**CLUSTER ANALYSIS OF PHYSICAL ACTIVITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A MULTICENTER STUDY**

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**AT A GLANCE COMMENTARY**

**Scientific Knowledge on the Subject**

Reduced physical activity has been reported in patients with chronic obstructive pulmonary disease (COPD), leading to increased risk of hospitalization and mortality. Thus, increasing physical activity in patients with COPD has become a priority. However, the heterogeneity of physical activity levels in patients with COPD is still insufficiently understood. To date, no large-scale study has investigated daily physical activity hourly patterns and cluster analysis based on physical activity measures in patients with COPD.

**What This Study Adds to the Field**

In a multicenter sample of 1001 patients with COPD, daily physical activity measures and hourly patterns were found to vary considerably depending on the clinical characteristic. Compared with healthy subjects, patients spent not only less time in higher intensities of physical activity, but also more time in lower intensities. Five clusters of patients were identified, each with distinct physical activity measures and hourly patterns. Compared to four other clusters, cluster 1 (the most inactive) spent less time in higher intensities and more time in lower intensities, whilst presenting with higher BMI, worse airflow limitation and disease severity, and more dyspnea. The present data show that outcome measures need to be clearly delineated when evaluating interventions aiming to promote PA in patients with COPD.

This article has an online data supplement, which is accessible from this issue's table of content online at [www.atsjournals.org](http://www.atsjournals.org)

**ABSTRACT**

**Rationale:** Physical activity (PA) in patients with chronic obstructive pulmonary disease (COPD) is insufficiently understood.

**Objectives:** To describe PA measures and hourly patterns in patients with COPD after stratification for clinical characteristics; to compare these measures and patterns between patients and healthy subjects; and to identify clusters of patients based on PA measures.

**Methods:** 1001 patients with COPD (65% men; age, 67 years; FEV1, 49% predicted) and 66 healthy subjects (45% men; age, 65 years; FEV1, 107% predicted) were studied. Daily PA measures and PA hourly patterns (i.e., the graphic representation of the mean intensity per hour during a day) were analyzed based on data from a multi-sensor armband. Principal component analysis (PCA) and cluster analysis were applied to PA data to identify subgroups.

**Measurements and main results:** Age, body mass index (BMI), dyspnea grade and the ADO index (including age, dyspnea, and airflow obstruction) were associated with PA measures and hourly patterns in patients with COPD. Compared to healthy subjects, patients had lower intensities of PA across hourly patterns. Five clusters were identified based on 3 components from the PCA, which accounted for 60% of variance. Importantly, cluster 1 - the most inactive cluster - was characterized by higher BMI, lower FEV1, worse dyspnea and higher ADO index compared to other clusters (*P*<0.05 for all).

**Conclusions:** Daily PA measures and hourly patterns in COPD are heterogeneous. Subgroups of patients could be identified based on PA data. These findings may be useful for interventions aiming to promote PA in COPD.

**Word count for the abstract:** 250 words.

**Keywords:** chronic obstructive pulmonary disease; physical activity; principal component analysis; cluster analysis.

**INTRODUCTION**

Patients with chronic obstructive pulmonary disease (COPD) undertake less physical activity (PA) compared to healthy individuals ([1-3](#_ENREF_1)), and this relative inactivity is related to a higher risk of hospital admission and mortality ([4-8](#_ENREF_4)). Since PA measures can be used as an outcome measure for clinical trials, a greater understanding of the clinical importance of physical activity and inactivity in COPD is needed.

To date, most studies investigating PA in patients with COPD have focused on the average daily value and its standard deviation ([9-14](#_ENREF_9)). Donaire-Gonzalez and colleagues ([15](#_ENREF_15)) were the first to perform more detailed analyses, showing that patients with COPD perform bouts of moderate-to-vigorous PA, and that the frequency of these bouts is inversely associated with the degree of airflow limitation. More detailed analyses may provide a better insight into daily PA of patients with COPD, but may also contribute to identify patients who benefit most from interventions, and this is important as interventions thus far have failed to demonstrate important increases in PA in patients with COPD ([13](#_ENREF_13), [16](#_ENREF_16), [17](#_ENREF_17)). Multiple other types of analyses to study PA in more depth are also available, such as daily PA hourly patterns (18, 19) and cluster analysis of PA measures (18, 20-22).

Plotting PA hourly provides a graphic representation of the average PA intensity per hour over the course of a day (19, 22, 23). This data can reveal whether specific physical activities are concentrated during certain periods of the day (23), but also whether and to what extent activities during weekdays and weekend days are performed in a similar manner ([18](#_ENREF_18)). Cluster analysis may be useful to identify subgroups of patients with similar PA characteristics (24), which may assist in targeting management strategies. PA hourly patterns and cluster analysis of PA measures have not been investigated in a large-scale study in patients with COPD. We hypothesize that distinct PA hourly patterns can be found in patients with different clinical characteristics or in comparison with healthy subjects, and that patients can be clustered into subgroups that associate with clinical characteristics.

Therefore, we aimed to i) describe PA measures and hourly patterns in patients with COPD after stratification for clinical characteristics, ii) compare PA measures and hourly patterns between patients with COPD and healthy subjects matched for gender, age and body mass index (BMI) and iii) identify clusters of patients with COPD based on PA measures with the goal of comparing clinical characteristics, PA measures and PA hourly patterns amongst these clusters.

**METHODS**

**Study design and participants**

In this multicenter, post-hoc cross-sectional study, objectively assessed PA data from the United Kingdom, Ireland, the Netherlands, Germany, Switzerland, Italy, Spain, the United States of America, Brazil, and Australia was analyzed. Published and/or unpublished PA data (with no overlapping analyses) as assessed by the SenseWear Armband or SenseWear Mini Armband activity monitors (both from BodyMedia Inc., Pittsburgh, PA, USA) was considered for the current analyses. Details of data sources are provided in the online supplement, including the references of previous reports that used the data under analysis. Subjects were included if they met the following inclusion criteria: COPD with a post-bronchodilator forced expiratory volume in the first 1 second (FEV1) / forced vital capacity (FVC) ratio <0.70 (25), stable condition (i.e., no recent exacerbation), and complete data for age, gender, BMI and daily PA measures (see *Assessments* section). Centers from the Netherlands and the UK also provided data on healthy elderly subjects, who were then pairwise-matched (1:1) for gender, age and BMI with a subgroup of patients with COPD. Ethics Board approval was obtained from the local ethics committees, and written informed consent was provided by participants, except for the data from Italy (n=23), which was obtained as part of routine clinical assessments.

**Assessments**

Demographics, anthropometrics, lung function, and clinical data were assessed; details can be found in the online supplement. The SenseWear Armband and SenseWear Mini Armband activity monitors were used to assess PA. These devices combine an accelerometer with different physiological sensors (a heat flux sensor, a galvanic skin response sensor, a skin temperature sensor, and a near-body ambient temperature sensor). Together with demographic characteristics, such as gender, age, height and weight, energy expenditure (EE) can be estimated using proprietary algorithms developed by the manufacturer. The SenseWear Armband has been shown to be valid both in field (26, 27) and in laboratory studies (28-30). The following thresholds proposed by the American College of Sports Medicine (ACSM) (31) were used to classify the intensity of activities: very light intensity, <2.0 metabolic equivalents of task (MET); light intensity, 2.0 to 2.9 METs; and moderate-to-vigorous intensity, ≥3.0 METs.

A minimum of 4 days (2 weekdays + Saturday + Sunday) was considered acceptable ([9](#_ENREF_9)), with the device being used for ≥22 hours·day-1 (32). Since PA measures during the week and the weekend are known to be different ([9](#_ENREF_9)), only recordings during waking hours and weekdays were considered for the cluster analysis, in order to reduce the variability of the data. Details on the selection of waking hour recordings can be found online. The PA measures represent the average of all valid weekdays. Weekend days were used only for the presentation of daily PA hourly patterns, which consist of a graphic representation of the intensity of PA per hour during the course of a day (18, 19, 22, 23). The software SenseWear Professional versions 6.1 and 7.0 were used for data analysis, providing minute-by-minute EE and METs. These two measures were stratified according to different criteria (and the combination of them): intensity (e.g., very light, light or moderate-to-vigorous intensity), duration (e.g., bouts of activity), period of the day (e.g., before or after midday), frequency (e.g., number of bouts per day); and presentation (e.g., absolute numbers or percentage of total). These stratifications were performed with Matlab R2012b (Mathworks Inc., USA) and led to 180 distinct variables referred to as features (Table E1, online supplement), which were used for clustering of patients.

**Statistical Analysis**

Continuous variables were expressed as median (interquartile range), as most variables presented non-normal distribution. Categorical variables were expressed as absolute and/or relative frequency. Mann-Whitney U test or Kruskal-Wallis test (post hoc Dunn) was used for comparing continuous variables, whilst the chi-square test was used for categorical variables. Spearman coefficient was used to investigate correlations, when appropriate. *P*<0.05 was considered significant and all statistical analyses were performed using SPSS 17.0 (SPSS, Chicago, Illinois, USA) or GraphPad Prism 5 (GraphPad Software, La Jolla, California, USA). Details about sample size calculation can be found in the online supplement.

Cluster analysis was adopted to identify subgroups with distinct PA profiles. Firstly, Principal Component Analysis (PCA) was used to reduce the high-dimensional feature set (180 dimensions) to a lower subspace useful for data visualization (3 dimensions). PCA transforms the data into a subset of linearly uncorrelated variables (i.e., principal components) so that the variance of the data in the low-dimensional representation is maximized. The components are constructed in a way that the first component has the largest possible variance under the constraint that it is uncorrelated with the others. Secondly, a k-means clustering algorithm with automatic selection of the number of clusters was applied to the 3 dimensional principal components space to separate the subjects into groups with distinct characteristics. The algorithm selects the number of clusters in a way that the corresponding clustering results are the most stable under small perturbations of the input dataset (33). The normalized mean over pairwise clustering distances was used as an instability measure (33). The features were first standardized using z-scores. Feature extraction, PCA and cluster analysis were performed using Matlab R2012b (Mathworks Inc., USA).

**RESULTS**

**General characteristics**

In total, 1001 patients with COPD were analyzed (Table 1). The number of subjects recruited from each country can be found online (Table E2). The majority of the patients were men, had normal-to-overweight BMI and moderate-to-severe degree of airflow limitation, were categorized to GOLD group D (i.e., high risk and more symptoms), and only a small proportion used LTOT.

**Daily PA measures and PA hourly patterns**

The median number of valid days was 6 (6 – 6) days, resulting in a total of 6074 valid PA days, of which 4049 (67%) were weekdays. Table 2 presents the daily PA measures during the weekdays. The smallest amount of time and lowest EE were spent in moderate-to-vigorous intensity. At this intensity, patients spent a median of 6 (0 – 22) min·day-1 in bouts of ≥10 minutes and 38 (17 – 79) min·day-1 in bouts of ≥2 minutes. Figure 1 presents the daily PA hourly patterns of the patients. A similar pattern can be observed between weekdays (Figure 1A) and weekend days (Figure 1B), and in both analyses the peak of intensity occurred before midday.

***Stratification for clinical characteristics***

Patients of older age, female gender, LTOT users, lower DLCO, higher mMRC dyspnea grade, higher BMI, higher ADO index, higher GOLD grade and patients from GOLD group D spent the smallest amount of time and lowest EE in moderate-to-vigorous intensity (Tables E3-E11, online supplement). Daily PA hourly patterns after stratification for the abovementioned clinical characteristics are presented in figures 2 and E1 (online supplement), showing a noticeable influence of age, BMI, mMRC dyspnea grades, and ADO index scores. The influence of GOLD grades or groups on these patterns was small. A weak but significant positive association existed between FEV1 (% predicted) and the time in activities of moderate-to-vigorous intensity (*r*s=0.20, *P*<0.0001; Figure 3).

***Patients with COPD versus healthy subjects***

Table 3 presents the general characteristics and daily PA measures in moderate-to-vigorous intensity of 66 healthy subjects and a subgroup of 66 patients with COPD, pairwise-matched for gender, age and BMI. As expected, subjects with COPD had worse lung function, higher mMRC dyspnea grade and worse PA measures compared to healthy subjects. The comparison of daily PA measures in very light and light intensities can be found in Table E12 (online supplement). Interestingly, patients with COPD spent more time in very light intensity than healthy subjects, but there was no difference for the time in light intensity. Figure 4 presents the daily PA hourly patterns of both groups. In general, healthy subjects performed their activities at higher intensities compared to patients with COPD, and this difference was more pronounced during weekdays.

**Cluster analysis of daily PA measures**

The PCA identified 3 components, which accounted for 60% of the total variance (first component, 34%; second component, 17%; third component, 9%). The most relevant features of the 1st component were the daily time in ≥2-min bouts of very light intensity, expressed as percentage of total assessment time; the daily time in ≥10-min bouts of very light intensity, in min·day-1; and the daily time in ≥10-min bouts of very light intensity, expressed as percentage of total assessment time. The most relevant of the 2nd component were the daily EE in moderate-to-vigorous intensity, the daily EE in ≥2-min of moderate-to-vigorous intensity, and the daily EE in ≥10-min bouts of moderate-to-vigorous intensity, all expressed as percentage of total EE. The most relevant of the 3rd component were the daily EE in very light intensity after midday, the daily EE in very light intensity, and the daily EE in ≥2-min bouts of very light intensity after midday, all in METs-min∙day-1.

Cluster analysis, performed on the 3 PCA components, identified five groups (Figure 5; see online supplement for a 3D video of Figure 5). Table 4 presents the general characteristics and PA measures of these groups. Cluster 1 was characterized by higher BMI, more dyspnea, higher ADO index, more time and EE in very light intensity, and less time and EE in light and moderate-to-vigorous intensities compared to other clusters. This cluster also had worse lung function compared to clusters 3 and 4, and apparently a higher proportion of GOLD D patients. Cluster 2 had the largest sample size with the most similar general characteristics and PA measures to the total sample. Cluster 2 also had more dyspnea and a higher ADO index than clusters 3 and 5. Similarly to cluster 1, this cluster spent more time and EE in very light intensity, and less time and EE in moderate-to-vigorous intensity than other clusters. Cluster 3 exhibited a higher FEV1 than cluster 2 and a higher FEV1/FVC ratio than clusters 1 and 2, whilst cluster 4 was younger than clusters 1 and 2 and had a lower BMI compared to cluster 2. Moreover, cluster 3 spent more time and EE in light intensity and less time and EE in moderate-to-vigorous intensity than clusters 4 and 5, whilst cluster 4 spent more time in light intensity compared to cluster 5. Cluster 5 had the smallest sample size (n=21) and was characterized by less time in very light intensity and more time in moderate-to-vigorous intensity compared to other clusters. Figure 6 presents the daily PA hourly patterns of the clusters. In all clusters the peak of intensity during the day occurred before midday, and in general, weekdays and weekend days presented a similar pattern, especially in more inactive clusters.

**DISCUSSION**

The present study provides detailed analyses of objectively measured PA in a multinational sample of 1001 patients with COPD. The principal findings were that, in patients with COPD, daily PA measures and hourly patterns vary considerably after stratification for clinical characteristics, such as age, BMI, and mMRC dyspnea grade. Also, patients with COPD exhibit PA hourly patterns at lower intensities in comparison with healthy subjects. Furthermore, patients with COPD can be clustered based on daily PA measures, with 5 clusters being identified, each with distinct PA measures and hourly patterns. Of note, a subgroup of patients with importantly compromised PA measures was observed (i.e., cluster 1).

**Daily PA measures, PA hourly patterns, and clinical characteristics**

Our results clearly show that PA is a heterogeneous outcome in patients with COPD, corroborating previous findings (1, 34, 35). Distinct daily PA measures were found after stratification for age (< or ≥ 67 years), gender (male or female), BMI (underweight to obese), mMRC dyspnea grade (0 to 4), LTOT (yes or no), DLCO (< or ≥ 51% predicted), ADO index (< or ≥ 4 points), GOLD grades (1 to 4) and GOLD groups (A to D) (Tables E3-E11). Our findings are broadly corroborated by previous literature on the determinants of PA in patients with COPD, as recently summarized by Gimeno-Santos et al (36). Interestingly, comparable time in very light and moderate-to-vigorous intensities was found between GOLD groups A and C, and B and D (Table E11). This suggests that symptoms, which discriminated between groups A/C and B/D, are better associated with PA measures than the degree of airflow limitation, which discriminated between groups A/B and C/D. Nonetheless, the influence of the GOLD 2011 classification on PA hourly patterns was less evident. Only age, BMI, mMRC dyspnea grade, and ADO index scores seemed to associate with PA hourly patterns (Figures 2 and E1). The stratification for GOLD grades (1 to 4) did not associate with PA hourly patterns, and this was supported by a weak association between FEV1 and the time in moderate-to-vigorous intensity (Figure 3). These findings and those of previous research suggest that the degree of airflow limitation only modestly determine PA in patients with COPD ([1](#_ENREF_1), [9](#_ENREF_9), [10](#_ENREF_10)).

**Healthy subjects versus patients with COPD**

Patients with COPD are physically less active compared to healthy subjects (1, 3, 32, 37). The present study is the first to confirm this finding after a pairwise matching for gender, age and BMI. To our knowledge, this study is the first large study to show that patients with COPD not only spend less time in moderate-to-vigorous intensity, but also more time in very light intensity, which can be considered a surrogate of sedentary time (i.e., activities between 1.0-1.5 METs) (38). There has been one smaller study that identified increased sedentary behavior in people with COPD with physical comorbidities compared to healthy subjects (37). However, most previous studies in COPD have only used moderate-to-high intensity PA measures to evidence the physical inactivity of the patients (9, 15, 39). Reducing the time in very light intensity without necessarily increasing the time in moderate-to-vigorous intensity may be an important strategy for achieving health benefits in patients with COPD ([4](#_ENREF_4)). Distinct PA hourly patterns were found in patients with COPD in comparison with healthy subjects, and this has not been shown previously. Patients with COPD perform their activities at a lower intensity compared with healthy subjects, and this difference was more evident during weekdays. PA hourly patterns also suggest that patients with COPD tend to be inactive during both weekdays and weekend days, whilst healthy subjects tend to be less active especially during weekend days.

**Clusters of patients with COPD based on daily PA measures**

The present study is the first to cluster patients with COPD based on daily PA measures. Indeed, five clusters were identified, each with distinct PA measures and hourly patterns. One very active cluster and one very inactive cluster were identified, but clusters in intermediate categories were also observed. Cluster 1 spent less time in moderate-to-vigorous intensity and more time in very light intensity compared to other clusters, with a very similar PA hourly pattern between weekdays and weekend days. This cluster is representative of an inactive lifestyle.

Only a few studies have used objectively measured PA data solely for clustering subjects, principally in children and middle-aged adults. In 10-to-12-year-old children, De Bourdeaudhuij and colleagues (40) were able to identify four clusters in each gender group, one of them with a mixed arrangement of PA (i.e., less time in moderate-to-vigorous intensity + less sedentary time). In our study, we also found a cluster with resembling characteristics (i.e., cluster 4, long very light intensity/long moderate-to-vigorous intensity), confirming that activities of moderate-to-vigorous intensity and sedentary activities are not two sides of one continuum (40). Indeed, clusters 4 and 5 were the only clusters to meet the recommendation of ≥30min·day-1 in ≥10-min bouts of moderate-to-vigorous intensity (31). On the other hand, more inactive clusters were also observed (clusters 1, 2 and 3). In middle-aged Chinese adults, Lee et al ([18](#_ENREF_18)) identified two clusters based on average counts per minute, one more active than the other. Male subjects from the less active cluster presented higher body fat percentage and older age than those from the active group ([18](#_ENREF_18)). In our study, patients from cluster 1 had older age, lower FEV1, higher BMI, worse dyspnea and higher ADO index than other clusters. Based on their characteristics, patients from this cluster may have a worse prognosis, but no follow-up data is available to confirm this hypothesis. Identifying clusters of subjects based on PA data may also be of clinical importance, as interventions thus far have failed to increase importantly PA measures in patients with COPD ([13](#_ENREF_13), [16](#_ENREF_16), [17](#_ENREF_17)). Interventions tailored to the needs of groups with specific PA profiles may lead to more important improvements in PA.

**Strengths and limitations of the findings**

Our sample is by far the largest and most diverse sample of patients with COPD with objectively assessed PA data ever studied. This allowed detailed analyses of daily PA, even identifying clusters of patients with COPD with similar PA measures, a true novelty within the COPD literature. PA hourly patterns were also investigated for the first time in a large-scale study in COPD, another important advance. All these analyses were only possible due to the use of objective methods of PA, another strength of our study.

Some methodological limitations are acknowledged, most of them related to this being a post-hoc cross-sectional analysis. Selection and information biases might be present, as parts of the data were collected with different purposes. Nevertheless, having patients from different studies and countries allowed us to have a more diverse sample, which may enhance the external validity of our findings. The clusters identified in our study were not validated, and this constitutes another limitation. Moreover, some of our findings need to be interpreted with caution in light of the number of multiple comparison tests performed.(41) Nonetheless, multiple findings in the same direction rather than a single statistically significant result are suggestive that these are not due to chance alone.

In a large and multicenter sample of patients with COPD, daily PA measures and hourly patterns were found to vary considerably depending on the clinical characteristic. Compared with healthy subjects, patients spent not only less time in higher intensities of physical activity, but also more time in lower intensities. Five clusters of patients were identified, each with distinct PA measures and hourly patterns. Compared to other clusters, cluster 1 (the most inactive) spent less time in higher intensities and more time in lower intensities, whilst presenting with higher BMI, worse airflow limitation and disease severity, and more dyspnea. The present data show that outcome measures need to be clearly delineated when evaluating interventions aiming to promote PA in patients with COPD.

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**FIGURE LEGENDS**

***Figure 1.*** Daily PA hourly patterns of the 1001 patients with COPD during weekdays (A) and weekend days (B). Data pooled per hour as mean (95% confidence intervals).

***Figure 2.***Daily PA hourly patterns of the patients with COPD after stratification for: A and B – modified Medical Research Council (mMRC) grades, data available for 868 subjects only; C and D – body mass index (BMI) classification; E and F – Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades (1 to 4); and G and H – GOLD groups (A to D). Figures A, C, E, and G represent weekdays, whilst figures B, D, F, and H represent weekend days. Data pooled per hour as mean (95% confidence intervals).

***Figure 3.*** Spearman’s correlation between FEV1 (% predicted) and the daily time in activities of moderate-to-vigorous intensity for 1001 patients with COPD (*r*s=0.20, *P*<0.0001).

***Figure 4.*** Daily PA hourly patterns of healthy subjects and matched patients with COPD during weekdays (A) and weekend days (B). Data pooled per hour as mean (95% confidence intervals).

***Figure 5.*** The five clusters identified. A: Graph in 3 dimensions presenting the three PCA components; B: Graph in 2 dimensions presenting the 1st and 2nd components; C: Graph in 2 dimensions presenting the 1st and 3rd components; and D: Graph in 2 dimensions presenting the 2nd and 3rd components. Details about the relationship between components and clusters can be found in the online supplement.

***Figure 6.*** Daily PA hourly pattern of the clusters of patients with COPD during weekdays (A and C) and weekend days (B and D), and before (A and B) and after (C and D) synchronization of the waking up moment. Data pooled per hour as mean (95% confidence intervals).

**TABLES**

**TABLE 1. GENERAL CHARACTERISTICS OF PATIENTS WITH COPD (n=1001)**

|  |  |
| --- | --- |
| Characteristic | Value |
| Age, yrs | 67 (61 – 72) |
| Male, % | 65 |
| Weight, kg | 74 (62 – 87) |
| Height, m | 1.70 (1.63 – 1.75) |
| BMI, kg·m-2 | 25.8 (22.5 – 29.6) |
| BMI classification, %  Underweight  Normal weight  Overweight  Obese | 7  37  34  22 |
| mMRC dyspnea grade\* | 2 (1 – 3) |
| Long-term oxygen therapy, %† | 10 |
| FEV1, L | 1.31 (0.91 – 1.79) |
| FEV1, % predicted | 49 (34 – 64) |
| FEV1/FVC, % | 45 (35 – 56) |
| DLCO, % predicted‡ | 51 (37 – 67) |
| ADO index\* | 4 (3 – 5) |
| GOLD 2007 classification 1 / 2 / 3 / 4, % | 9 / 40 / 34 / 17 |
| GOLD 2011 classification A / B / C / D, %\* | 29 / 16 / 17 / 38 |

Data expressed as absolute/relative frequency, or median (interquartile range). BMI: body mass index; mMRC: modified Medical Research Council; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; DLCO: diffusion capacity of the lung for carbon monoxide; ADO: age dyspnea obstruction index; GOLD: Global Initiative for Chronic Obstructive Lung Disease. \*Data available for 868 subjects; †Data available for 707 subjects; ‡Data available for 505 subjects.

**TABLE 2. DAILY PHYSICAL ACTIVITY MEASURES DURING WEEKDAYS IN PATIENTS WITH COPD**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | General physical activity | | | |
| PA measure | Very light intensity | Light intensity | | Moderate-to-vigorous intensity |
| Time, min∙day-1  Before midday  After midday  Total | 283 (236 – 347)  514 (449 – 577)  803 (710 – 901) | 49 (31 – 74)†  88 (53 – 123)†  142 (92 – 194)† | | 21 (10 – 42)†,‡  27 (13 – 59)†,‡  52 (26 – 99)†,‡ |
| EE, METs-min∙day-1  Before midday  After midday  Total | 364 (274 – 502)  668 (521 – 858)  1032 (822 – 1327) | 154 (95 - 263)†  273 (167 – 413)†  435 (291 – 655)† | | 110 (46 – 232)†,‡  147 (65 – 310)†,‡  267 (132 – 550)†,‡ |
|  | Bouts of physical activity | | | |
| PA measure | Very light intensity | | Light intensity | Moderate-to-vigorous intensity |
| Time, min∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 273 (225 – 338)  503 (435 – 569)  781 (683 – 884)  215 (167 – 284)  436 (352 – 526)  657 (539 – 780) | | 37 (22 – 59)†  67 (37 – 97)†  107 (65 – 156)†  3 (0 – 8)†  4 (0 – 14)†  7 (0 – 22)† | 15 (6 – 34)†,‡  20 (8 – 47)†,‡  38 (17 – 79)†,‡  2 (0 – 11)†  3 (0 – 13)†,‡  6 (0 – 22)† |
| Frequency, bouts∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 21 (17 – 25)  27 (21 – 34)  48 (39 – 58)  7 (6 – 9)  11 (9 – 13)  18 (16 – 21) | | 11 (7 – 16)†  19 (11 – 26)†  31 (20 – 41)†  0 (0 – 1)†  0 (0 – 1)†  1 (0 – 2)† | 4 (2 – 8)†,‡  5 (2 – 10)†,‡  10 (5 – 17)†,‡  0 (0 – 1)†  0 (0 – 1)†  1 (0 – 2)† |
| Average duration, min∙bout-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 13 (10 – 17)  18 (13 – 27)  16 (12 – 21)  29 (24 – 36)  37 (29 – 50)  34 (28 – 43) | | 3 (3 – 4)†  3 (3 – 4)†  3 (3 – 4)†  10 (0 – 13)†  11 (0 – 13)†  12 (0 – 14)† | 4 (3 – 5)†,‡  4 (3 – 5)†,‡  4 (3 – 5)†,‡  10 (0 – 15)†,‡  11 (0 – 15)†  13 (0 – 16)†,‡ |
| EE, METs-min∙day-1\*  ≥2-minute  Before midday  After midday  Total  ≥10-minute  Before midday  After midday  Total | 347 (261 – 490)  648 (501 – 845)  1000 (783 – 1298)  273 (193 – 411)  572 (410 – 783)  847 (626 – 1168) | | 118 (67 – 205)†  211 (119 – 335)†  340 (204 – 523)†  6 (0 – 26)†  14 (0 – 47)†  26 (0 – 77)† | 86 (29 – 187)†,‡  106 (41 – 255)†,‡  205 (86 – 436)†,‡  9 (0 – 61)†,‡  12 (0 – 69)†  36 (0 – 132)† |

Data expressed as median (interquartile range). EE: energy expenditure; MET: metabolic equivalent of task. \*The time, frequency and EE in bouts of physical activity were averaged out over the total number of valid days, whilst the duration of bouts of physical activity was averaged out over the total number of bouts available. †*P*<0.05 vs very light intensity; ‡*P*<0.05 vs light intensity.

**TABLE 3. GENERAL CHARACTERISTICS AND DAILY PHYSICAL ACTIVITY MEASURES IN MODERATE-TO-VIGOROUS INTENSITY OF HEALTHY SUBJECTS AND MATCHED PATIENTS WITH COPD**

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic/PA measure | Healthy subjects | Matched patients with COPD | *P*-value |
| General characteristics  N | 66 | 66 |  |
| Age, yrs | 65 (61 – 70) | 65 (61 – 70) | 1.00 |
| Male, % | 45 | 45 | 1.00 |
| BMI, kg·m-2 | 25.3 (22.9 – 28.1) | 24.9 (22.4 – 27.9) | 0.65 |
| FEV1, % predicted | 107 (97 – 117) | 43 (29 – 63) | <0.0001 |
| FEV1/FVC, % | 78 (75 – 82) | 42 (32 – 54) | <0.0001 |
| mMRC dyspnea grade, points\* | 0 (0 – 0) | 2 (1 – 3) | <0.0001 |
| Physical activity measures in moderate-to-vigorous intensity  Time, min∙day-1 | 101 (57 – 163) | 47 (30 – 95) | <0.0001 |
| EE, METs-min∙day-1 | 461 (271 – 797) | 213 (123 – 435) | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 82 (38 – 138) | 37 (15 – 83) | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 29 (10 – 73) | 6 (0 – 20) | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 17 (10 – 25) | 9 (5 – 17) | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 2 (1 – 4) | 0 (0 – 1) | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 5 (4 – 7) | 4 (3 – 5) | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 16 (13 – 21) | 12 (0 – 14) | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 362 (212 – 712) | 164 (65 – 376) | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 107 (47 – 417) | 23 (0 – 121) | <0.0001 |

Data expressed as absolute/relative frequency, or median (interquartile range). See Tables 1 and 2 for definition of abbreviations. \*Data available for 48 healthy subjects and 59 patients with COPD.

**TABLE 4. GENERAL CHARACTERISTICS AND DAILY PHYSICAL ACTIVITY MEASURES OF CLUSTERS OF PATIENTS WITH COPD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristic/PA measure | Cluster 1  (very long very light intensity/very short moderate-to-vigorous intensity) | Cluster 2  (very long very light intensity/ short moderate-to-vigorous intensity) | Cluster 3  (long very light intensity/short moderate-to-vigorous intensity) | Cluster 4  (long very light intensity/long moderate-to-vigorous intensity) | Cluster 5  (intermediate very light intensity/very long moderate-to-vigorous intensity) | *P*-value |
| General characteristics  N | 216 | 415 | 184 | 165 | 21 |  |
| Age, yrs | 68 (62 – 74) | 67 (61 – 72) | 67 (60 – 72) | 63 (58 – 70)†,‡ | 63 (56 – 68) | <0.0001 |
| Male, % | 67 | 67 | 51 | 76 | 67 | 0.32 |
| BMI, kg·m-2 | 30.4 (26.5 – 34.7) | 25.7 (22.6 – 29.0)† | 24.9 (22.2 – 27.4)† | 23.1 (20.3 – 26.8)†,‡ | 22.5 (18.3 – 30.9)† | <0.0001 |
| FEV1, % predicted | 44 (32 – 58) | 48 (34 – 61) | 57 (41 – 71)†,‡ | 50 (36 – 68)† | 51 (39 – 70) | <0.0001 |
| FEV1/FVC, % | 43 (34 – 55) | 44 (34 – 55) | 50 (38 – 61)†,‡ | 47 (36 – 57) | 49 (38 – 64) | 0.002 |
| mMRC dyspnea grade, points\* | 2 (1 – 3) | 2 (1 – 3)† | 1 (1 – 2)†,‡ | 1 (0 – 3)† | 1 (0 – 2)†,‡ | <0.0001 |
| ADO index\* | 5 (3 – 6) | 4 (3 – 5)† | 4 (3 – 5)†,‡ | 4 (3 – 5)† | 3 (2 – 4)†,‡ | <0.0001 |
| GOLD 2007 classification 1 / 2 / 3 / 4, % | 4 / 34 / 43 / 19 | 8 / 38 / 35 / 19 | 18 / 46 / 23 / 13 | 9 / 42 / 31 / 18 | 10 / 43 / 33 / 14 | 0.17 |
| GOLD 2011 classification A / B / C / D, %\* | 18 / 19 / 16 / 47 | 28 / 15 / 17 / 40 | 44 / 16 / 16 / 24 | 31 / 13 / 20 / 36 | 44 / 6 / 28 / 22 | 0.02 |
| Physical activity measures in very light intensity  Time, min∙day-1 | 955 (904 – 1042) | 823 (768 – 879)† | 706 (641 – 769)†,‡ | 675 (604 – 735)†,‡ | 516 (456 – 621)†,‡,§ | <0.0001 |
| EE, METs-min∙day-1 | 1356 (1165 – 1730) | 1022 (854 - 1222)† | 855 (729 – 1118)†,‡ | 789 (692 – 1019)†,‡ | 853 (661 – 1884)† | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 946 (894 – 1033) | 802 (746 – 858)† | 682 (611 – 744)†,‡ | 647 (573 – 707)†,‡ | 480 (428 – 591)†,‡,§ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 890 (815 – 968) | 680 (622 – 745)† | 534 (452 – 601)†,‡ | 490 (415 – 561)†,‡ | 340 (254 – 444)†,‡,§ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 33 (26 – 39) | 50 (42 – 57)† | 54 (48 – 61)†,‡ | 54 (47 – 65)†,‡ | 46 (43 – 59)† | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 17 (14 – 20) | 20 (17 – 22)† | 18 (16 – 20)†,‡ | 17 (15 – 20)‡ | 12 (11 – 16)†,‡,§,ǁ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 29 (23 – 36) | 16 (14 – 19)† | 12 (10 – 15)†,‡ | 11 (10 – 14)†,‡ | 10 (8 – 13)†,‡ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 53 (43 – 65) | 35 (30 – 41)† | 29 (25 – 34)†,‡ | 27 (24 – 32)†,‡ | 26 (22 – 32)†,‡ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 1344 (1145 – 1709) | 988 (827 – 1186)† | 810 (687 – 1074)†,‡ | 748 (650 – 976)†,‡ | 832 (606 – 1730)† | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 1257 (1068 – 1632) | 836 (693 – 1050)† | 628 (516 – 862)†,‡ | 589 (467 – 779)†,‡ | 704 (420 – 1185)† | <0.0001 |
| Physical activity measures in light intensity  Time, min∙day-1 | 57 (35 – 79) | 139 (113 – 167)† | 245 (208 – 282)†,‡ | 167 (134 – 209)†,‡,§ | 121 (87 – 163)†,§,ǁ | <0.0001 |
| EE, METs-min∙day-1 | 196 (121 – 305) | 408 (320 – 517)† | 725 (591 – 958)†,‡ | 526 (366 – 735)†,‡,§ | 416 (227 – 1093)†,§ | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 38 (19 – 56) | 105 (85 – 130)† | 205 (175 – 244)†,‡ | 126 (97 – 161)†,‡,§ | 79 (50 – 120)†,§,ǁ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 0 (0 – 3) | 8 (3 – 16)† | 46 (32 – 65)†,‡ | 8 (3 – 16)†,§ | 0 (0 – 4)‡,§,ǁ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 13 (7 – 17) | 30 (24 – 36)† | 49 (40 – 56)†,‡ | 37 (31 – 46)†,‡,§ | 28 (20 – 37)†,§,ǁ | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 0 (0 – 0) | 1 (0 – 1)† | 3 (2 – 5)†,‡ | 1 (0 – 1)†,§ | 0 (0 – 0)‡,§ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 3 (3 – 3) | 3 (3 – 4)† | 4 (4 – 5)†,‡ | 3 (3 – 4)†,§ | 3 (3 – 3)‡,§,ǁ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 0 (0 – 11) | 12 (11 – 13)† | 14 (13 – 15)†,‡ | 12 (10 – 14)†,§ | 0 (0 – 11)‡,§,ǁ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 131 (68 – 215) | 317 (241 – 408)† | 620 (510 – 801)†,‡ | 390 (263 – 586)†,‡,§ | 307 (159 – 748)†,§ | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 0 (0 – 12) | 26 (10 – 54)† | 155 (99 – 240)†,‡ | 26 (8 – 54)†,§ | 0 (0 – 19)‡,§,ǁ | <0.0001 |
| Physical activity measures in moderate-to-vigorous intensity  Time, min∙day-1 | 15 (7 – 27) | 48 (30 – 70)† | 68 (43 – 96)†,‡ | 166 (136 – 219)†,‡,§ | 361 (332 – 458)†,‡,§ | <0.0001 |
| EE, METs-min∙day-1 | 90 (40 – 192) | 235 (138 – 349)† | 327 (198 – 527)†,‡ | 805 (616 – 1134)†,‡,§ | 2693 (1694 – 5886)†,‡,§ | <0.0001 |
| Time in ≥2-min bouts, min∙day-1 | 9 (4 – 19) | 36 (20 – 54)† | 51 (29 – 72)†,‡ | 145 (118 – 190)†,‡,§ | 336 (293 – 433)†,‡,§ | <0.0001 |
| Time in ≥10-min bouts, min∙day-1 | 0 (0 – 3) | 5 (0 – 14)† | 9 (3 – 18)†,‡ | 60 (38 – 91)†,‡,§ | 209 (161 – 317)†,‡,§ | <0.0001 |
| Frequency of ≥2-min bouts, bouts∙day-1 | 3 (1 – 5) | 9 (6 – 13)† | 13 (8 – 17)†,‡ | 26 (20 – 33)†,‡,§ | 41 (35 – 52)†,‡,§ | <0.0001 |
| Frequency of ≥10-min bouts, bouts∙day-1 | 0 (0 – 0) | 0 (0 – 1)† | 1 (0 – 1)†,‡ | 3 (2 – 5)†,‡,§ | 10 (8 – 13)†,‡,§ | <0.0001 |
| Average duration of ≥2-min bouts, min∙bout-1 | 3 (2 – 4) | 4 (3 – 5)† | 4 (3 – 5)† | 6 (5 – 7)†,‡,§ | 8 (7 – 11)†,‡,§ | <0.0001 |
| Average duration of ≥10-min bouts, min∙bout-1 | 0 (0 – 11) | 12 (0 – 14)† | 13 (10 – 16)†,‡ | 17 (15 – 21)†,‡,§ | 20 (17 – 25)†,‡,§ | <0.0001 |
| EE in ≥2-min bouts, METs-min∙day-1 | 56 (20 – 123) | 173 (92 – 280)† | 251 (146 – 392)†,‡ | 704 (544 – 992)†,‡,§ | 2583 (1589 – 5348)†,‡,§ | <0.0001 |
| EE in ≥10-min bouts, METs-min∙day-1 | 0 (0 – 20) | 25 (0 – 70)† | 47 (13 – 105)†,‡ | 300 (171 – 513)†,‡,§ | 1635 (1102 – 2590)†,‡,§ | <0.0001 |

Data expressed as absolute/relative frequency, or median (interquartile range). See Tables 1 and 2 for definition of abbreviations. \*Data available for 198 subjects in Cluster 1, 367 subjects in Cluster 2, 159 subjects in Cluster 3, 126 subjects in Cluster 4, and 18 subjects in Cluster 5; †*P*<0.05 vs Cluster 1; ‡*P*<0.05 vs Cluster 2; §*P*<0.05 vs Cluster 3; ǁ*P*<0.05 vs Cluster