PARADOXICAL MOVEMENT OF THE LOWER RIB CAGE AT REST AND DURING EXERCISE IN COPD PATIENTS

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ABSTRACT

Paradoxical inward displacement of the costal margin during inspiration is observed in many COPD patients at rest but its importance is unclear.

We studied 20 patients (FEV1=32.6±11.7, FRC=186±32%pred) and 10 healthy controls at rest and during symptom-limited incremental exercise. With optoelectronic plethysmography we quantified the phase shift between pulmonary and abdominal ribcage volumes and the percentage of inspiratory time the rib cage compartments moved in opposite directions using control data to define the normal range of movement.

Eight patients showed lower ribcage inspiratory paradox (P+) at rest while 12 patients did not (P-). This was unrelated to resting lung function or exercise tolerance.

Total end-expiratory chest wall volume (EEVcw) increased immediately when exercise began in P+ patients, but later in exercise in P- patients (p<0.001). This difference in EEVcw was mainly due to a greater increase of end-expiratory pulmonary ribcage volume (p<0.001) in P+ patients. During exercise, dyspnoea increased similarly in the two groups, while leg effort increased more markedly in the patients without paradox (p<0.01).

We conclude that lower ribcage paradox at rest is reproducible, associated with early-onset hyperinflation of the chest wall and predominant dyspnoea at end-exercise. When paradox is absent, the sense of leg effort becomes a more important symptom limiting exercise.

Running title: Rib cage paradox in COPD

INTRODUCTION

In healthy people inspiration occurs as a result of the coordinated action of the chest wall muscles. As the diaphragm flattens, the incompressible abdominal contents displace the abdominal wall outwards. The ribcage comprises two linked compartments: the lung apposed part (pulmonary rib cage, RC,p) expanded by inspiratory rib cage muscle action and submitted to pleural pressure, and the diaphragm apposed part (abdominal rib cage, RC,a) expanded as this muscle contracts and submitted to abdominal pressure. During inspiration the expansions of the abdomen and both ribcage compartments are in phase, a relationship that persists when the subject exercises although now end-expiratory lung volume is actively reduced by increased expiratory abdominal muscle action [1].

In Chronic Obstructive Pulmonary Disease (COPD) the situation is different. Here, the diaphragm is flatter and the respiratory drive is increased [2]. In this condition, the effectiveness of the diaphragm is less than in normal subjects, the expansion of the lower rib cage caused by diaphragmatic contraction is smaller than in normal subjects and consequently it is possible that an uncoordinated expansion of the two rib cage compartments occurs, leading to rib cage distortion [3, 4]. Before the advent of objective measurements of chest wall volume, clinical observation had identified patients who exhibited paradoxical (inward) movement of their lower ribcage on inspiration [5, 6, 7, 8]. Such inspiratory paradoxical motion of the lower rib cage is common in COPD [7, 8] and has been proposed as an aid to diagnosis [9]. However, until now it has not been quantified or related to other forms of respiratory behavior or the symptoms which limit exercise.

Previously, we have used Opto-Electronic Plethysmography (OEP) to identify differences in the behaviour of the rib cage and abdominal compartments of COPD patients during rest and

exercise [10, 11, 12, 13]. However, we did not study the effect of within-breath asynchrony between different rib cage compartments. We hypothesized that the presence of lower rib cage paradoxical movement would relate to the pattern of the end-expiratory and end-inspiratory chest wall volume changes during exercise. To test this we defined the normal range of lower rib cage paradox by studying a group of age-matched healthy controls and then measured regional chest wall volumes at rest and during exercise in stable COPD. Additionally, to investigate the relevance of paradoxical lower rib cage movement to exercise undertaken in daily life, we measured exercise performance and symptoms during self-paced corridor walking.

METHODS

Subjects

We studied 20 male patients who met the clinical and physiological diagnostic criteria for COPD [14]. All patients were or had been tobacco smokers, were less than 75 years old and had a post-bronchodilator FEV1/FVC <0.7, a pre-bronchodilator FEV1 <50% predicted and showed <10% improvement in FEV1 after inhaled bronchodilator drugs. Patients were not known to have paradoxical lower rib cage movement prior to the study and no specific examination for the presence of Hoover's sign [5, 6] was undertaken. No patient had experienced a COPD exacerbation requiring treatment in the previous six weeks. All were treated with inhaled corticosteroids and long-acting inhaled bronchodilators together with short-acting rescue therapy. In addition, we recruited 10 healthy age-matched volunteers who followed the same measurement protocol as follows. Subjects had normal spirometry for their age and an FEV1/FVC value >0.7.

Protocol

All assessments were made on a single study day. After clinical review, spirometry and plethysmographic lung volumes were measured in all subjects and repeated in the COPD patients 15 minutes after 400 μg Salbutamol given via a spacer device. Each COPD patient performed two six-minute walking tests with a 20 minute rest period between testing. The first walk was used to familiarise the patient with the test and only data from the second walk are reported. After a 20 minutes rest during which the OEP reflective markers were applied (see below), patients were seated on the cycle ergometer and asked to execute three Slow Vital Capacity (SVC) and three Forced Vital Capacity (FVC) maneuvers followed by two minutes of

quiet breathing (QB) to establish baseline values for the chest wall volumes. After this, subjects undertook the incremental exercise protocol described below. Subject started pedalling, first unloaded for 2 minutes, and then with an incremental load of 5 watts per minute until exhaustion.

The research protocol was approved by the district research ethics committee and informed consent was obtained from each participant.

Measurements

Subdivisions of lung volumes were measured to ATS standards in a body plethysmograph (Medgraphic Autolink 1085D, MedicalGraphics, St Paul, MN, USA) . Flow was measured at the mouth by a screen pneumotachograph and integrated to display the flow-volume loop from which spirometry and flow indices were derived.

Self-paced corridor walking tests were performed according to standard protocols with a standardised walking course [15]. Subjects walked at their maximal pace along an elliptical 40 meter course. They were asked to cover as much ground as possible while maintaining a steady pace without running during the allotted time. No encouragement was given, and subjects were informed each minute of the time remaining. The patients were allowed to stop, but they could start again, if possible, within the allocated 6 min. Distance covered in 6 min was recorded, together with oxygen saturation and HR from a lightweight pulse oximeter (Minolta PulseOx 3i, USA). During exercise subjects were asked to rate their breathlessness and the sense of leg effort every minute on a 10-point modified Borg category scale.

Incremental exercise was performed while seated on an electrically braked cycle ergometer. With the subjects breathing through a mouth piece with a nose clip, breath by breath

ventilatory variables were derived from the flow signal detected by a pneumotachograph system (Medical Graphics, St Paul, MN, USA). Oxygen consumption and carbon dioxide production were measured using a paramagnetic sensor and infrared carbon dioxide analyser, respectively, as part of an exercise testing system (Medical Graphics, St Paul, MN, USA). The flow signal was synchronised to that of the motion analyser used for OEP and sent to a personal computer for subsequent analysis. Oxygen saturation was measured by pulse oximetry (Biox 3700e, Ohmeda, Louisville, CO, USA) and cardiac frequency was determined using the R-R interval from a 4-lead electrocardiogram. During the exercise tests, subjects were asked to rate their breathlessness and legs effort every minute on the same Borg category scale used in the walking tests.

Kinematics of the chest wall (see below) were measured by Opto-Electronic Plethysmography (OEP System, BTS, Milano, Italy). In brief, the volumes displaced by the three compartments of the chest wall were measured by 89 retro-reflective markers placed on the trunk of the subject according to precise anatomical reference points. Marker positions were captured by 6 TV cameras (3 in front and 3 behind the subject) operating at 60 frames per second and synchronised with coaxial infrared flashing LEDs. The three-dimensional coordinates of the markers were calculated with stereo-photogrammetry and linked with a mesh of triangles to create the surface embedding the trunk. The volume of the trunk enclosed by the surface was obtained through a computing algorithm based on the Gauss' theorem [16].

Data analysis

Modeling of the chest wall. The chest wall was modelled in three compartments: pulmonary rib cage (RC,p), abdominal rib cage (RC,a), and abdomen (AB). Thus, the total volume

displaced by the chest wall (CW) was calculated as the sum of the volumes displaced by the individual compartments. The boundaries between the three portions were represented by a transversal section placed at the level of the xiphoid process(between RC,p and RC,a) and another surface positioned at the level of the lower costal margin (between RC,a and AB) (figure 1). The time courses of the volume of each region (Vrc,p, Vrc,a, Vab), along with their sum (Vcw) was processed to obtain a breath-by-breath assessment of both ventilatory pattern and operational chest wall volumes [1, 4, 16].

Chest wall volume data were standardized for the duration of each test to allow comparisons between different subjects as a percentage of maximum exercise. Comparisons were also made using minute ventilation as a percentage of the maximum value reached and as an absolute value.

Quantitative analysis of the paradoxical movement of the lower rib cage. The presence of paradoxical lower rib cage motion was established by comparing the time courses of Vrc,p, and Vrc,a. In each patient the volume tracings were normalized with respect to time to allow ensemble averaging over three reproducible consecutive breaths randomly chosen within the period of interest (either quiet breathing or during exercise at different levels) and to derive an 'average' respiratory cycle at each level of workload. Inspiratory and expiratory phases of the breathing cycles were derived from the Vcw signal. From these average breaths asynchronous and paradoxical motion between the two rib cage compartments were then assessed by calculating the following parameters (Figure 2 for graphical illustrations):

a. Phase shift (θ) between Vrc,a and Vrc,p, as indicated by the degree of opening of the Lissajou figure produced when these two volumes were plotted against each other. This

was measured as the ratio of the distance delimited by the intercepts of the Vrc,p vs. Vrc,a dynamic loop on a line parallel to the X-axis at 50% of pulmonary rib cage tidal volume (m), divided by RC,a tidal volume (s), as $\theta=\sin^{-1}(m/s)$, an approach adopted by others [17]. In this system a phase angle of 0 represents completely synchronous movement of the compartments and 180° total asynchrony.

b. Inspiratory paradox time (IP), defined as the fraction of the inspiratory time during which the abdominal rib cage volume decreased (see dashed area in Fig. 2).

Patients were subdivided into those showing paradox at rest (P+) and those who did not (P-). This grouping was based on threshold values of IP and θ, obtained at rest before the various maneuvers in the 10 healthy volunteers and defined as values two standard deviations beyond the respective means. To confirm the validity of these measurements three different breaths were selected under the same workload in both the control and COPD subjects and the data compared to the initial estimate. In three COPD patients the data on the first incremental test were repeated on a subsequent day to determine whether differences in marker position positioned by different experimenters or day to day variability in the subjects breathing influenced the classification of paradoxical movement.

As an alternative parameter to θ for the quantification of the degree of opening of the Lissajou figure in the Vrc,p - Vrc,a plot, we also considered the hysteresivity index η [18]:

$$\eta = \left[\left(\pi \cdot \Delta Vrc,p \cdot \Delta Vrc,a / 4A \right)^{2} - 1 \right]^{-\frac{1}{2}}$$

where $\Delta Vrc,p$ and $\Delta Vrc,a$ are respectively the tidal volumes of the pulmonary and abdominal rib cage and A is the area bounded by the Vrc,p - Vrc,a loop.

In a post-hoc analysis we examined whether the presence of tidal expiratory flow limitation at rest was related to our indices of paradoxical lower rib cage movement and the behavior of patients during exercise. The flow signal was integrated to obtain flow-volume loops during rest, forced expiratory maneuvers and maximal exercise. To correct the drift of the volume signal obtained from the integration of the flow measured at the mouth we positioned the loops accordingly to the values of chest wall volume measured at TLC during inspiratory capacity maneuvers performed at rest before the various maneuvers during which the loops to be compared were recorded. Expiratory flow limitation was considered present at rest when >50% of the tidal breath met or exceeded the expiratory boundary of the maximal flow-volume loop [19].

Statistical analysis

Data are presented as mean (SD) unless otherwise stated. Differences between anthropometric, spirometric, and exercise data sets were tested using Wilcoxon and Mann-Whitney tests for paired and unpaired data, respectively with appropriate adjustment for multiple comparisons. To evaluate the influence of rib cage paradox and exercise intensity on ventilatory parameters and operational volumes a two way analysis of variance (ANOVA) was performed. Statistical significance was assumed if the null-hypothesis was rejected with a probability of $p < 0.05$.

RESULTS

Anthropometric characteristics, spirometry values and subdivision of lung volumes are reported in Table 1.

Defining the occurrence of paradoxical rib cage movement at rest

The magnitude of volume change, its timing and the phase angle relationship of the RC,p and RC,a regions are shown for three typical subjects in figure 2, while all the individual Vrc,a and Vrc,p time courses and Vrc,p-Vrca loops are presented in the online supplement. Using a difference of at least two standard deviations above the mean value for the normal subjects (99% C.I.) gave a threshold for the upper limit of normal of 14.0 degrees for phase angle and 20.3% for the IP%. When three different breaths were chosen and the analysis repeated similar values were obtained and no individual would have been classified as showing rib cage paradox, even if only one criterion were used (see online supplement).

Among the COPD patients, 8 subjects met both criteria for paradox (P+) while the remaining 12 did not (P-). Of these, 7 subjects showed no evidence of paradox by either criteria, 4 showed only an abnormal phase angle and one an increased IP (fig. 3a).

Both indices of paradoxical lower ribcage movement lay close to the upper limit of normal in the P- subjects but were clearly separate from those in the P+ subjects at rest (p<0.001) (fig. 4). The reproducibility of the % inspiratory time and phase angle in the COPD patient data was good. No patient would have been re-classified had different breaths been chosen. Likewise we did not see any difference among the replicate data on three different occasions both at rest and during exercise (see online supplement).

When hysteresivity η was plotted instead of phase angle against IP to investigate rib cage paradox (fig. 3b), among the COPD patients, 9 subjects showed values of both IP and η above threshold. Of these, 8 subjects were previously classified as P+, and the remaining was the one with above-threshold IP and below-threshold θ.

Tidal expiratory flow limitation

Among the P+ patients, all showed clear evidence of expiratory flow limitation at rest using our flow-volume criteria (see above). Among the P- patients, 9 of the 12 where flow limited and three of these flow limited patients had a value of phase angle above the threshold (see online supplement, fig. E4).

Paradoxical ribcage movement during exercise

The time courses of the phase angle and %IP during unloaded, half maximal and maximal exercise are shown in fig. 4. At rest, the P+ group showed, by definition, high mean phase angle and %IP than the P- group. During exercise, the phase angle did not change significantly in the control and the P- groups, but in the P+ group the phase angle fell at maximal exercise so that there was no longer any significant difference between the P+ and the P- groups. The %IP patterns, like the phase angle, were similar throughout for the control and P- groups, but, unlike the phase angle, increased substantially during exercise, approaching the levels of the P+ group.

Spirometry, lung volumes and exercise performance in the COPD

The presence of rib cage paradox was not associated with statistically significant differences in spirometry or any measurement of resting lung volume when compared to patients who did not show this finding. There were no significant differences in the maximum workload, peak oxygen consumption achieved, maximum minute ventilation or breathing pattern between the two groups of COPD patients (table 2).

Chest wall volumes during incremental exercise.

None of the normal subjects showed evidence of an increased end-expiratory total chest wall volume (EEVcw) at end-exercise relative to their baseline values and all showed an early fall in EEVcw as exercise began (Fig. 5). In contrast, P+ subjects showed an early increase in EEVcw (Fig.6a) and this was maintained up to the maximum workload, exceeding the values of the spontaneous breathing by a mean of 328 ml. In contrast, P- subjects maintained an EEVcw similar to the baseline value up to approximately 50% of maximum workload. EEVcw slowly rose thereafter showing a late hyperinflation of 297 ml at end exercise, a value similar to that of the P+ subjects (when volumes were expressed as change from baseline as in fig. 6) but statistically different from the healthy volunteers ($p<0.001$). These findings were similar when data where expressed using minute ventilation either as a percentage of the maximum or as an absolute value (fig. 6b) .

The time course of the end-expiratory and end-inspiratory regional chest wall volumes differed significantly between the healthy subjects and the two COPD groups (fig. 7). In P+, RC,p end-expiratory volumes rose immediately after the onset of exercise while this volume increased to a lesser degree in P- and normals ($p<0.001$). End-expiratory volumes of RC,a increased during exercise in a similar way in P+ and P- groups, while in healthy subjects they

remained constant up to approximately 60% of the maximum workload and then increased on average by 316 ml at end exercise. In healthy subjects the abdominal volume at end-expiration significantly fell throughout the exercise while at end exercise the two COPD groups reached values identical on average to those measured during quiet breathing.

Symptoms and self-paced exercise.

Data for the symptom intensity of dyspnoea and leg effort for both incremental and self-paced exercise and total distance walked for both P+ and P- patients are presented in table 2 while the symptoms at rest, the mid-point of exercise testing and end-exercise are shown in fig. 8. The intensity of dyspnoea reported at end-exercise was similar in the two groups with both types of exercise. However, the symptom intensity of leg effort was significantly less in P+ patients during incremental exercise ($p<0.01$) with a similar trend in the self-paced walk test ($p<0.05$). The difference between dyspnoea and sense of leg effort severity was statistically significant in both types of test ($p<0.01$ or less). Oxygen saturation and heart rate data did not show significant differences between P+ and P- groups for either corridor walking or cycling test.

DISCUSSION

Although the movement of the rib cage during the respiratory cycle normally tracks the change in lung volume, this is not always the case in patients with obstructive lung disease, as has been recognised by clinicians for many years [5, 6]. Magnetometer studies have identified different patterns of behaviour in the upper and lower rib cage [2, 7, 8] but our data are the first to provide a quantitative three-dimensional assessment of the effect of lower rib cage paradox on chest wall volumes, ventilatory pattern and symptoms at rest and during exercise. We observed that COPD patients with paradox increased their end-expiratory chest wall volume as soon as exercise began while those without lower rib cage paradox only hyperinflated their chest wall towards the end of incremental exercise. These changes were reflected in the symptoms reported during exercise with dyspnoea being the major complaint when paradox was present, irrespective of whether the exercise was incremental or self-paced. This suggests that different patterns in the timing of end-expiratory chest wall volume change [12] relates to patient symptoms and can be reliably predicted by rib cage movement assessed under resting conditions.

We defined paradoxical rib cage movement by quantifying the asynchrony between the two rib cage regions during inspiration. We followed the model proposed by Ward et al [20] and used by others reporting data with opto-electronic plethysmography [1, 4] in which the rib cage is considered as formed by two sub-compartments, i.e. the part that is apposed to the lung, the pulmonary rib cage, and the part apposed to the diaphragm, the abdominal rib cage. The boundary between the pulmonary and the abdominal rib cage was defined by a surface identified by a set of markers placed at the level of the xiphisternum (fig. 1) and this does not

change with diaphragm movement. Thus in COPD patients the abdominal rib cage volume may not precisely correspond to the true area of apposition but is best considered as representing the lower rib cage where the muscles inserted and acting in that area differ from those influencing upper rib cage volume.

While previous workers have used changes in the lateral and antero-posterior dimensions of the rib cage to do this [7, 8], our approach was based on the analysis of volume variation, obtained by integrating the three-dimensional motion of multiple surface markers. Thus our data are not strictly comparable to those obtained by two-dimensional analysis of lower ribcage movement alone, and they provide a description of normal or paradoxical inspiratory motion that includes and integrates changes of dimensions in multiple directions. We used a conservative definition of paradox based on the relative movement of the upper and lower rib cage regions which was only considered to be significant when there were changes beyond the normal range in both the percentage of inspiratory time where paradox was seen and in the phase angle shift. The latter index provided a measure of the degree of chest wall distortion while the former indicated how much of the inspiratory period was affected. We were able to classify individuals in a binary fashion although the variables themselves are likely to represent a continuous spectrum of severity as can be seen in fig. 3 and table E1. Each of these measurements proved relatively reproducible in both healthy subjects and those with COPD when different breaths were ensemble averaged to generate the data. Moreover, differences in individual operators positioning the markers on different days did not influence the results nor did the classification if resting paradoxical rib cage movement change if different breaths were used to define it.

When a different index like the hysteresivity of the Vrc,p-Vrc,a loop was considered instead of the phase shift angle, the classification did not change substantially. Only one patient who

previously showed an increased percentage inspiratory paradox without an apparently abnormal phase angle shift would have been re-classified as belonging to the P+ group. Interestingly, this patient showed relatively early onset of chest wall hyperinflation during exercise.

Our data were primarily observational rather than mechanistic. Like the investigators who identified Hoover's sign clinically, [9, 21] we found no relationship between the presence of lower ribcage paradox and resting lung function. The only significant differences we found between P+ and P- groups were for weight and BMI, suggesting that paradox may be commoner as weight increases. This needs to be confirmed in a larger population of patients. However, a selective activation of different respiratory muscle groups might explain the relationship between the presence of rib cage paradox at rest and the increased end-expiratory volume of the pulmonary rib cage at the onset of exercise in the P+ subjects. These patients may exhibit an increase in ribcage and related accessory muscle tonic activation. More detailed studies to understand the basis of resting paradox defined as we have are now underway. Future experiments are needed to correlate paradoxical movement of the lower rib cage to diaphragm shape and length of the area of apposition, as recently proposed by preliminary studies based on ultrasound [2, 22, 23] and magnetic resonance [24] imaging.

Exercise modified the different components of paradox in different ways. In normal and P-COPD subjects the phase angle was unchanged by exercise, while in P+ patients it only decreased at maximum workload, but even then did not reach the values seen in the healthy subjects and COPD patients without resting paradox. This result may reflect the increasing

volume, and therefore decreasing compliance, of the pulmonary ribcage as hyperinflation develops, with a concomitant increase in the mechanical linkage between the two rib cage portions. In contrast, in the normal and P- subjects the percentage of inspiratory paradox time tended to increase at the onset of exercise and to remain constant thereafter, approaching levels similar to those seen in the P+ group. This result may be attributed to the insertional action of the expiratory abdominal muscles on the lower rib cage [1, 4], even though abdominal end-expiratory volume decreases substantially only at the onset and during exercise in the healthy (fig. 7).

All the P+ patients showed an early increase of total chest wall end-expiratory volume. This was mainly due to the increase of the pulmonary rib cage volume, presumably to cope with the expiratory action of the lower ribcage, which was not seen in the P- patients. The early onset of chest wall hyperinflation in P+ patients was unexpected and was not related to the duration of exercise or the severity of airflow obstruction or baseline pulmonary hyperinflation. Retrospective classification of the presence of tidal expiratory flow-limitation showed that all the 8 P+ patients were flow-limited compared to 9 out of 12 P- patients. None of the P- patients exhibited chest wall hyperinflation at the onset of exercise. These results suggest that paradoxical motion rather than the presence of tidal EFL determines early chest wall hyperinflation. .

Breathlessness and sense of leg effort increased during exercise in patients with and without ribcage paradox, although the relative importance of each symptom differed. At the end of cycle exercise end-inspiratory chest wall volume which is not influenced by gas compression

and blood shift effects, approached the critical inspiratory reserve volume associated with neuromechanical dissociation [25] in both groups. However the P+ patients were less likely to report severe sense of leg effort than the P- patients leaving breathlessness as their principal complaint at the end of exercise. This is in keeping with previous reports of symptom limitation in severe COPD [26] and the predominance of effort in P- subjects was replicated during the self-paced corridor testing. These differences were not related to degree of oxygen desaturation, peak workload or exercise duration. The early-onset of dynamic hyperinflation of the chest wall is the likeliest explanation for the predominance of dyspnoea in P+ patients. In P- patients other factors such as the onset of peripheral muscle fatigue which limits exercise in some COPD patients may have been more important [27].

Our study was designed to identify reliable objective criteria for the presence of paradoxical lower ribcage movement and test whether these predicted physiological differences during exercise in stable hyperinflated COPD patients. Although our criteria resemble the subjective ones described by Hoover [6] ,we did not select our patients on the basis of a clinical diagnosis of Hoover's sign and we did not record this to avoid the risk of biasing our results. Others have examined resting lower rib cage movement using the OEP method in patients defined clinically as having Hoover's sign and reported that Hoover's sign did not correlate with the level of hyperinflation and therefore rib cage distortion and hyperinflation appear to be independent factor limiting ventilatory function in stable COPD patients [21].

In summary, we have shown that abnormal lower rib cage movement is not just a clinical curiosity but that it identifies important physiological differences in the chest wall volumes

during exercise and these translate into different patterns of reported symptoms. The early onset of hyperinflation in those with paradox helps to explain why differences seen in incremental exercise are still present during lower intensity self paced exercise, which relates to the daily activity undertaken by COPD patients.

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FIGURES LEGENDS

Figure 1: Markers' positioning on the front (left) and the back (right) of the subject and geometrical models of the chest wall compartments (center) for analysis by opto-electronic plethysmography (OEP).

The markers are positioned on approximately horizontal rows at the level of: the clavicular line; the manubrio-sternal joint (angle of Louis); the nipples; the xiphoid process; the lower costal margin; the umbilicus; and the anterior superior iliac crest. Surface landmarks for the vertical columns are: the midlines; both anterior and posterior axillary lines; the midpoint of the interval between the midline and the anterior axillary line and the midpoint of the interval between the midline and the posterior axillary line; and the midaxillary lines. Extra markers are added bilaterally at the midpoint between the xiphoid and the most lateral portion of the 10th rib, in the region overlying the lung-apposed rib cage, and in corresponding posterior positions. Volume displacement of the chest wall is calculated by triangulating the surface and integrating the subtended volume. The actual triangulation for the different considered compartments of the chest wall (pulmonary or upper rib cage (RC,p); abdominal or lower rib cage (RC,a); abdomen (AB)) is shown in the right panel. To allow a better understanding, each compartment is represented slightly shifted in the vertical direction.
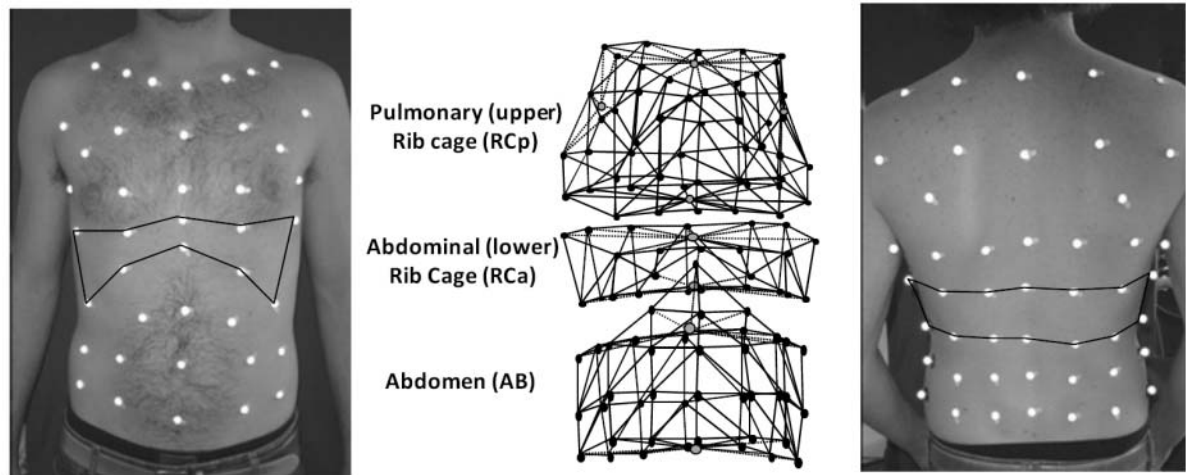
Figure 2: *Top panel*: time courses of the volumes of the upper rib cage, lower rib cage, abdomen and total chest wall (Vrc,p, Vrc,a, Vab and Vcw respectively) during two consecutive breaths at rest in a control subject (left), in a COPD patient without paradoxical movement between Vrc,p and Vrc,a (centre) and in a COPD patient with paradoxical movement between Vrc,p and Vrc,a (right). Inspiratory paradox time (IP) of the lower rib cage is represented by the grey dashed areas shown in the top right panel. *Bottom panel*: dynamic loops of Vrc,p vs Vrc,a during quiet breathing. Loops refer to the data shown in the top panel ensemble averaged on the respiratory cycle time. The phase shift (θ) is calculated as $\theta = \arcsin(m/s)$ (see text) .
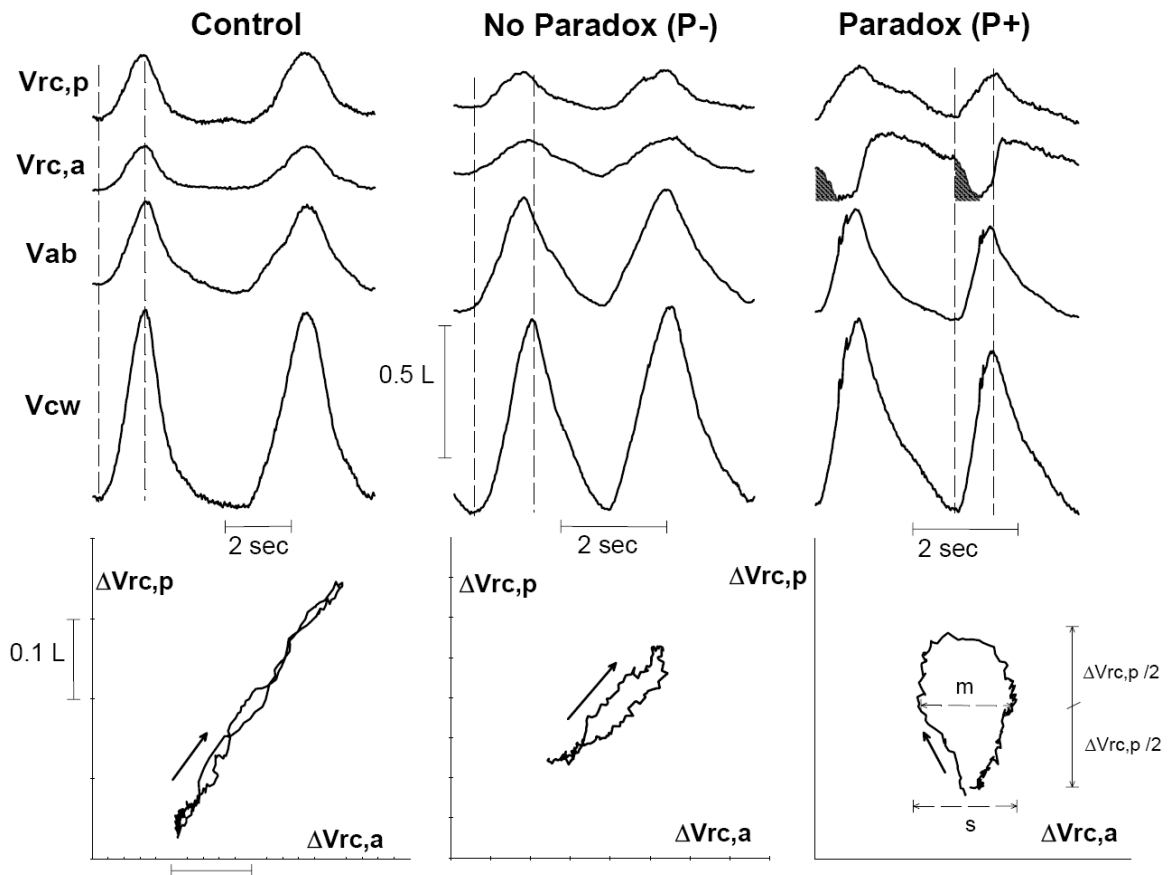
Figure 3: left: Relationship between phase of upper vs. lower rib cage (θ) and inspiratory paradox time (IP) of the lower rib cage. Dashed lines represent the thresholds as defined as 2 standard deviations beyond the mean values of IP and θ observed in healthy subjects at rest. Right: Relationship between hysteresivity of upper vs. lower rib cage (η) and inspiratory paradox time (IP) of the lower rib cage. Dashed lines represent the thresholds as defined as 2 standard deviations beyond the mean values of IP and η observed in healthy subjects at rest.
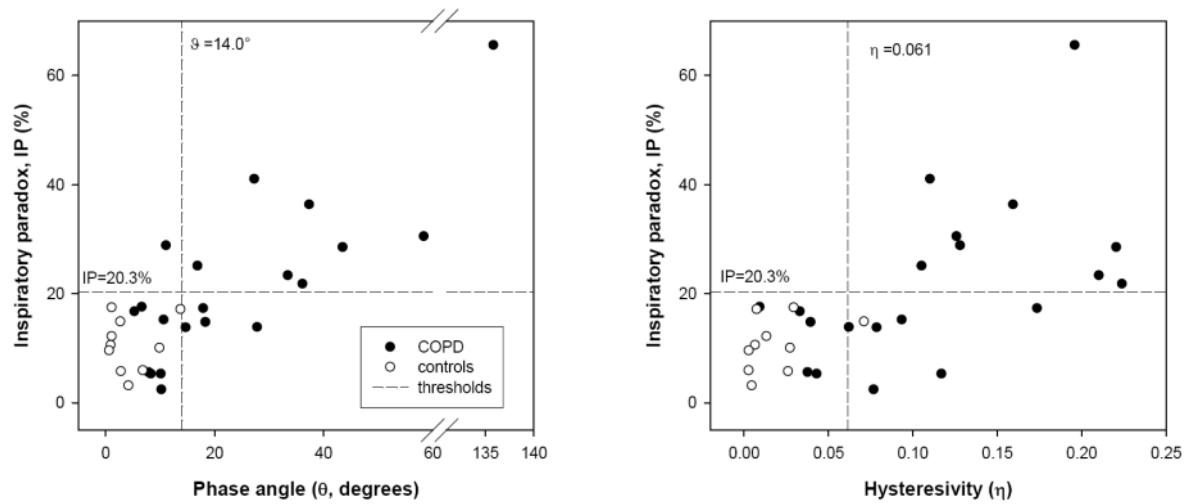
Figure 4: Mean ± S.E. of phase shifts (*left panel*) and paradox inspiratory times (*right panel*) during exercise between upper (pulmonary) rib cage and lower (abdominal) rib cage. Triangles: control subjects Closed circles: P+. Open circles : P-. QB: quiet breathing, UL: unloaded exercise. *p<0.05, **p<0.01, ***p<0.001 P+ vs P-. † p<0.05, †† p<0.01, ††† p<0.001 P+ Vs Control.
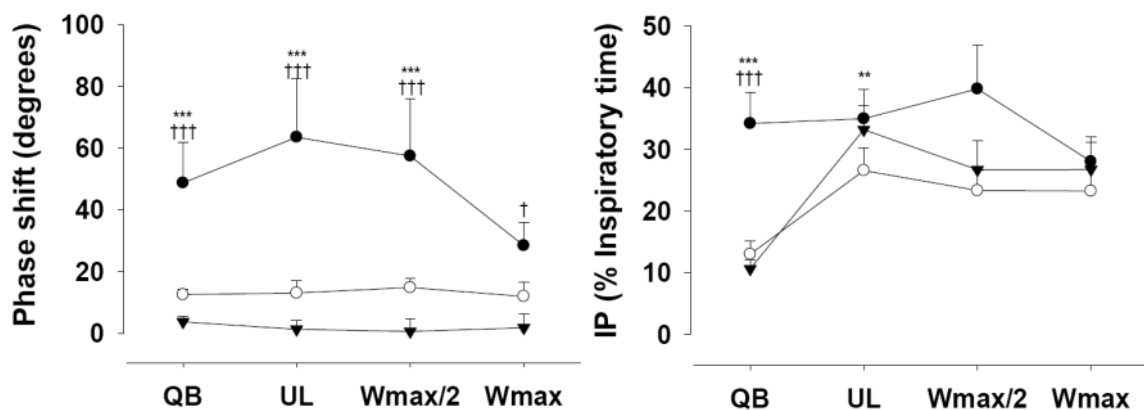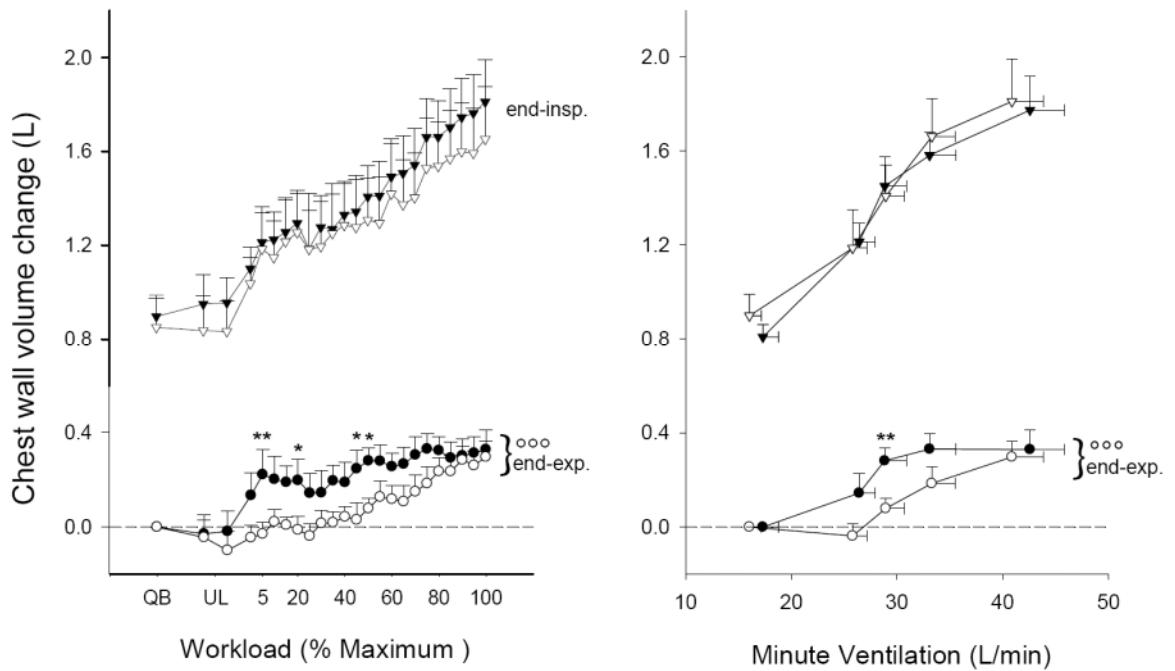

Figure 5: Mean ± S.E. end-expiratory and end-inspiratory total chest wall volume variations during exercise (expressed as percentage of the chest wall volume at Total Lung Capacity

(TLC)) in the COPD patients and in the Control group. Closed symbols: P+, open symbols P-, grey symbols: controls. QB: quiet breathing, UL: unloaded exercise. °°°p<0.001 P+ vs P- (overall data) .
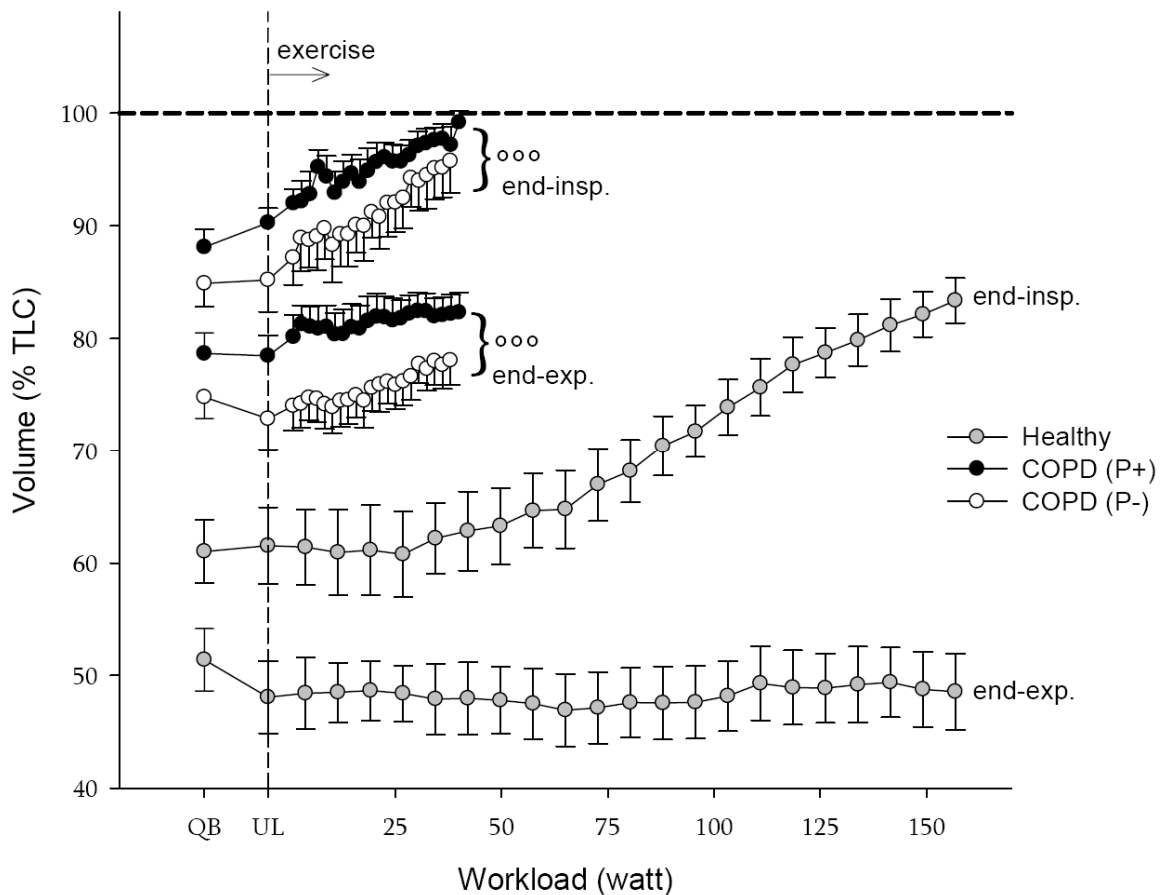

Figure 6: Mean ± S.E. end-expiratory and end-inspiratory total chest wall volume variations during exercise (expressed as chest wall volume variations from chest wall volume at FRC during quiet breathing, QB) in the COPD patients as a function of workload (6a) and minute ventilation (6b). Closed symbols: P+, open symbols P-. UL: unloaded exercise, 0%: onset of the load. *p<0.05, **p<0.01, ***p<0.001 P+ vs P- (at same levels of exercise). ° p<0.05, °° p<0.01, °°° p<0.001 P+ vs P- (overall data).

Figure 7: Mean ± S.E. end-expiratory and end-inspiratory volumes variations of RC,p (upper plots), RC,a (middle plots) and AB (lower plots) during exercise in the COPD group (*left panel*) and in the Control group (*right panel*). Closed symbols: P+, open symbols P-, grey symbols: Controls. QB: quiet breathing, UL: unloaded exercise, 0%: onset of the load. ° $p<0.05$, °° $p<0.01$, °°° $p<0.001$ P+ vs P- (overall data) .
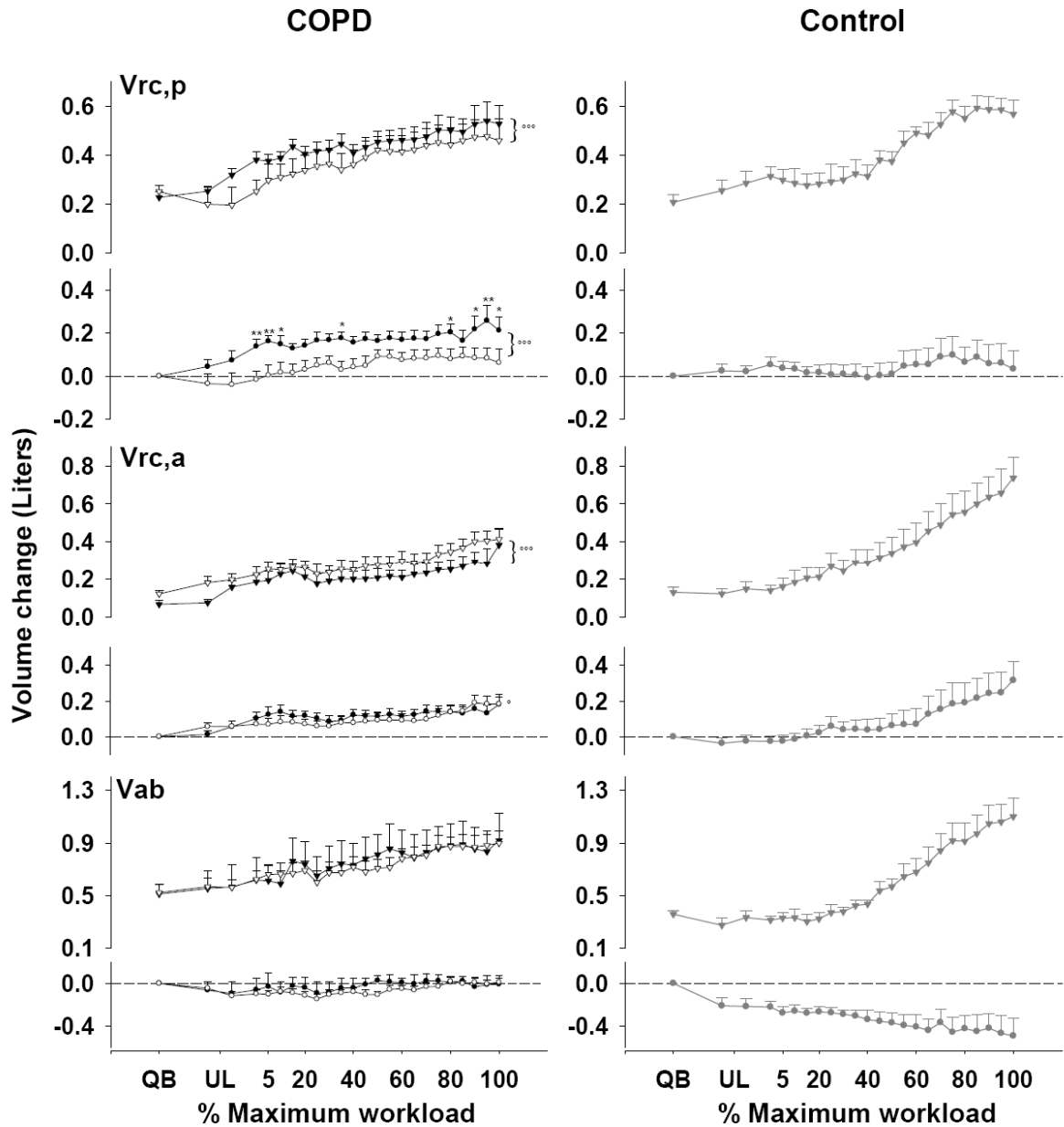
Figure 8: Dyspnoea, legs effort and difference between the two symptoms (dyspnoea and legs effort) during the six minute walking test (left panels) and exercise (right panels). Black bars: P+. White bars: P-. . *p<0.05, **p<0.01, ***p<0.001 P+ vs P- (at same levels of exercise). ° p<0.05, °° p<0.01, °°° p<0.001 P+ vs P- (overall data). Data are reported as mean ± S.E.
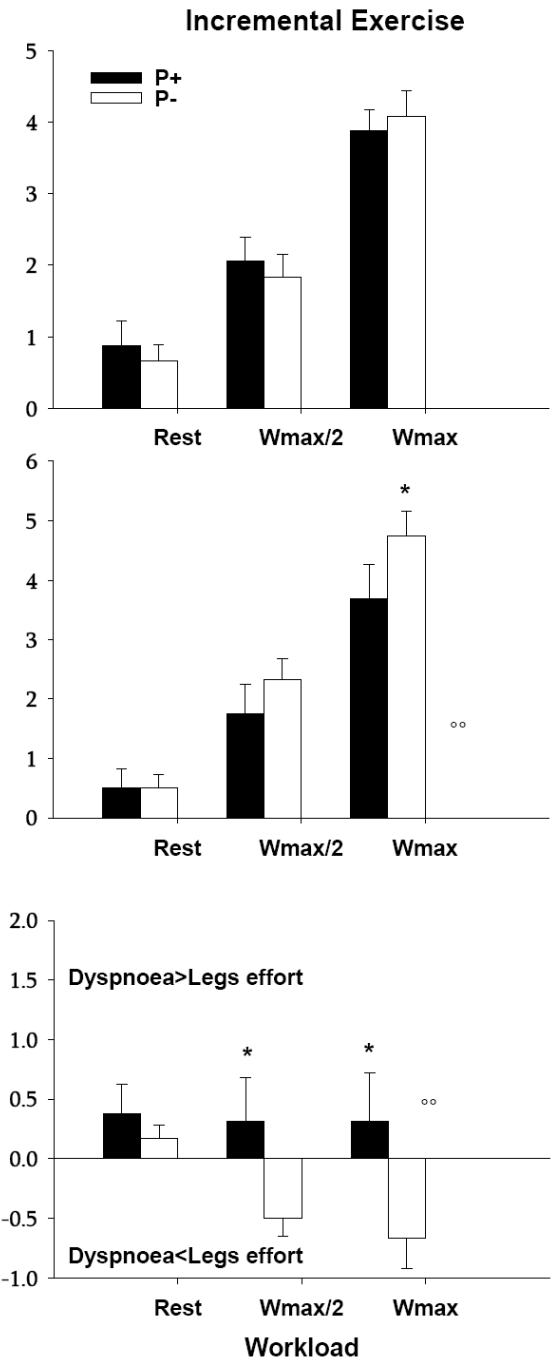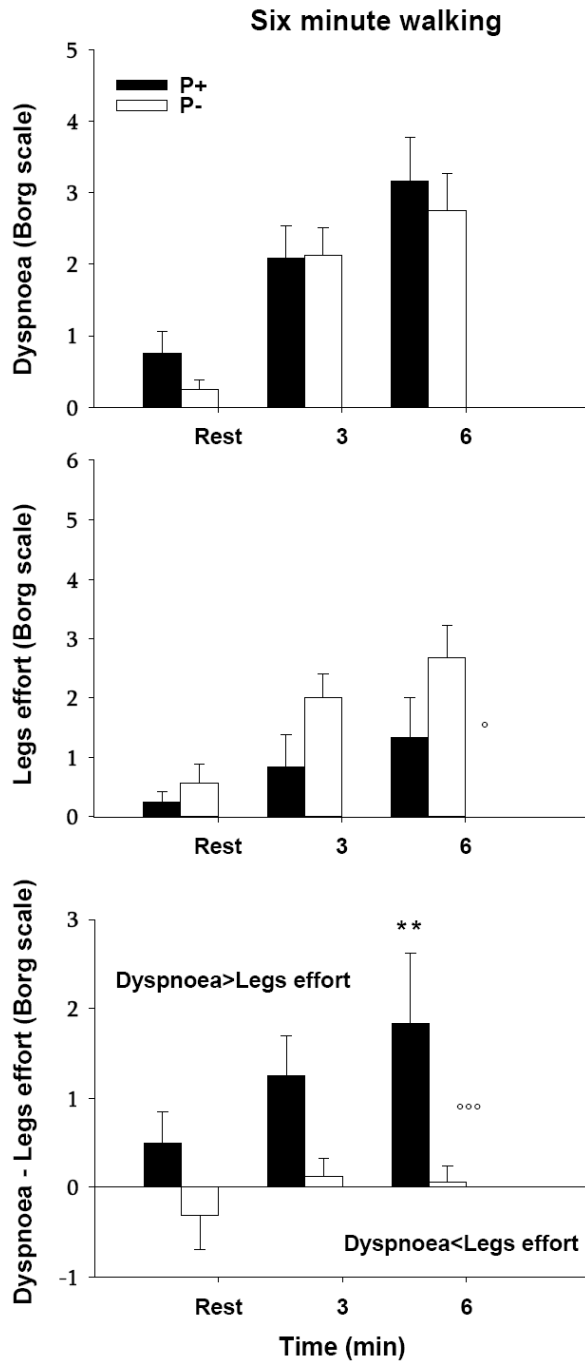
Table 1: Patients' characteristics. Anthropometric characteristics, spirometric values and subdivision of lung volumes in COPD and healthy subjects (*p<0.05, P+ vs P-). BMI, Body Mass Index; FVC, Forced Vital Capacity; FEV1, Forced Expiraotry Volume in 1 sec; TGV, Total Gas Volume; RV, Residual Volume; SVC, Slow Vital Capacity; IC, Inspiratory Capacity; %pred, percentage of predicted value. Data are expressed as mean (SD).

	Control group (n=10)	COPD All (n=20)	P+ (n=8)	P- (n=12)
Age (yrs)	65 (7)	66 (7)	69 (6)	65 (7)
Height (cm)	173 (6)	174 (6)	175 (6)	173 (7)
Weight (Kg)	77.0 (7)	69 (14)	76 (16)	63 (11) *
BMI (Kg/m^2)	25.6 (1.6)	22.5 (3.9)	24.6 (4.3)	21.0 (2.9) *
FVC (L)	5.0 (1.29)	2.9 (0.78)	2.87 (0.77)	2.87 (0.83)
FVC (%pred)	117.7 (29.5)	66.0 (16.5)	65.9(14.4)	66.6 (17.7)
FEV1 (L)	3.3 (0.5)	1.0 (0.3)	0.9 (0.2)	1.1 (0.4)
FEV1 (%pred)	102.8 (12.7)	32.6 (11.7)	28.0 (6.1)	35.6 (13.6)
FEV1/FVC (%)	67.0 (11.6)	36.3 (9.4)	31.9 (5.7)	39.3 (10.4)
FEV1/FVC (%pred)	89.9 (15.2)	48.9 (12.6)	43.1 (7.9)	52.7 (13.9)
TGV (L)	3.7 (0.7)	6.5 (1.5)	6.8 (0.7)	6.2 (1.7)
TGV (%pred)	108.6 (20.7)	186.4 (31.5)	189.1 (24.1)	179.1 (34.5)
RV (L)	2.9 (0.7)	5.6 (1.1)	5.7 (07)	5.4 (1.3)
RV (%pred)	129.9 (29.2)	239.5 (48.9)	241.2 (35.5)	227.9 (49.8)
TLC (L)	7.0(0.9)	8.6 (1.4)	8.6 (0.9)	8.2 (1.5)
TLC (%pred)	106.7 (11.2)	125.7 (15.5)	126.7 (12.2)	123.9 (16.6)
RV/TLC (%)	40.1 (7.4)	66.0 (7.2)	66.0 (6.0)	65.0(9.1)
RV/TLC (%pred)	124.8 (21.3)	188.3 (15.9)	184.3 (18.2)	194.6 (20.5)
SVC (L)	4.2 (0.6)	3.0 (0.7)	3.0 (0.7)	3.0 (0.9)
SVC (%pred)	98.4 (8.9)	68.4 (12.1)	68.2 (11.1)	69.8 (15.1)
IC (L)	3.3 (0.6)	1.9 (0.4)	1.8 (0.5)	2.03 (0.3)
IC (%pred)	103.9 (14.7)	61.0 (12.3)	56.6 (14.3)	64.3 (9.9)

[†] p<0.05

Table 2: Resting and end exercise ventilatory pattern, metabolic and cardiac variables Breathing pattern (breathing frequency, F; tidal volume, V_T; minute ventilation, V_E; inspiratory time, T_I), oxygen consumption (VO_2), CO_2 production (VCO_2), respiratory exchange ratio (RER), end-tidal $CO2$ ($P_{ET}CO_2$), oxygen saturation (SaO_2), heart rate and symptoms at rest and during peak cycle exercise in the healthy and COPD (all, patients with paradoxical motion of the lower rib cage, P+ and without, P-). Exercise tolerance data (maximum cycle exercise workload and 6-min walking distance) are also reported. **: $p<0.01$ (P+ vs P-). Data are expressed as mean (SD).

	Control (n=10)		COPD All (n=20)		COPD P+ (n=8)		COPD P- (n=12)	
	Rest	Peak exercise	Rest	Peak exercise	Rest	Peak exercise	Rest	Peak exercise
F (breaths•min⁻¹)	16 (4)	28 (5)	21 (4)	31 (8)	22 (3)	31 (7)	20 (5)	30 (9)
V_T (L)	0.67 (0.12)	2.45 (0.58)	0.86 (0.26)	1.42 (0.36)	0.80 (0.16)	1.42 (0.29)	0.89 (0.30)	1.41 (0.41)
V_E (L•min⁻¹)	11.4 (2.7)	67.40 (17.20)	16.34 (3.59)	40.54 (8.92)	16.65 (3.25)	42.00 (9.38)	16.13 (3.92)	39.58 (8.89)
T_I (sec)	1.50 (0.26)	1.04 (0.19)	1.07 (0.29)	0.87 (0.38)	1.03 (0.27)	0.79 (0.29)	1.11 (0.32)	0.94 (0.45)
Duty cycle (%)	39.6 (6.0)	46.2 (2.5)	35.6 (5.4)	39.8 (5.8)	34.7 (5.6)	39.4 (5.3)	36.1 (5.6)	40.1 (6.5)
VO_2 (L•min⁻¹)	0.33 (0.10)	1.75 (0.42)	0.32 (0.06)	0.78 (0.19)	0.34 (0.0)	0.75 (0.18)	0.31 (0.07)	0.80 (0.20)
VO_2 (ml•Kg⁻¹•min⁻¹)	4.45 (1.57)	22.73 (5.02)	4.56 (1.31)	11.08 (3.16)	4.69 (1.29)	10.37 (2.59)	4.48 (1.37)	11.55 (3.52)
VCO_2 (L•min⁻¹)	0.27 (0.07)	2.19 (0.59)	0.28 (0.06)	0.77 (0.19)	0.30 (0.05)	0.74 (0.18)	0.27 (0.06)	0.78 (0.21)
RER	0.83 (0.11)	1.25 (0.11)	0.87 (0.07)	0.98 (0.10)	0.89 (0.05)	0.99 (0.10)	0.86 (0.08)	0.97 (0.11)
$P_{ET}CO_2$ (mmHg)	35.5 (4.3)	39.5 (4.7)	29.9 (5.0)	33.3 (5.9)	30.7 (7.1)	35.6 (7.5)	27.6 (3.3)	31.6 (4.1)
SaO_2 (%)	97 (4)	96 (3)	93 (3)	93 (2)	95 (1)	93 (1)	92 (3)	92 (2)
Heart rate (beat•min⁻¹)	89 (19)	120 (12)	93 (14)	122 (17)	94 (10)	121 (4)	93 (20)	124 (18)
Dyspnoea	0 (0.0)	4.4 (3.8)	0.7 (0.2)	4.0 (1.1)	0.9 (0.9)	3.9 (0.8)	0.7 (0.7)	4.1 (1.2)
Sense of Leg Effort	0 (0.0)	5 (3.6)	0.5 (0.2)	4.3 (1.6)	0.5 (0.9)	3.7 (1.6)	0.5 (0.77)	4.7 (1.4) (**)
Predominant symptom (Dyspnoea - Leg Effort)	0 (0.0)	-0.6 (0.6)	0.2 (0.1)	-0.3 (0.2)	0.4 (0.7)	0.3 (1.2)	0.2 (0.4)	-0.7 (0.7) (**)
Maximum workload (watt)	153 (35)		43 (19)		42 (20)		44 (19)	
6 min walking distance (m)	—		291 (12)		290 (93)		291 (63)	