was a linear relationship between Poes/T_I and PTIoes throughout exercise.

We conclude that the determination of inspiratory muscle load indices at rest may be useful in pulmonary rehabilitation programmes, for identifying those patients with COPD who do not develop exercise induced metabolic acidosis. Our results indicate that exercise hyperpnoea produces a different pattern of inspiratory muscle output (when analysed in terms of the pressure developed, as well as the duration of contraction and rate of pressure development) in patients with and without identifiable AT.
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Patients with chronic obstructive pulmonary disease (COPD) generally have limited exercise capacity because of reduced ventilatory capacity [1, 2]. Several approaches for reducing the ventilatory limitation have been defined. Reduction of exercise metabolic acidosis by exercise training is a potential approach to reducing the ventilatory effort for a given level of work. Exercise training, therefore, is considered to be a cornerstone of rehabilitation programmes for COPD patients [3, 4]. A training programme above the anaerobic threshold (AT) was shown to be more effective than one below the AT [5]. However, not all patients with COPD develop metabolic acidosis during exercise. Previous studies have examined quantitative relationships between pulmonary function at rest and

exercise metabolic acidosis, in order to correlate the reduced or absent exercise metabolic acidosis with specific defects in the respiratory system [6]. Variables examined as determinants of exercise metabolic acidosis include expiratory spirometric data and diffusing capacity. But, pulmonary function data at rest cannot be used to distinguish individual patients who would or would not develop metabolic acidosis [6]. In addition to reduced expiratory airflow and impaired gas exchange, patients with COPD are also susceptible to reduction of inspiratory muscle strength [7]. The increased airway resistance and hyperinflationary characteristic of COPD affect respiratory muscle function. The increased resistance imposes a greater than normal load on the inspiratory muscles,

whilst hyperinflation imposes a mechanical disadvantage on the inspiratory muscles by shortening their fibres.

We wanted to determine whether assessment of inspiratory muscle load indices, measured during breathing at rest, could improve our ability to predict which COPD patients would not reach the AT. Our study examined the following questions in detail: 1) Can inspiratory muscle load indices be used to predict which patients with COPD would not develop exercise metabolic acidosis? and 2) Does the increased mechanical load during exercise hyperpnoea produce a different pattern of inspiratory muscle output (when analysed in terms of the pressure developed, as well as the duration of contraction and the rate of pressure development) in patients with and without identifiable AT?

Methods

Subjects

For the purpose of this study, we defined chronic airflow obstruction as clinically stable primary pulmonary disease with the following characteristics: 1) ratio of forced expiratory volume in one second (FEV_1) to forced vital capacity (FEV_1/FVC) of less than 70%; 2) total lung capacity greater than 80% of the predicted value; and 3) change in FEV_1 after bronchodilator inhalation of less than 15%. Thirty ambulatory male out-patients fulfilled this definition of COPD. Their mean age was 55±8 yrs (range 44–76 yrs), mean weight was 68±11 kg (range 52–86 kg), and mean height 169±10cm (range 155–188 cm). Respiratory impairment ranged from mild to severe [8]. None had evidence of endocrine, orthopaedic or primary cardiac disorders. Patients with clinical or electrocardiographic evidence of coronary artery disease, hypertension or cor pulmonale were excluded. Chronic medications included aminophylline and inhaled beta-adrenergic agents. The serum aminophylline levels were in the therapeutic range in all patients. No patient was on oral steroids. Patients gave institutionally reviewed informed consent for participation in this study, which was approved by the local Ethics Committee.

Protocol

Lung function analysis consisted of spirometry and plethysmography. Spirometry and the 12 s maximum voluntary ventilation (12 s-MVV) test were performed by using an open system, with integration of the flow signal; whole body plethysmography was carried out by the constant volume method (Jaeger, Würzburg, Germany). FVC, FEV_1, and total lung capacity (TLC) were also compared with the reference values given by the European Community for Coal and Steel [9]. Sniff-assessed maximal oesophageal pressure ($Poes_{max}$) was used as a parameter for global inspiratory muscle strength [10]. Sniff trials were performed at resting end-expiration. The oesophageal pressure was arbitrarily assigned zero at the start of each sniff trial, therefore, only pressure changes relative to the initial level were recorded. The patients were instructed that their sniffs be short, full strength and executed through the nose with the mouth closed. Noseclips were not used. The period allowed between sniffs was 30–40 s. When a plateau of sniff Poes was reached (usually within five sniffs), an extra 10 maximal sniffs were carried out to make sure that there was no further increase. The highest oesophageal pressure was then selected for analysis. Progressive, incremental tasks were performed on an electrically braked cycle ergometer (Jaeger, Würzburg, Germany) whilst the patient breathed room air. Each patient sat at rest on the bicycle for 4 min. Work rate was then increased (25 W every 2 min) to maximum tolerated exercise.

Continuous measurements and technical details

Minute ventilation ($\dot{V}E$), tidal volume (VT), breathing frequency (fb), oxygen uptake (Vo_2) and carbon dioxide output (Vco_2) were measured from the analysis of the expirate every 30 s using a computerized system (EOS Sprint, Jaeger, Würzburg, Germany). This system features pneumotachographic airflow measurement and a mixing chamber for metabolic rate measurement. Daily calibration of this system was accomplished with a 2 l syringe and precision gas mixtures. The expired and inspired gas flows, both measured with a separate pneumotachograph (model PT18, Jaeger, Würzburg, Germany) connected to a pressure transducer (model PT, Jaeger), were continuously recorded on a Beckman strip-chart recorder (model 511A, Fullerton, CA, USA). The oesophageal pressure swings at rest and during exercise were also recorded on the strip-chart recorder immediately below the flow tracings. For the recording of the oesophageal pressure swings, the same equipment was used as for the sniff trials. The catheter was described in detail previously [11]. A flexible, distilled-water perfused catheter was first passed through the nose into the stomach with its distal end, and by observing the pressure signal, it was then withdrawn until it reached the middle third of the oesophagus [12]. The proximal end of the catheter was connected to a pressure transducer (Gould-Statham, P231D, Cleveland, OH, USA).

During exercise, the onset of inspiratory muscle activity was identified on the pressure tracing as the point of sharp decline in Poes, which sometimes preceded the beginning of inspiratory flow. The intrinsic positive end-expiratory airway pressure - the inspiratory pressure developed before the onset of inspiratory flow - was also considered for the calculation of inspiratory muscle load. From the oesophageal pressure-time graphs thus obtained, at least eight breathing cycles of each load increment were chosen (two breathing cycles per 30 s) for calculating the oesophageal pressure-time integral by manually digitizing. It was expressed as a fraction of the patient's maximal oesophageal pressure and total breath cycle duration (Ttot). This parameter was called the oesophageal pressure time index: $PTIoes = Pbreath/Poes_{max} \times TI/Ttot$. (Pbreath is the average inspiratory oesophageal pressure

developed per tidal breath, $Poes_{max}$ is the maximal pressure that can be developed by the patient and T_I/T_{tot} is the fraction of inspiration to total breathing cycle duration). Inspiratory time (T_I), respiratory cycle duration (T_{tot}) and the resultant T_I/T_{tot} were measured directly from the Poes tracings. The pressure-time curves were also used to compute the mean rate of pressure development (peak inspiratory pressure/time to peak pressure, $Poes/T_I$). Whereas the oesophageal pressure time index takes into account the pressure developed by the inspiratory muscles and the relationship between contraction- and relaxation time, the $Poes/T_I$ values reflect the mean pressure change during inspiration. The Hill-equation indicates that the energy cost of skeletal muscle contraction depends on the pressure developed, the duration and the velocity of contraction [13]. The PTIoes and $Poes/T_I$ values were used as indirect representation of these factors. Heart rate (HR) was measured from the R to R interval of the electrocardiogram, recorded from a 3-lead configuration. Arterial blood pressure was measured every 2 min by sphygmomanometer. Blood from an indwelling radial artery catheter (modified Seldinger technique) was sampled at rest, and every other minute during the phase of incremental exercise, for determining arterial O_2 and CO_2 partial pressure (Pao_2 and $Paco_2$ respectively) and arterial blood pH. Plasma bicarbonate was determined using the Henderson-Hasselbach equation, and standard bicarbonate was calculated using the nomogram of SIGGAARD-ANDERSON and ENGEL [14]. Standard bicarbonate was used in the further analysis.

Data analysis

Anaerobic threshold was determined by the $\dot{V}o_2$ at which there was a fall in plasma standard bicarbonate. Thereby a log-log plot of bicarbonate *versus* $\dot{V}o_2$ was used. This method was previously described in detail by BEAVER *et al.* [15]. The patients were subdivided into two groups, depending on whether there was an identifiable AT. PTIoes and $Poes/T_I$ served as inspiratory muscle load indices at rest. The third parameter used for characterizing inspiratory muscle load at rest was the $Raw/Poes_{max}$ ratio, as it was shown that this parameter is a major determinant of lung impedance and ventilatory capacity in COPD patients [16, 17]. In order to analyse the changes caused by exercise hyperpnoea with respect to the pressure development, the duration and the velocity of contraction of the inspiratory muscles, $Poes/T_I$, was plotted against PTIoes for each separate patient. For each patient, a single linear regression was initially fit to all data and used for later statistical comparisons. Then a second line was fitted to the data. Regression lines were calculated for all possible divisions of the data into two contiguous groups, and the pair of lines yielding the least-pooled residual sum of squares was chosen to represent the best fit. An analysis of variance determined whether a significant ($p<0.01$) reduction in the total sum of squares was achieved by adding the second line segment. The corresponding $\dot{V}o_2$ value was determined at the intersection of the two lines of the most appropriate model. This $\dot{V}o_2$ value was statistically compared with the $\dot{V}o_2$ at which there was a fall in plasma standard bicarbonate (AT).

Statistical analysis involved linear regression analysis, analysis of variance (ANOVA) and discriminant analysis, in order to discriminate the two groups with respect to inspiratory muscle load at rest, inspiratory muscle strength, and lung function parameters. All data are presented as mean±SD. A probability level of $p<0.05$ was considered statistically significant.

Results

Table 1 shows the anthropometric characteristics, pulmonary and respiratory muscle function parameters of the 30 patients with COPD. They were divided into two groups for comparison, on the basis of exercise metabolic acidosis development. Group 1 had 18 patients, in whom anaerobic threshold could be detected by the fall in plasma standard bicarbonate. Group 2 consisted of 12 patients, in whom the AT during exercise could not be differentiated. Mean Raw was significantly greater in the Group 2 patients. Group 1 patients had slightly higher mean maximal oesophageal pressure and MVV values, although they were not statistically significant. All other pulmonary function data at rest were also not statistically different in the two groups. No patient in either group had a Pao_2 lower than 8 kPa and a $Paco_2$ value greater than 6 kPa at rest. Examination of the blood gas and pH responses at peak exercise showed that no patient became severely hypoxaemic with exercise; only one patient in Group 2 had an end-exercise Pao_2 lower than 8 kPa. The breathing pattern at rest did not allow distinction between patients with and without exercise metabolic acidosis.

Table 1. – Anthropometric, lung function and respiratory muscle data in Group 1 patients (anaerobic threshold could be detected) and in Group 2 patients (anaerobic threshold could not be detected).

	Group 1 n=18	Group 2 n=12
Age yrs	58±6	54±12
Height cm	169±9	168±9
Weight kg	69±10	67±12
FVC *l*	2.84±0.82	2.49±0.67
FVC % pred	76±16	71±11
FEV_1 *l*	1.18±0.39	0.94±0.31
FEV_1 % pred	41±16	37±8
FEV_1/FVC %	43±14	38±9
TLC *l*	7.7±2.3	7.3±3.1
TLC % pred	140±18	135±21
RV *l*	4.93±1.9	4.80±2.12
RV/TLC %	63±8	66±7
Raw $cmH_2O·l^{-1}$	4.9±2.12	7.03±1.2*
$Poes_{max}$ cmH_2O	55.8±13.2	46.3±20.1
MVV *l*	45.4±13.7	38.6±12.4

Data are presented as mean±SD. *: $p<0.05$ *vs* Group 1 patients; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; TLC: total lung capacity; RV: residual volume; Raw: mean airway resistance; $Poes_{max}$: sniff assessed maximal oesophageal pressure; MVV: maximal voluntary ventilation measured over 12 s.

Table 2. – Resting values and exercise data at highest workload in the 30 COPD patients

	Rest		End-exercise	
	Group 1 n=18	Group 2 n=12	Group 1 n=18	Group 2 n=12
$\dot{V}O_2$ $l·min^{-1}$	0.34±0.12	0.32±0.10	1.36±0.55	1.05±0.41
HR $b·min^{-1}$	81.8±8.8	83.3±8.0	147.4±10.2	144.5±12.4
$\dot{V}E$ $l·min^{-1}$	11.9±2.7	10.8±1.4	44.8±13.7	35.0±9
$\dot{V}E$/MVV %	29±5	34±6	99±25	91±30
$\dot{V}t$ l	0.57±0.1	0.46±0.09*	1.3±0.4	0.95±0.15*
fb $br·min^{-1}$	20.8±3.7	24.0±4	35.4±6.1	37.4±9.1
T_I s	1.06±0.16	0.97±0.23	0.63±0.13	0.56±0.13
T_I/tot %	36.8±3.9	37.0±5.0	35.9±4.6	33.8±6.1
HCO_3^- $meq·l^{-1}$	23.9±0.9	24.1±1.1	19.2±1.4	23.4±1.2+
Pao_2 kPa	9.23±1.0	9.14±1.29	8.89±1.10	8.65±1.35
$Paco_2$ kPa	5.33±0.73	5.88±1.04	5.64±0.67	6.09±1.12

$\dot{V}O_2$: oxygen uptake; HR: heart rate; $\dot{V}E$: minute ventilation; VT: tidal volume; fb: breathing frequency; T_I: inspiratory time; T_I/Ttot: inspiratory duty cycle; HCO_3^-: plasma standard bicarbonate; Pao_2 and $Paco_2$: arterial partial pressure of oxygen and carbon dioxide respectively; *: p<0.05; +: p<0.01 vs Group 1 patients

Table 3. – Inspiratory muscle load indices at rest in the 30 COPD patients

	Group 1 n=18	Group 2 n=12	p
Raw/Poes$_{max}$ $s·l$	0.091±0.041	0.160±0.065	<0.01
Poes/T_I $cmH_2O·s^{-1}$	9.92±3.46	18.13±7.5	<0.05
PTIoes	0.048±0.016	0.081±0.017	<0.001
Pbreath/Poes$_{max}$ %	13.2±3.3	21.9±6.6	<0.001
T_I/Ttot %	36.8±3.9	37.0±5.0	NS

Raw/Poes$_{max}$: ratio of mean airway resistance to sniff-assessed maximal oesophageal pressure; Poes/T_I: peak inspiratory pressure/time to peak pressure; PTIoes: oesophageal pressure time index; Pbreath: average inspiratory oesophageal pressure developed per tidal breath; T_I/Ttot: fraction of inspiration to total breathing cycle duration; PTIoes: Pbreath/Poes$_{max}$ × T_I/Ttot; COPD: chronic obstructive pulmonary disease. NS: nonsignificant.

However, mean tidal volume at end-exercise was significantly higher in those who developed metabolic acidosis (table 2).

Discriminant analysis was performed to predict those COPD patients without detectable AT during exercise. PTIoes, Poes/T_I, and Raw/Poes$_{max}$ were the quantitative measurements at rest which discriminated the Group 1 from the Group 2 patients. These three variables were significantly higher in the Group 2 patients (table 3). Discriminant analysis was successful in classifying all of the Group 2 patients correctly. Classification results are given in table 4.

Table 4. – Classification results of discriminant analysis performed in order to predict those COPD patients with and without detectable anaerobic threshold during exercise*

Actual group	Predicted group					
	1		2		Total	
	n	%	n	%	n	%
1	15	83.3	3	16.7	18	100
2	0	0.0	12	100.0	12	100

*: PTIoes, Poes/T_I, Raw/Poes$_{max}$ were the quantitative measurements at rest which discriminated among Group 1 (AT was detected in 18 subjects) and Group 2 (no AT could be defined in 12 subjects), (p<0.001). For abbreviations see legend to table 3.
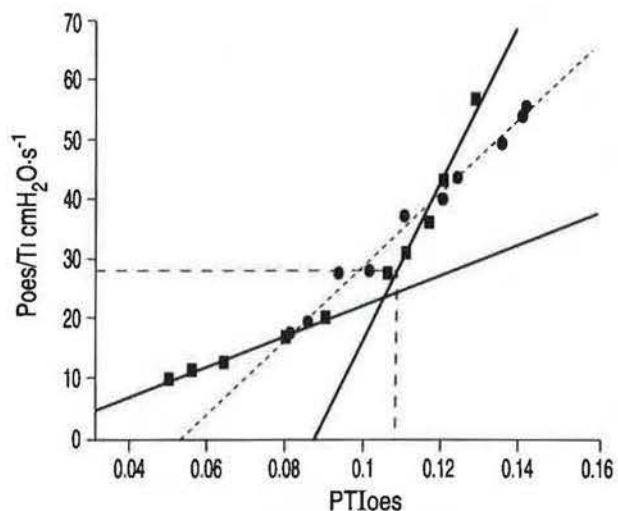

Fig. 1. – Relationship between Poes/T_I and PTIoes characterizing inspiratory muscle output in the two patient groups during exercise. Circles and squares represent the mean values for the patients without and with detectable anaerobic threshold (AT) at every 10% increment of maximum oxygen uptake ($\dot{V}O_2$max), beginning with 10%. A single linear regression was used in Group 2 patients (no detectable AT), whereas a two segment model resulted in the best fit in Group 1 patients. The mean $\dot{V}O_2$ at the intersection was not significantly different from the $\dot{V}O_2$ at the AT. The two dashed lines indicate the PTIoes and Poes/T_I values at the AT. Poes/T_I: mean rate of pressure development during inspiration (peak inspiratory pressure/time to peak pressure); PTIoes: oesophageal pressure time index.

When Poes/Ti was plotted against PTIoes, ANOVA could show no significant reduction in the total sum of squares through recalculation of the initial linear regression model in the 12 patients without detectable AT (Poes/Ti = 630 × PTIoes - minus 33.1; r=0.93). In the remaining 18 subjects, a two segment model resulted in the best fit (fig. 1). The linear regression of the first segment was: Poes/Ti = 266 × PTIoes - 3.5; r=0.09; and of the second segment it was: Poes/Ti = 1,365 × PTIoes - 118.9; r=0.88. The mean $\dot{V}O_2$ at the intersection (0.88 ± 0.23 $l\cdot min^{-1}$) was not significantly different from the $\dot{V}O_2$ at the AT (0.93 ± 0.26 $l\cdot min^{-1}$; p>0.05).

Discussion

Our study showed that using inspiratory muscle load indices at rest, we can satisfactorily predict which COPD patients are not able to develop metabolic acidosis during exercise, and that there is a different relationship between Poes/Ti and PTIoes during exercise hyperpnoea in COPD patients with and without detectable AT.

Since conventional lung function parameters cannot be relied upon to predict which COPD patients will develop exercise metabolic acidosis [6, 18, 19], it is all the more important that our result enables us to make that prediction. Quantitative testing of inspiratory muscle function has previously been applied to other clinical problems, including prediction of the likelihood of successful weaning from mechanical ventilation [20], and peak oxygen consumption in patients with COPD [21, 22]. With this study, we show that inspiratory muscle load decisively affects exercise capacity at submaximal workloads.

Measurement of the ventilatory responses to exercise provides useful information about the control of breathing in healthy people and in patients with pulmonary disease [23]. The ventilatory responses were analysed either in terms of fb and V_T, or in terms of Ti/Ttot and V_T/Ti. However, until now, it was not known how the inspiratory muscles respond to the increased ventilation load and impedance load during exercise hyperpnoea in COPD patients. When we analyse inspiratory muscle output in terms of pressure developed, duration of contraction, and rate of pressure development, we see that the inspiratory muscles react differently to exercise hyperpnoea.

The pressure time index, which describes inspiratory muscle performance, is widely used to predict respiratory muscle endurance time or O_2 consumption [24, 25]. In our study we used PTIoes, which includes both the relative force (Pbreath/Poes$_{max}$), and duration of contraction (Ti/Ttot). PTIoes reflects, therefore, the balance between the mechanical impediments to breathing and the capacity of the respiratory muscles to cope with them. Since we did not measure the relaxation pressure-volume curves of the chest wall, we cannot exactly say how much of the oesophageal pressure swing generated by each breath is caused by active muscle contraction. It was certain, however, that a pronounced recruitment of the inspiratory muscles was necessary, because at end-exercise the ratios of peak inspiratory pressure/Poes$_{max}$ were $56.6\pm9.7\%$ and $72.1\pm7.1\%$ for the Group 1 and Group 2 patients respec-

tively. The recoil pressure of the chest wall is only about -2.5 cmH$_2$O at functional residual capacity (FRC) [26]. The Poes$_{max}$ values used in calculating the ratio were static measurements at FRC at rest. It is known, however, that COPD patients have pulmonary hyperinflation during exercise [27]. The increase in end-expiratory lung volume would be expected to reduce the capacity of the inspiratory muscles to generate pressure. The ratio of peak inspiratory pressure/Poes$_{max}$ was, therefore, probably even higher than our results indicated.

Apart from the impedance component of inspiratory muscle load, Pbreath is also related to mean inspired flow (V_T/Ti). Hence, PTIoes (Pbreath/Poes$_{max}$ × Ti/Ttot) is related to minute ventilation (V_T/Ti × Ti/Ttot). Accordingly, at constant Ti/Ttot the oesophageal pressure time integral within one breath (Pbreath × dTi) is related to tidal volume. Poes/Ti on the other hand reflects flow and breathing frequency (fb is directly proportional to 1/Ti at constant Ti/Ttot). Recent studies have demonstrated that the pressure time index may be of limited value to characterize the load on the inspiratory muscles, when inspiratory flow changes appreciably [28, 29]. Therefore, it seems reasonable to relate PTI to the mean rate of pressure development (Poes/Ti). The PTIoes - Poes/Ti relationship can thus be compared with the $\dot{V}E$-V_T relationship, known as the Hey plot [30]. Both slopes have the dimensions of frequency. In healthy subjects, a shift from primarily V_T to predominantly increased fb occurs at or near the AT. In our study, no clear inflection point of the $\dot{V}E$-V_T relationship could be identified in 10 of the 18 Group 1 patients. On the other hand, in all Group 1 patients, an inflection point could be identified when Poes/Ti was plotted against PTIoes. The $\dot{V}O_2$ at this point corresponded to the $\dot{V}O_2$ at the AT determined by the fall in plasma standard bicarbonate. In COPD patients, who have lung function as well as inspiratory muscle function impairment, the impedance component of inspiratory muscle load plays a decisive part in addition to the ventilatory component. The PTIoes and Poes/Ti values reflect not only the ventilation load and the given breathing pattern, but in addition they also take into consideration the impedance component of respiratory muscle load. In the Group 1 patients at below AT levels, Poes/Ti rose slowly, associated with an increase of Pbreath×dTi. Above the AT, further increases in PTIoes are met with changes in the rate of pressure development, preventing the increase in Pbreath×dTi that would otherwise occur. The increase of Poes/Ti above the AT enables one to keep the duty cycle constant throughout exercise, in spite of the increasing ventilatory requirements. Indeed, an increase of contraction velocity, just like an increase of PTIoes, demands more energy [29]; by keeping the duty cycle constant, however, one ensures an optimal diaphragmatic blood flow. It could be shown in animal experiment that the highest diaphragmatic blood flow per breathing cycle is achieved at duty cycles of 0.4, regardless of the pressure generated [31]. If the changes in the rate of pressure development did not prevent a greater increase of Pbreath×dTi, Ttot would have to be increasingly lengthened to keep the duty cycle in the optimal range.

In the Group 2 patients, the Pbreath/Poes$_{max}$ ratio was

already higher at rest, in comparison with the Group 1 patients, and at end-exercise, higher values of Pbreath/ Poes$_{max}$ were reached than in Group 1 patients. The duty cycle was, however, the same in both groups. For the Group 2 patients, the only way to prevent further increase in Pbreath×dTi and PTioes is by changing the rate of pressure development. Their Poes/Ti values actually increased sharply right at the beginning of the exercise test, so that in contrast to the Group 1 patients, no inflection point in the PTioes - Poes/Ti relationship could be identified.

To summarize, our study shows that inspiratory muscle load indices at rest can be used to predict which COPD patients are not able to develop exercise metabolic acidosis. Furthermore, facing increased breathing load during exercise hyperpnoea the two patient groups adopt a different pattern of inspiratory muscle output, when muscle output is analysed in terms of pressure developed, duration of contraction and rate of pressure development. The results of our study provide new insight into the regulation of breathing in response to exercise hyperpnoea in COPD patients.

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