Research clerkship project report:

Dynamic hyperinflation during metronome-paced tachypnea and the correlation with the activity status in COPD (Mozart)

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Dutch summary (Nederlandse samenvatting)
Eén van de factoren die dyspnoe veroorzaakt in COPD patiënten is dynamische hyperinflatie. Dynamische hyperinflatie zou vervolgens weer tot verminderde dagelijkse activiteit kunnen leiden. Echter, weinig studies hebben gezocht naar een relatie tussen dynamische hyperinflatie en dagelijkse activiteit.
Ons primaire doel was om de relatie te onderzoeken tussen dagelijkse activiteit en dynamische hyperinflatie, opgewekt door metronoom-geïnduceerde tachypneu, op het gebied van 1) de snelheid van ontstaan en verdwijnen van dynamische hyperinflatie en 2) de mate van dynamische hyperinflatie, bij patiënten met COPD.
Er waren 35 proefpersonen met stabiel COPD geïncludeerd. Dagelijkse activiteit werd gemeten met een 3D-accelerometer. Proefpersonen ondergingen metronoom-geïnduceerde tachypneu, met secundaire inspiratoire capaciteit manoeuvres. De mate van dynamische hyperinflatie werd gedefinieerd als een verandering in de inspiratoire capaciteit als een percentage van de totale longcapaciteit.
Er waren geen significante correlaties gevonden tussen dagelijkse activiteit en parameters 1) en 2) zoals boven genoemd.
Alhoewel we geen relaties hebben gevonden tussen dynamische hyperinflatie en dagelijkse activiteit zou statische hyperinflatie wel een bruikbare marker kunnen zijn met betrekking tot verminderde dagelijkse activiteit.

Summary
One of the factors causing dyspnoea in COPD patients is dynamic hyperinflation which could on its turn limit daily physical activity. However, few studies have investigated if there is a relation between daily activity and dynamic hyperinflation.
Our main objectives were to investigate the relationships between daily physical activity and dynamic hyperinflation induced by metronome-paced tachypnea, in terms of 1) development rate and recovery rate of dynamic hyperinflation and 2) the degree of dynamic hyperinflation, in patients with COPD.
35 patients with stable COPD were included. Daily physical activity was assessed using a 3D-accelerometer. Subjects underwent metronome-paced tachypnea and inspiratory capacity manoeuvres. In the quantification of the degree of dynamic hyperinflation, the change in the inspiratory capacity as a percentage of the total lung capacity was used to correct for body height.
No significant correlations were found between daily physical activity and the parameters 1) and 2) as mentioned above.
Although we did not find any relation between dynamic hyperinflation and daily physical activity, static hyperinflation could be a useful marker to indicate reduced daily physical activity.
Table of contents

Dutch summary (Nederlandse samenvatting) ................................................................. 2
Summary .......................................................................................................................... 2
Introduction ................................................................................................................... 4
Research questions ....................................................................................................... 6
Methods .......................................................................................................................... 6
  Subjects ....................................................................................................................... 6
  Procedures ................................................................................................................. 7
Results ............................................................................................................................. 12
  General baseline characteristics ............................................................................... 12
  Daily activity ............................................................................................................... 12
  The relation between daily activity and the development rate of dynamic hyperinflation .................................................................................................................. 13
  The relation between daily activity and the recovery rate of dynamic hyperinflation ........................................................................................................... 14
  The relation between daily activity and the degree of dynamic hyperinflation .......... 15
  The relation between daily activity and a change in Borg-score .............................. 16
  Exploratory analysis: static hyperinflation and daily activity ...................................... 16
Discussion ...................................................................................................................... 17
Conclusion ..................................................................................................................... 19
Literature ......................................................................................................................... 19
Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem. In 2020, COPD is projected to rank fifth worldwide in terms of burden of disease and third in terms of mortality(1).

The severity of COPD can be graded according to GOLD stage. The GOLD stage is based on the predicted value of the forced expiratory volume in one second. The lower the forced expiratory volume in one second as a percentage of the predicted value is, the higher the GOLD-stage is and the more severe the COPD becomes (Table 1 (1)).

<table>
<thead>
<tr>
<th>GOLD Stage</th>
<th>Severity</th>
<th>FEV₁ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>Mild</td>
<td>≥ 80%</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>50% ≤ FEV₁ &lt; 80%</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>30% ≤ FEV₁ &lt; 50%</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very severe</td>
<td>FEV₁ &lt; 30%</td>
</tr>
</tbody>
</table>

*Definition of abbreviation: COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.*

COPD is not only characterized by symptoms of dyspnea, chronic cough, and sputum production, but also by a decreased exercise performance and a reduced physical activity level (2-5).

One of the factors causing dyspnoea in COPD patients is dynamic hyperinflation which could on its turn limit daily physical activity (6-8). Symptomatic patients with COPD are dyspnoic, even during daily activities. This leads to inactivity and subsequently to physical deconditioning. This results in a vicious circle of inactivity and disease progression that affects the quality of life highly(1,9). Furthermore, subjects with COPD who perform some level of regular physical activity have a lower risk of both respiratory mortality and hospital admission(10). Additionally, physical exercise decreases morbidity due to COPD(11).

Patients with COPD use expiratory muscles and increase their pleural and alveolar pressures during exercise, just as healthy individuals do. In this way it’s possible to completely breathe out the increased tidal volume before the next expiration starts. Consequently this causes an increase in the expiratory airflow. However, the airways of patients with COPD might collapse when the pleural pressure is positive, so that an increase in expiratory airflow is prevented(12,13). Due to this collapse the expiration cannot be entirely completed before the next expiration begins causing a progressive hyperinflation which is called dynamic hyperinflation. It occurs during physical activity in the presence or absence of static hyperinflation(14,15).

It is common knowledge that static hyperinflation is partly responsible for a sensation of dyspnea in patients with COPD. This knowledge is derived from studies that found a relief of dyspnea after lung volume reduction surgery(16-18). Static hyperinflation is defined as the increase, above the upper limits of natural variability, of the total lung capacity, the residual volume or the ratio of the residual volume and the total lung capacity(19). The different lung volumes are shown in figure 1(20).
Dynamic hyperinflation is defined as an increased end-expiratory lung volume during exercise. The end-expiratory lung volume during exercise and the inspiratory capacity together create the total lung capacity which always has to remain constant. Therefore an increase of the end-expiratory lung volume has to be accompanied by a decrease of the inspiratory capacity (figure 1). The end-expiratory lung volume can only be measured directly through additional pulmonary function testing, such as, respectively the helium dilution technique, the nitrogen washout technique, body plethysmography or chest radiography(21). It’s more practical to use decreased inspiratory capacity as a substitute for the increased end-expiratory lung volume(22,23).

![Figure 1](image.png)

Figure 1(20): Normal spirogram and subdivision of lung volume. Inspiratory capacity (IC), Functional residual capacity (FRC) (during breathing the FRC becomes the end expiratory lung volume (EELV)), inspiratory reserve volume (IRV), tidal volume (TV), expiratory reserve volume (ERV), residual volume (RV), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), vital capacity (VC), and total lung capacity (TLC).

Dynamic hyperinflation occurs during physical activity. Since metronome-paced tachypnea induces dynamic hyperinflation by visual or auditory support to encourage a fixed respiratory rate, it is a simple substitute of physical activity to cause dynamic hyperinflation (24). Metronome-paced tachypnea is a cost-effective and a relative patient-friendly method and it provides a very accurate way to quantify dynamic hyperinflation in a study population. It’s not only possible to determine the degree of dynamic hyperinflation in this manner accurately, but also other methods of quantification could be theoretically devised, such as the rate of developing dynamic hyperinflation during a particular respiratory rate. Determining the rate of developing dynamic hyperinflation during metronome-paced tachypnea could be a new, useful and accurate method to quantify dynamic hyperinflation.

Garcia-Rio et al. found that daily physical activity of patients with COPD is mainly associated with the degree of dynamic hyperinflation, regardless of severity classification (r=-0.73; P=0.001). However, no studies have investigated the relation between the rate of developing dynamic hyperinflation and daily activity in COPD-patients. Furthermore, the relation between the rate of recovery after having developed dynamic hyperinflation and daily activity is unknown.

Our main objective is to investigate if there is a relation between daily activity measured with a 3D-accelerometer and, induced by metronome-paced tachypnea, the rate of developing dynamic hyperinflation.
Our secondary objectives are to investigate if there is a relation between daily activity measured with a triaxial accelerometer and, induced by metronome-paced tachypnea, respectively, the rate of recovery after having developed dynamic hyperinflation and the degree of dynamic hyperinflation.

The Borg scale (1-10) is used to assess the subjective sense of dyspnea in patients with COPD\(^{(25-27)}\). The higher the number indicated on the Borg scale by a subject with COPD is, the worse his or her sense of dyspnoe is supposed to be.

Consequently, an additional secondary objective is to investigate if a change in Borg-score, measured as the difference between Borg-score before and after metronome-paced tachypnea, and daily activity, determined with an accelerometer, are related.

Static hyperinflation remains a meaningful variable in the context of overall hyperinflation with regard to subjects with COPD. Therefore, from an exploratory perspective we also want to investigate a relation between static hyperinflation and daily activity.

**Research questions**

Primary research question:

Are the rate of developing dynamic hyperinflation, induced by metronome-paced tachypnea, and daily activity, determined with an accelerometer, related?

Secondary research questions:

Are the rate of recovery after having developed dynamic hyperinflation, induced by metronome-paced tachypnea, and daily activity, determined with an accelerometer, related?

Are the degree of dynamic hyperinflation, induced by metronome-paced tachypnea, and daily activity, determined with an accelerometer, related?

Are a change in Borg-score, measured as the difference between Borg-score before and after metronome-paced tachypnea, and daily activity, determined with an accelerometer, related?

Additional explorative research question:

Are static hyperinflation, measured by use of spirometry and the helium dilution technique, and daily activity, determined with an accelerometer, related?

**Methods**

**Subjects**

This study was performed at the department of Pulmonary Medicine of Medisch Spectrum Twente, a training hospital in Enschede, The Netherlands, between the 22th of August 2013 and the 15th of January 2014. In total 35 patients were included. Inclusion criteria were COPD GOLD II and III, the ability to read and speak Dutch, an age between 40-80 years old, and a
signed informed consent. Exclusion criteria were GOLD stage I and IV, clinical signs of a COPD exacerbation, impairment of hearing or vision, use of long-term oxygen therapy, a history of asthma, serious psychiatric comorbidity, participation in a COPD rehabilitation program in the previous 3 months, serious comorbidity with a reduced life expectancy, restrictive lung disease (Total lung capacity < 80% of the predicted value), chronic lung disease other than COPD, a history of myocardial infarction, heart failure or cardiac arrhythmia in the previous 6 months that required treatment, and an inability to travel to the hospital. The procedure of receiving approval by the Medical Ethical Committee of the Medisch Spectrum Twente Hospital was arranged by the student responsible for this project report and this study. All patients were treated according to standard care.

Procedures

Physical activity
In this study we used the same triaxial accelerometer as Tabak et al. have used to ascertain the activity status in COPD patients(28). To accomplish this a smartphone (HTC Desire/ HTC Desire S) and a motion sensor (ProMove 3D wireless inertial sensor, Inertia Technology) were used. The motion sensor is a triaxial accelerometer that measures acceleration. The average value of the three axes of motion were then calculated and converted into activity outcome IMA (Integral modulus of body acceleration). IMA per minute was used as our activity outcome. The outcome measure was calculated by use of the method of Bouten et al.(29), that can be highly related to energy expenditure(29,30). Both the sensor-unit and smartphone were worn on the patient's belt. Daily activity was measured in our study for 7 consecutive days during waking hours(31).

Diary
Participants kept a diary in these 7 days to prevent measurement errors. Previous studies have shown that respectively two and three days of measurements are required to reliably determine the daily activity in GOLD II and GOLD III patients (3,32). Sundays are shown to be days with less activity and higher variety among the less severe COPD-patients(5). Literature shows that recording your steps in a diary already causes a substantial increase in activity level in the first measurement week compared to a blinded baseline activity measurement(33). As such, Clemes and Parker advised the first three days of a baseline measurement to be treated as a familiarization period. Consequently, we chose a measurement period of 7 days, with exception of sundays, unless sundays were part of the familiarization period. Participants were asked to continue their daily routines during measurements.

Metronome-paced tachypnea
At the second visit participants underwent metronome-paced tachypnea and secondary inspiratory capacity maneuvers. A web based metronome was used to acquire a fixed respiratory rate, that was shown to participants with a laptop(34). The metronome was first demonstrated to ensure that participants were able to hear the tones and to familiarize them with it. The participants were free to determine their own tidal volume, as long as they were breathing with at least the volume of their tidal volume at resting rate. This does not only approximate natural conditions, but also ensures that dynamic hyperinflation develops. The respiratory rate was set at 30 per minute(35). Every patient underwent one episode of metronome-paced tachypnea. The duration of the episode of tachypnea was 60 s. In this way the End-tidal CO\textsubscript{2} would stay within limit(35).
Oxycon Pro
Respiratory physiology during metronome-paced tachypnea was measured using Oxycon Pro (CareFusion)(36,37). Oxycon Pro is a breath- by- breath system consisting of a face mask with a turbine and integrated CO$_2$ en O$_2$ electrodes and a pulse oximeter. Before the episode of tachypnea and 1 minute after the episode of tachypnea was finished an inspiratory capacity maneuver was performed.

An inspiratory capacity maneuver consisted out of a maximal inspiration after a normal expiration. Because 2 inspiratory capacity measurements were carried out, correction for drifting could be applied(Fig.3). Consequently, throughout the course of the curve the change in the inspiratory capacity could be deduced.

Drifting
Drifting is a general phenomenon that can be defined as a gradual change in the zero line of an instrument that is assumed to be stable(Fig.2). This can occur when a slowly passing parameter is measured. During registration of respiration this occurs mainly during measurements of the tidal volume. Because inhaled air is being heated up and provided with water vapour completely, exhaled air is composed differently and is subsequently measured as a larger volume. Although drifting was corrected in advance (the ATP-BTPS correction), in general there always remains a slight deviation.

![Image](drifting.png)
**Pulmonary Function**

Spirometry and determination of the residual volume through helium dilution were performed (Pneumotach, CareFusion) when the term of the latest measurements exceeded 24 months.

**Hyperinflation**

The degree of dynamic hyperinflation was determined as the difference in the end-expiratory lung volume at the start and at the end of a period of metronome-paced tachypnea. This difference in inspiratory capacity in liters is used as a determinant of daily activity.

We did not only define dynamic hyperinflation as a change in the inspiratory capacity, but also as a change in the inspiratory capacity as a percentage of the total lung capacity. In this manner dynamic hyperinflation is corrected for height (38). A change in the inspiratory capacity as a percentage of the total lung capacity was used as a determinant of daily activity.

**Static hyperinflation**

We define static hyperinflation as a the ratio between the residual volume as a percentage of the total lung capacity, determined through measurements, and the reference value of this ratio. We think this is the most accurate definition of static hyperinflation. Static hyperinflation was used as an additional determinant of daily activity.

**Development and recovery rate of dynamic hyperinflation**

We used time coefficients to determine the development and recovery rate of dynamic hyperinflation. The department of technical medicine of the University of Twente developed a script, named VERDI, using MATLAB®(39,40) to determine these time coefficients. MATLAB® is a programming language just as the more common known programming language JAVA®. By use of this programming language applications can be developed. MATLAB® is used for mathematical purposes, such as data analysis, drawing of curves, the deduction of time coefficients and curve fitting. Curve fitting is a function of MATLAB®,
which is used to devise a curve based on a specific formula, for example the logarithmic formula \( a + b \times \ln(t) \). Subsequently, MATLAB® “fits” this formula in the best possible way to the data and provides for accurate values for parameters “a” and “b” in this formula. “a” is a constant and “b” is a time coefficient. Thus, the script VERDI is a program written by use of MATLAB® which we used to calculate time coefficients with regard to the development and recovery of dynamic hyperinflation.

Five different time coefficients were used to describe the development and recovery rate of dynamic hyperinflation:

1. **The logarithmic curve fit** where time coefficients could be derived from(Fig. 3). That is, VERDI searched for a shape of the formula \( a + b \times \ln(t) \) that corresponded most with the data. The time coefficient “b” is used as a determinant of daily activity. In case of the development rate this means that the higher the time coefficient is, the faster dynamic hyperinflation develops. In case of the recovery rate this means that the higher the time coefficient is, the faster dynamic hyperinflation dissolves. This variable is dimensionless, so it has no unit.

2. To investigate whether the development and recovery rate of dynamic hyperinflation could be quantified more easily, a method was developed by which the average incline per time unit could be determined. This crude approach made a trend line (Fig. 3). The time coefficient of the trend line is used as a determinant of daily activity. In case of the development rate this means that the higher the time coefficient is, the faster dynamic hyperinflation develops. In case of the recovery rate this means that the higher the time coefficient is, the faster dynamic hyperinflation dissolves. This variable is a crude approach and doesn’t have a specific unit.

3. **The time coefficient \( \tau \).** This time coefficient is equal to the time when the inspiratory capacity is reduced to 63,2% of the original inspiratory capacity(Fig.4). This percentage is based on a specific value of time regarding natural processes (logarithmic or exponential processes). By definition, the time coefficient \( \tau \) is the time when 63,2% \( (1-1/e) \) of the maximum value of a system is reached. This time coefficient is, among other things, used by the electro-technology in circuits that contain resistors and capacitators. In this case the time coefficient indicates the duration when a capacitor is charged at 63,2% of its maximum value. The larger the time coefficient \( \tau \) is, the longer it takes for the capacitor to become fully charged. Regarding the development rate of dynamic hyperinflation (as a change in inspiratory capacity), a similar time coefficient can be applied, which means that a small value of this time coefficient results in a fast development of dynamic hyperinflation(40). In case of the recovery this means that the smaller this time coefficient is, the faster dynamic hyperinflation dissolves. The time coefficient \( \tau \) is used as another determinant of daily activity.
4. The ‘area under the curve’ (AUC). This is the surface beneath the minima of the data during metronome-paced tachypnea. This parameter is presented as the relation between different surfaces beneath the curve (Fig. 3). The development rate is in this case described by the ratio of A+B/B. B is the surface beneath the trend line. By use of this method normalization of differences in lung volumes takes place. That is, a tall person inherently has large lungs (38). Consequently, surface B is relatively large in comparison with a person who has a normal or small body height. By use of the ratio A+B/B we try to normalize this difference in lung volume. The value of the ratio A+B/B is used as a determinant of physical activity. The larger this ratio is, the faster dynamic hyperinflation develops. The recovery rate is in this case described by the ratio D/C+D. D is the surface beneath the trend line. This ratio is inverted in comparison with A+B/B, because D in relation to B (both the surfaces beneath the trend lines) is much larger. The value of the ratio D/C+D is also used as a determinant of physical activity. The larger this ratio is, the faster dynamic hyperinflation dissolves.

5. The time of having reached maximum dynamic hyperinflation in seconds is also used as a determinant of daily activity. The smaller this value is, the faster dynamic hyperinflation develops.

**Borg score**

Borg scale (1-10) before and directly after metronome-paced tachypnea was examined (25-27). This test was performed to assess if a change in the Borg scale is linked with dynamic hyperinflation and activity status. It could be expected that if subjects experienced a sense of dyspnea by means of dynamic hyperinflation this could subsequently result in diminished daily activity. Thus, a change in borgscore is used as a determinant of daily activity.
Statistical analysis
First of all, histograms were used to determine if continuous variables were normally distributed. Subsequently, continuous variables were displayed as mean with SD or as median with interquartile range, dependent on the distribution. Hereafter, scatterplots were made to assess the association between two continuous variables. The degree of association was determined by either Pearson’s or Spearman’s correlation test as applicable.

Results

General baseline characteristics
The baseline characteristics and pulmonary function of the group of subjects included in the study are shown in Table 1.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
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<th>N=35</th>
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<tbody>
<tr>
<td>Males, N(%)</td>
<td>23 (66%)</td>
</tr>
<tr>
<td>Current smokers, N(%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>Participants in exercise-training program in preceding 3 months of study, N(%)</td>
<td>19 (54%)</td>
</tr>
<tr>
<td>GOLD II, N(%)</td>
<td>14 (40%)</td>
</tr>
<tr>
<td>III, N(%)</td>
<td>21 (60%)</td>
</tr>
<tr>
<td>BMI (SD)</td>
<td>28 (4)</td>
</tr>
<tr>
<td>VC, % pred (SD)</td>
<td>93 (20)</td>
</tr>
<tr>
<td>TLC, % pred (SD)</td>
<td>106 (14)</td>
</tr>
<tr>
<td>RV%TLC (SD)</td>
<td>46 (7)</td>
</tr>
<tr>
<td>FRC%TLC (SD)</td>
<td>62 (8)</td>
</tr>
<tr>
<td>FEV1, % pred (SD)</td>
<td>51 (12)</td>
</tr>
<tr>
<td>FEV1%VC (SD)</td>
<td>41 (9)</td>
</tr>
<tr>
<td>Median Age, yrs (IQR)</td>
<td>65 (59-70)</td>
</tr>
</tbody>
</table>

Definitions of abbreviations: BMI: body mass index; VC = vital capacity; TLC = total lung capacity; RV%TLC = residual volume as a percentage of the total lung capacity; FRC%TLC = functional residual capacity as a percentage of the total lung capacity; FEV1 = forced expiratory volume in 1 second; FEV1%VC = forced expiratory volume in 1 second as a percentage of the vital capacity.

Daily activity
Daily activity divided by GOLD stadium is shown in Figure 5. There was no significant difference (p=0.893) in median daily activity between patients with GOLDII (median IMA = 256 (201-389)) and GOLDIII ((median IMA = 273 (204-388 )).
Figure 5: IMA = activity outcome. The red line indicates the daily activity of a 27 year old healthy male with a fulltime desk job. As shown in this figure both GOLDII and GOLDIII groups have a lower median IMA score than the reference line.

The relation between daily activity and the development rate of dynamic hyperinflation

A

B

C

D
Figure 6: relation between daily activity measured with an accelerometer and (A) the time coefficient of the trend line that described the development rate of dynamic hyperinflation (B) the time coefficient of the logarithmic curve fit that described the development rate of dynamic hyperinflation (C) the time coefficient (tau) of the delta-IC curve that described the development rate of DH (D) the time of having reached maximum DH (Spearman’s rho) (E) the area under the curve that described the development rate of DH (Pearson’s correlation coefficient). DH = dynamic hyperinflation. IMA = activity outcome.

Between daily activity and the different time coefficients which described the development rate of dynamic hyperinflation no significant correlations were found (Figures 6A-6E).

The relation between daily activity and the recovery rate of dynamic hyperinflation
Between daily activity and the different time coefficients which described the recovery rate of dynamic hyperinflation no significant correlations were found (Figures 7A-7D).

**The relation between daily activity and the degree of dynamic hyperinflation**

Between daily activity and the degree of dynamic hyperinflation no significant correlations were found (Figure 8A-8B).
The relation between daily activity and a change in Borg-score

![Graph](image1)

*Figure 9:* relation between daily activity measured with an accelerometer and a change in Borg score (Spearman’s rho). IMA = activity outcome.

Between daily activity and a change in Borg score no significant correlation was found (Figure 9).

Exploratory analysis: static hyperinflation and daily activity

![Graph](image2)

*Figure 10:* relation between daily activity measured with an accelerometer and static hyperinflation (Spearman’s rho). IMA = activity outcome.

A negative correlation between daily physical activity and static hyperinflation was found (Figure 10).
Discussion

The absence of any correlation between daily activity and the degree of dynamic hyperinflation is contrary to results from more recently published studies. Garcia-Rio et al. had a study design that resembled ours and they did establish a negative association between the degree of dynamic hyperinflation (change in end-expiratory lung volume during exercise), induced with a cycle-ergometer, and daily activity, measured with a triaxial accelerometer (41). The difference is that we used metronome-paced tachypnea instead of a cycle-ergometer. Nonetheless, we feel that it is unlikely that this explains the observed difference since the metronome-paced tachypnea test has shown good overall accuracy to identify subjects who are susceptible to develop dynamic hyperinflation during cardiopulmonary exercise testing (CPET) (42).

On the other hand, it’s not unthinkable cycle-ergometry would result in an increased physiological demand in comparison with metronome-paced tachypnea. Subsequently, cycle-ergometry could lead to more dynamic hyperinflation. However, we compared by use of a one sample T-test our mean change in end-expiratory lung volume (1.10 L) with the mean change in end-expiratory lung volume of Garcia-Rio et al. (0.44 L) (41). Consequently, we had a significantly higher degree of dynamic hyperinflation (mean difference= 0.66; P<0.001).

It’s mentioned in current literature that not all subjects with COPD are susceptible to dynamic hyperinflation (41,42). It so happened that during our first measurements we discovered that patients breathing with a smaller tidal volume than at rest did not develop dynamic hyperinflation. This was probably due to low airflow so the smaller airways couldn’t collapse and air trapping was prevented.

When we coached the subjects to breath with at least the same tidal volume as at rest we saw an improvement. However, still some subjects didn’t develop dynamic hyperinflation (17%). Some of the patients who did not show dynamic hyperinflation were seen to breath with pursed lips. This caused an expiratory positive airway pressure (EPAP), which has been shown to reduce dynamic hyperinflation (43).

It is common practice lung volumes are defined as the percentage of the predicted value (19,44,45). This way, measured lung volumes can be related to the reference value of subjects with the same age, gender, body height or ethnic group (19,45). A single absolute value of a measured lung volume is relatively meaningless. Reference values of dynamic hyperinflation aren’t yet investigated. Nonetheless, the total lung capacity is related to body height (38). Consequently, measured lung volumes can be defined as the percentage of the total lung capacity to correct for body height. Therefore, we defined dynamic hyperinflation as a change in inspiratory capacity as the percentage of the total lung capacity. The effect of a similar absolute degree of dynamic hyperinflation could result in a different sense of dyspnea regarding a tall individual in comparison to a small subject, as a result of a difference in the total lung capacity. However, also with this corrected dynamic hyperinflation we observed no relation with daily activity.

Although other studies did find a relation between daily activity and dynamic hyperinflation, these same studies described dynamic hyperinflation as the absolute value of a change in end-expiratory lung volume, as the absolute value of a change in inspiratory capacity (24,41,46), or as the absolute value of a change in inspiratory capacity as a percentage of the inspiratory capacity at rest (8,42). By doing so, the results of the studies in which absolute values were used (24,41,46) are insignificant. The results of the studies in which a change in inspiratory
capacity as a percentage of the inspiratory capacity at rest (8,42) were used as an improvement of the former, because they used some baseline lung function variable to relate to. Nonetheless, a change in inspiratory capacity as a percentage of the total lung capacity corrects for body height. The question remains, if these studies had corrected for body height, would they still have found a relation between daily activity and dynamic hyperinflation?

A reason we didn’t see a relation between daily activity and dynamic hyperinflation could be because of the presence of static hyperinflation in these subjects since Hannink et al. mentioned that dynamic hyperinflation was inversely related to static hyperinflation (47). We were not able to confirm this inverse relation in our explorative analyses (r = -0.173; P = 0.371). An explanation for this discrepancy could be the result of the differences in definitions used. Hannink et al used the inspiratory reserve volume (IRV) during exercise as a reflection of static hyperinflation (47), while we used the ratio of the measured residual volume and the percentage of the total lung capacity divided by the reference value of this ratio. While the inspiratory reserve volume is a reflection of static hyperinflation, an increase in the reserve volume as the percentage of the total lung capacity is a commonly used method to measure static hyperinflation in a verified accurate way (19, 44, 45).

The majority of our patients having static hyperinflation (75%), which alone can result in reduced activity, could explain why dynamic hyperinflation had no noticeable effect on daily activity. That is, our explorative analyses showed that there was a significant negative relation between static hyperinflation and daily activity (r = -0.393; P = 0.020).

A difference between the study of Garcia-Rio et al. and our study is that they excluded subjects who were engaged in any exercise-training programme in the previous 3 months before participating in the study, while we only excluded patients who took part in a COPD rehabilitation programme in the previous 3 months. Consequently, to check if a difference in this exclusion criterium could offer a possible explanation for not finding a relation between dynamic hyperinflation and daily activity, we performed additional subgroup analyses with regard to subjects who either were or were not engaged in any exercise-training programme in the preceding 3 months of the study. Still, no significant correlations between the degree of dynamic hyperinflation and daily activity were observed. Nonetheless, these subgroup analyses revealed that subjects who were not engaged in any exercise-training programme in the previous three months before participating in this study showed an even stronger negative correlation between daily activity and static hyperinflation (r = -0.528; P = 0.035). No significant correlation between static hyperinflation and daily activity was found in subjects who were engaged in such a programme.

Garcia-Rio et al. did find a relation between dynamic hyperinflation and daily activity (41). We wanted to investigate if differences in the characteristics of the subjects of our studies could offer an explanation. Thereafter, we wanted to investigate differences in baseline characteristics with regard to Garcia-Rio et al. (41) by use of a one sample T-test. The baseline lung function parameters which were used in their study were not all the same as ours so we could only compare the mean age, the body-mass index, the residual volume as the percentage of the total lung capacity and, subsequently as the percentage of the predicted value, the total lung capacity and the forced expiratory volume in 1 second. Only the residual volume as the percentage of the total lung capacity showed a significant difference (Garcia-Rio et al.: 57%; ours: 46%; difference in means: p < 0.001). A trend was seen between the forced expiratory volume in 1 second as the percentage of the predicted value. This makes sense, because Garcia-Rio et al. also included GOLD I and IV subjects (41). Although only the residual
volume as the percentage of the total lung capacity showed a significant difference, this still doesn’t explain the absence of a relation between daily activity and dynamic hyperinflation.

The script VERDI(40) that was used to determine the time coefficients had some disadvantages. First of all, to analyze the curves you first had to manually select the area where dynamic hyperinflation started to develop and where dynamic hyperinflation reached its plateau.

Subjects had to maintain a regular respiratory rate with a tidal volume that also remained relatively constant, or else they would start with metronome-paced tachypnea at a higher end-expiratory lung volume level, which could suggest a larger increase of dynamic hyperinflation than was actually the case.

Furthermore, the inspiratory capacity-manoeuvres that were necessary to correct for drifting had to be both performed at the maximum capability of the subjects, otherwise the correction for drifting would not be exact. That would consequently influence the determination of dynamic hyperinflation.

Although this study produced some interesting results, this study group remains the result of a sample size calculation which reflects only a small part of the total COPD population. Moreover, this study group consisted only of the COPD patients which have an indication for a consultation with a pulmonary specialist (7% (48)). The results of this study could be a poor reflection of the remaining 93% of COPD patients in The Netherlands that only have consultations with a general practitioner or a different specialist.

Conclusion
We did not find any relation between daily physical activity and dynamic hyperinflation in terms of 1) development rate and recovery rate of dynamic hyperinflation and 2) the degree of dynamic hyperinflation, in patients with COPD. Nonetheless, static hyperinflation could be a useful marker to indicate reduced daily physical activity. No relation was found between daily activity and a change in Borg scale.

Literature


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