**CLUSTER ANALYSIS OF OBJECTIVELY MEASURED PHYSICAL ACTIVITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A MULTICENTER CROSS-SECTIONAL STUDY**

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**ABSTRACT**

**Rationale:** Detailed analyses of physical activity (PA) measures have been insufficiently explored in patients with chronic obstructive pulmonary disease (COPD).

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

**Methods:** 1001 patients with COPD (65% men; median age and FEV1: 67 years and 49% predicted) and 66 healthy subjects were studied. 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 k-means cluster analysis were applied to PA data to identify subgroups.

**Measurements and main results:** Age, body mass index (BMI), dyspnea grade and ADO index were associated with PA measures and hourly patterns in patients with COPD. Compared to healthy subjects, patients presented PA hourly patterns at lower intensities. Five clusters were identified based on 3 components from the PCA, which accounted for 60% of the total 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:** PA measures and hourly patterns are heterogeneous in COPD. Subgroups of patients could be identified based on physical activity data. These findings may be useful for interventions aiming to promote PA in COPD.

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

**INTRODUCTION**

Patients with chronic obstructive pulmonary disease (COPD) have lower physical activity (PA) measures compared to healthy subjects,(1-3) which is related to higher risk of hospital admission and mortality.(4-7) As PA measures can be used as outcome for clinical trials, as well as a possible target for therapy, a greater awareness of the clinical importance of physical inactivity in COPD is needed amongst healthcare professionals and scientists.(REF\_ERSStatementonPA\_tobeincluded)

To date, most studies investigating PA in patients with COPD have focused on the average daily value and its standard deviation.(8-11) Donaire-Gonzalez and colleagues(12) were the first to perform a more detailed analysis, 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.(12) More detailed analyses may provide a better insight into daily PA of patients with COPD and may also be of clinical importance, as interventions thus far have failed to demonstrate consistent important increases in PA measures in patients with COPD.(13, 14) Multiple other types of analysis are also available if the aim is to study PA in depth, such as daily PA hourly patterns,(15) and even cluster analysis of PA measures.(15-18)

PA hourly patterns consist of a graphic representation of the average PA intensity per hour during the course of a day.(18, 19) They can reveal whether specific physical activities are concentrated during certain periods of the day,(19) but also whether and to what extent activities during weekdays and weekend days are performed in a similar manner.(15) Complementarily, cluster analysis is useful to identify subgroups of patients with similar PA characteristics.(20) To the best of our knowledge, PA hourly patterns and cluster analysis of PA measures have not been investigated in patients with COPD.

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

**METHODS**

**Study design and participants**

In this multicenter and retrospective 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 were 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) were considered for the current analyses. References of previously published data can be found online (Table E1). Subjects were included if they met the following inclusion criteria: COPD with a post-bronchodilator forced expiratory volume in the first 1 s (FEV1) / forced vital capacity (FVC) ratio <0.7(21), stable condition (i.e., no recent exacerbation), and complete data for age, gender, BMI and daily PA measures (see *Physical activity assessment* section for details). All studies were approved by the local medical ethical committees, and written informed consent was obtained from participants, except for the data from Italy (n=23), which were obtained as part of routine clinical assessments.

Demographics, anthropometrics, lung function, and clinical data were collected: age, gender, BMI, FEV1 (% of predicted), FEV1/FVC ratio, diffusion capacity of the lung for carbon monoxide (DLCO, % of predicted), symptoms of dyspnea by the modified Medical Research Council (mMRC) dyspnea grade,(22) use of walking aids (yes/no), and use of long-term oxygen therapy (LTOT, yes/no). In addition, the ADO index was calculated(23), and participants were stratified by BMI (underweight, <18.5 kg∙m-2; normal weight, 18.5 to 24.99 kg∙m-2; pre-obese, 25 to 29.99 kg∙m-2; or obese, ≥ 30 kg∙m-2) or GOLD classifications (2007, 1 to 4; and 2011, A to D).(21, 24) GOLD 2011 classification (A to D) was based on the degree of airflow limitation (GOLD grades 1 to 4) and symptoms (mMRC dyspnea grades 0 to 4).

Centers from the Netherlands and the UK also provided for the current analysis data on healthy elderly subjects. The healthy subjects were pairwise-matched (i.e., 1:1) for gender, age and BMI with a subgroup of patients with COPD.

**Physical activity assessment**

The SenseWear Armband and SenseWear Mini Armband activity monitors were used for the assessment of PA. These devices combine an accelerometer with different physiological sensors (i.e., 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 in both field(25, 26) and laboratory studies.(27-29) The following thresholds proposed by the American College of Sports Medicine (ACSM)(30) 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,(8) with the device being used for ≥22 hours·day-1.(31) Since PA measures during week and weekend are known to be different,(8) for the cluster analysis only recordings during waking hours (i.e., all sleeping hours were deleted) and weekdays were considered, in order to reduce the variability of the data. 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 mean (95% confidence intervals) intensity of PA per hour during the course of a day. Previous studies have shown that PA hourly patterns can provide important information.(15, 19) 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 distinct 180 variables referred as features (Table E2, online supplement), which were used for clustering the 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 for identifying subgroups with distinct PA measures. Firstly, Principal Component Analysis (PCA) was used to perform dimensionality reduction. The high-dimensional feature set (180 dimensions) was projected to a lower dimensional space of principal components that is practical for data visualization (3 dimensions). PCA derives principal components as linearly uncorrelated variables, that represent the dataset variance. Principal components are ordered according to their variance, starting with the largest variance. Subsequent component has the largest variance orthogonal to (i.e., uncorrelated with) the preceding components. Secondly, a k-mean clustering algorithm was applied to the principal component space to partition the dataset into clusters with distinct characteristics, The first three principal components were supplied to k-means clustering. The k-means algorithm forms clusters with convex shape and the results are stable under small perturbations of the input dataset. The normalized mean over pairwise clustering distances was used as convergence[?] measure. The features were first standardized using z-scores. Feature extraction, PCA and clustering analyses were performed using Matlab R2012b (Mathworks Inc., USA).

**RESULTS**

**General characteristics**

In total, 1001 patients with COPD were analyzed (Table 1). The majority of the patients included in the analysis were men, with moderate-to-severe degree of airflow limitation, belonged to GOLD D (i.e., high risk and more symptoms), and only a small proportion used LTOT and/or walking aids.

**Daily physical activity measures and 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 weekdays. The smallest amounts of time and EE were spent in moderate-to-vigorous intensity. Considering 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 and weekend days, and in both analyses the peak of intensity occurred before midday.

***Stratification for clinical characteristics***

Patients of older age, female gender, LTOT users, walking aid users, lower DLCO, higher mMRC dyspnea grade, higher BMI, higher ADO index, higher GOLD grade and patients from GOLD group D spent the lowest amounts of time and EE in moderate-to-vigorous intensity (Tables E3-E12, online supplement). Figure 2 presents the daily PA hourly patterns after stratification for the abovementioned clinical characteristics, showing a noticeable influence of age, BMI, mMRC dyspnea grade, and ADO index scores. The influence of GOLD grades and GOLD 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).

***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 E13 (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 hourly PA 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 physical activity measures**

Five clusters were identified based on three principal components from the PCA (Figure 5; see online supplement for a 3D video of Figure 5), which accounted for 60% of the total variance in the dataset (first component, 34%; second component, 17%; third component, 9%). The most relevant features included in the 1st principal 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 features in the 2nd principal 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 features of the 3rd principal 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.

Table 4 presents the general characteristics and PA measures of the 5 clusters identified: cluster 1 (n=216; very long very light intensity/very short moderate-to-vigorous intensity), cluster 2 (n=415; very long very light intensity/ short moderate-to-vigorous intensity), cluster 3 (n=184; long very light intensity/short moderate-to-vigorous intensity), cluster 4 (n=165; long very light intensity/long moderate-to-vigorous intensity), and cluster 5 (n=21; intermediate very light intensity/very long moderate-to-vigorous intensity). 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. Clusters 4 and 5 were the only clusters to meet the recommendation of ≥30 min·day-1 (in ≥10-min bouts) in activities of moderate-to-vigorous intensity.(30) Figure 6 presents the hourly PA 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 objectified PA in a multinational sample of 1001 patients with COPD. The principle findings were that daily PA measures and hourly patterns are heterogeneous amongst patients with COPD after stratification for clinical characteristics, such as age, BMI, and mMRC dyspnea grade. Secondly, patients with COPD in addition to demonstrating lower PA measures, also exhibit hourly PA patterns at lower intensities in comparison with healthy subjects. 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).

**Clinical characteristics, and daily physical activity measures and hourly patterns**

Our results clearly show that PA is a very heterogeneous outcome, corroborating previous findings.(1, 32, 33) 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), use of walking aids (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-E10). Most of these clinical characteristics have been recently explored as determinants and/or outcomes of PA in a systematic review by Gimeno-Santos et al.(34). The results found by these authors broadly corroborate our findings. One of the few characteristics not investigated in their study was the degree of disease severity as assessed by the GOLD 2011 classification.(34) Interestingly, comparable time in very light and moderate-to-vigorous intensities was found between groups A and C, and B and D (Table E8), suggesting that symptoms are better associated with PA measures than the degree of airflow limitation. Nonetheless, the influence of the GOLD 2011 classification on PA hourly patterns is less evident. Only age, BMI, mMRC dyspnea grade, and ADO index scores seemed to materially affect PA hourly patterns (Figure 2). The stratification for GOLD grades (1 to 4) seems not to be associated with PA hourly patterns, and this is supported by a weak association found in our study between measures of lung function and PA (Figure 3). These findings and those of previous research suggest that lung function only modestly determine PA in patients with COPD.(1, 8, 9)

**Healthy subjects versus patients with COPD**

Patients with COPD are physically less active compared to healthy subjects.(1, 3, 31) 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 also one of the first 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 could be considered a surrogate of sedentary time (i.e., activities between 1.0-1.5 METs).(35) Most previous studies in patients with COPD have only used measures related to activities of high intensity (e.g. time in moderate-to-vigorous intensity) to evidence the physical inactivity of these patients,(8, 12, 36), ignoring PA at very light and light intensities. Reducing the time in very light intensity without necessarily increasing the time in moderate-to-vigorous intensity can be an important strategy for achieving health benefits in patients with COPD.(4) Distinct PA hourly patterns were found in patients with COPD in comparison to healthy subjects, and this has not been shown previously. Patients with COPD develop their activities at a lower intensity compared to healthy subjects, and this difference is more evident during weekdays. We believe that patients with COPD tend to be more inactive during both week and weekend, whilst healthy subjects tend to be less active especially during weekends.

**Clusters of patients with COPD based on daily physical activity 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 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 (Table 4), with a very similar PA hourly pattern between weekdays and weekend days.

Only a few studies have used objectively measured PA measures solely for clustering subjects, principally in children and middle-aged adults. In 10-to-12-year-old children, De Bourdeaudhuij and colleagues(37) were able to identify four clusters in each gender group, based on the time in activities of moderate-to-vigorous intensity and in sedentary activities. Besides clusters with very distinct PA measures (e.g., active or inactive), these authors also found one cluster with a mixed arrangement (i.e., less time in moderate-to-vigorous intensity + less sedentary time). In our study, we also found a cluster with such 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.(37) Indeed, cluster 4 together with cluster 5 (intermediate very light intensity/very long moderate-to-vigorous intensity) were the only clusters to meet the recommendation of ≥30min·day-1 in ≥10-min bouts of moderate-to-vigorous intensity.(30) On the other hand, more inactive clusters were also observed (clusters 1, 2 and 3). Based on their worse PA measures, patients from these clusters may have a worse prognosis,(4, 5) but no follow-up data is available to confirm this hypothesis. In middle-aged Chinese adults, based on average counts per minute Lee et al.(15) identified two clusters, 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.(15) In our study, patients from cluster 1 presented older age, lower FEV1, higher BMI, worse dyspnea and higher ADO index than the other clusters. These findings may explain, at least in part, the physical inactivity in these patients.

**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 us to perform a 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 COPD, another important advance. All these analyses were only possible due to the use of objective methods of PA, another strength in our study.

Some methodological limitations are acknowledged, most of them related to the study design adopted (i.e., a retrospective post-hoc analysis). A degree of 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.(38) Nonetheless, rather than a single statistically significant result, multiple findings in the same direction are suggestive that these are not due to chance alone.

In a large and multicenter sample of patients with COPD, five clusters of subjects were identified based on PA measures, each with very characteristic PA measures and hourly patterns (from a very inactive to a very active cluster). Compared to other clusters, cluster 1 (the most inactive) spent less time in higher intensities and more time in lower intensities, besides presenting higher BMI, worse airflow limitation, more dyspnea and worse disease severity. 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 are pooled per hour as mean (95% confidence intervals).

***Figure 2.***Daily PA hourly patterns of the patients with COPD after stratification for clinical characteristics during weekdays (A, C, E, G, I, K, M, O, Q, and S) and weekend days (B, D, F, H, J, L, N, P, R, and T). The daily PA hourly patterns were stratified for: A and B – age groups (< or ≥ median, 67 years); C and D – gender; E and F – body mass index (BMI) classification; G and H – modified Medical Research Council (mMRC) grades, data available for 868 subjects only; I and J – long-term oxygen therapy (LTOT) use (yes or no), data available for 707 subjects only; K and L – walking aids use (yes or no), data available for 705 subjects only; M and N – diffusion capacity of the lung for carbon monoxide (DLCO) groups (< or ≥ median, 51% predicted), data available for 505 subjects; O and P – ADO index groups(< or ≥ median, 4 points); Q and R – Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades (1 to 4); and S and T – GOLD groups (A to D). Data are 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 are 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 are 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 |
| Walking aid, %‡ | 3 |
| 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 705 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. \**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 4.