

## Physical activity in patients with chronic obstructive pulmonary disease

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## **ABSTRACT**

**We aimed to measure physical activity in patients with COPD, to identify the disease stage at which physical activity becomes limited, to investigate the relationship of clinical characteristics with physical activity, to evaluate the predictive power of clinical characteristics identifying very inactive patients, and to analyze the reliability of physical activity measurements.**

**163 patients with COPD (GOLD I –IV; BODE 0 –10) and 29 patients with chronic bronchitis (normal spirometry; former GOLD stage 0) wore activity monitors that recorded steps per day (SPD), minutes of at least moderate activity (MMA), and physical activity levels (PAL) for 5 days (3 weekdays, 1 weekend).**

**Compared to patients with chronic bronchitis SPD, MMA, and PAL were reduced from GOLD stage II/BODE score 1 on, from GOLD stage III/BODE score 3/4 on, and from GOLD stage III/BODE score 1 on, respectively. Reliability of physical activity measurements improved with the number of measured days and with higher GOLD stages. Moderate relationships were observed between clinical characteristics and physical activity. GOLD stages III and IV predicted best very inactive patients.**

**Physical activity is reduced in patients with COPD from GOLD stage II/BODE score 1 on. Clinical characteristics of patients with COPD only incompletely reflect their physical activity.**

**Keywords:**

- 1. chronic obstructive pulmonary disease**
- 2. clinical COPD**
- 3. activities of daily living**
- 4. 6MWD**

Physical activity is an important clinical parameter related to morbidity and mortality in many chronic diseases [1]. In chronic obstructive pulmonary disease (COPD) the level of physical activity reported by the patients is related to lung function decline [2], hospitalizations [3], and mortality [4].

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting energy expenditure [1]. Physical activity can be quantified with self-reported questionnaires [5-7], motion sensors like pedometers or accelerometers [5;7], and with methods assessing free-living energy expenditure such as the doubly labeled water technique [6]. Self-reported physical activity is often subject to recall bias [7], correlates only poorly with objectively quantified physical activity in patients with COPD [8;9], and does not provide an accurate estimate of free-living energy expenditure [6]. Pedometers and accelerometers generate objective data in terms of quantifying steps or body movements performed over a period of time [5]. However, estimating total daily energy expenditure from body movement counts has been shown to be inaccurate [10;11]. Recently, a multisensor armband (SenseWear Pro Armband, BodyMedia, Inc., Pittsburgh, PA) became available. It incorporates a biaxial accelerometer that records steps per day, and physiological indicators of energy expenditure. In patients with COPD the SenseWear Pro Armband provides a valid and reproducible estimate of energy expenditure during slow to moderate paced walking in a laboratory setting [12], and a high correlation between steps per day and movement counts as measured by a different accelerometer [13].

Physical activity in terms of body movements, walking time, and standing time has been shown to be reduced in patients with severe COPD [14;15]. However, it is currently unknown at which clinical stage of the disease limitations of physical activity show up first. Furthermore, the relationships between physical activity and clinical

characteristics reflecting the disease severity like the degree of airway obstruction, distance walked in 6 minutes, reported grade of dyspnea by the patient, and clinical stages of COPD need to be investigated as data are inconclusive so far or have never been evaluated. For example some authors found substantial correlations between airway obstruction and physical activity [8] [14], while others found no [16] [17] or only loose [15] relations. Previous studies indicate that 6-minute walk distance might best reflect physical activity [8] [15], while a recent study found airway obstruction to better correlate with physical activity than 6-minute walk distance [18].

Habitual physical activity is known to be highly variable [19] [20]. Therefore, reliability of physical activity measurements needs further studies in patients with COPD as it is currently unknown how many days of physical activity measurement are needed to reliably measure physical activity in patients with COPD. With the present study we aimed to measure physical activity in a substantial number of patients with COPD, to investigate the relationships between clinical characteristics and physical activity, to assess the predictive power of clinical characteristics identifying very inactive patients, and to analyze the reliability of physical activity measurements. A group of patients with normal lung function and symptoms of chronic bronchitis, who were matched for social and lifestyle associated confounders of physical activity, served as a control.

## **METHODS**

### **Study population**

We recruited 170 patients with COPD (128 males, 42 females) and 30 patients with chronic bronchitis (23 males, 7 females) between February and November 2006 at the Pulmonary Research Institute at Hospital Grosshansdorf, Schleswig-Holstein, Germany. Details of the COPD population at the institute have been published previously [13]. Patients with COPD had to be free of an exacerbation for at least 2 months. Postbronchodilator spirometry was performed using established reference values [21]. Patients with chronic bronchitis served as a control group matched for social and lifestyle associated confounders of physical activity such as smoking habits, alcohol consumption, and educational status [22] [23]. They fulfilled the criteria of being “at risk” (stage 0) for COPD according to the former staging system of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), i.e. chronic cough and sputum production but normal spirometry [24]. The study was approved by the local ethics committee of Schleswig-Holstein, and participants gave their written informed consent. Eight patients (7 with COPD and 1 with chronic bronchitis) were excluded from analysis (see below and fig. 1).

### **Physical activity - clinical characteristics of COPD patients**

All patients with COPD were classified according to the current GOLD criteria [25] and the criteria of the BODE (body mass index, airway obstruction, dyspnea, exercise capacity) index [26].

Dyspnea was assessed by the modified medical research council dyspnoea scale (MMRC), which is part of the BODE Index [26]. Furthermore, medical research council dyspnoea scale (MRC; same descriptors as MMRC) has been shown to be a simple method categorising patients with COPD in terms of their disability [27].

Levels of dyspnea are graded as follows: grade 0, "I only get breathless with strenuous exercise"; grade 1, "I get short of breath when hurrying on the level or up a slight hill"; grade 2, "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"; grade 3, "I stop for breath after walking 100 yards or after a few minutes on the level"; grade 4, "I am too breathless to leave the house".

The 6-minute walk test was conducted according to current guidelines on a 30-m corridor [28]. The 6-minute walk test measures the global and integrated responses of all organ systems involved during exercise [28], has been shown to be an important parameter related to morbidity and mortality in COPD [29;30], and is also part of the BODE index [26].

Receiver operating characteristic curves (ROCs) were used to analyse the sensitivity, specificity, and accuracy of the clinical characteristics (GOLD stages, BODE score, 6-minute walk distance, airway obstruction (forced expiratory volume in one second [FEV<sub>1</sub>], MMRC) in serving as a predictor of a very inactive patients with COPD. The positive and negative predictive values and likelihood ratios were calculated.

### **Physical activity – parameters and measurement**

Parameters of physical activity were, steps per day, minutes of at least moderate activity (defined as any physical activity > 3 metabolic equivalents [MET]), and the physical activity level. Physical activity was measured using a multisensor armband (SenseWear Pro Armband, BodyMedia, Inc., Pittsburgh, PA) that is worn on the upper right arm over the triceps muscle. The armband was described in a validation study for patients with COPD [12]. Briefly, it incorporates a biaxial accelerometer that records steps per day and physiological sensors of energy

expenditure. We calculated physical activity level by dividing total daily energy expenditure by whole-night sleeping energy expenditure [13]. A physical activity level  $\geq 1.70$  defines an active person [6], 1.40-1.69 defines a predominantly sedentary person [6], and  $< 1.40$  defines a very inactive person [31]. A person with a physical activity level of 1.2 is usually chair- or bed-bound [31].

### **Physical activity - days of analysis**

Patients wore the SenseWear Armband for 8 days. To get the armband, they came to the Pulmonary Research Institute on the first day, and they came back on the last day to return the device. The first and last days were not used for analysis because of an incomplete measurement of the day and a bias due to the fact that they had to come to the institute. Therefore, data from 6 days (4 weekdays plus Saturday and Sunday) of measurement were available for most patients.

Patients were told to wear the armband 24 hours per day with the exception of the time spent on personal hygiene. Wearing time was recorded by the armband. For a valid day of activity measurement, the threshold was set at 22 hours and 30 minutes of wearing time (94% wearing time per day). Days below that threshold were excluded from analysis.

As one aim was to assess the day-to-day variability of physical activity, including the amount of physical activity performed on weekdays *versus* weekend days, we excluded legal and religious holidays falling on a weekday (fig.1).

As another aim was to compare the physical activity between patients of different disease stages according to GOLD or BODE we tried to keep the study population as large as possible. 8 patients had to be excluded from analysis due to the fact that a weekend day was missing or less than 3 regular weekdays were available. In the remaining 192 patients 1114 measurement days were available, of whom 154



patients had a measurement of 4 weekdays, Saturday, and Sunday, and 38 patients had a measurement of 3 weekdays, Saturday and Sunday, respectively. To keep the study population with 192 patients we systematically excluded the fourth weekday in 154 patients (fig.1), grouped the days of measurement into weekday-1, weekday-2, weekday-3, Saturday, and Sunday, and analysed 960 days of activity monitoring.

### **Physical activity – variability and reliability of measurement**

The variability of physical activity between days was analyzed by repeated-measures ANOVA. First, we determined whether mean physical activity per day was different across all measured days. In the case of a significant difference between all measured days we analyzed whether this was caused by a difference between Saturday and weekdays, Sunday and weekdays, or a difference between weekdays themselves.

The reliability of physical activity measurement was assessed by the intra-class correlation coefficient. The equation is  $\text{intra-class correlation coefficient} = \sigma_b^2 / [\sigma_b^2 + (\sigma_w^2 / k)]$ , where  $\sigma_b^2$  is the between-subject variance,  $\sigma_w^2$  is the within-subject variance, and  $k$  is the number of measurement days. An intra-class correlation coefficient  $\geq 0.8$  indicates that the measured physical activity captures at least 80% of the variation of physical activity of the group and is the generally accepted value for a multiple-day intra-class correlation in accelerometer studies [32-34]. We calculated the intra-class correlation coefficient for every possible combination of days. To ensure that no bias resulted from exclusion of the fourth weekday in 154 patients we compared the mean values of the physical activity parameters assessed on 5 days (3 weekdays, weekend) versus six days (4 weekdays, weekend).

## **General statistics**

General statistics included ANOVA for linear trend, LSD post hoc analysis, and parametric and nonparametric correlations. Data analysis was performed with the Statistical Package for Social Science (SPSS; Chicago, IL), version 14.0.

## **RESULTS**

Characteristics of the patients are given in table 1, table 2, and table E1 of the online depository.

Steps per day, minutes of at least moderate activity, and the physical activity level decreased with the clinical stages according to GOLD or BODE (fig. 2A-2C; fig. 3A-3C). Furthermore, physical activity decreased with the grade of dyspnea (fig. 4A-4C). Steps per day, minutes of at least moderate activity, and the physical activity level decreased from patients with chronic bronchitis to patients in GOLD stage IV by 69 percent, 69 percent, and 61 percent, respectively (fig. 2A-2C). Compared to patients with chronic bronchitis the proportion of sedentary COPD patients markedly increased in GOLD stage I, BODE score 0, and in COPD patients reporting to get breathless with strenuous exercise only (MMRC 0) (fig. 5A-5C). The proportion of very inactive patients markedly increased in GOLD stages III and IV, in patients from BODE score 2 on, and in patients quoting dyspnea of MMRC grade 2 or higher (fig. 5A-5C). Compared to patients with chronic bronchitis steps per day, minutes of at least moderate activity, and the physical activity level were significantly reduced in COPD patients from GOLD stage II/BODE score 1 on, from GOLD stage III/BODE score 3/4 (quintile 4) on, and from GOLD stage III/BODE score 1 on, respectively (fig. 2A-2C; fig. 3A-3C). Patients reporting MMRC grade 1 dyspnea or higher had a reduced physical activity (fig. 4A-4C).

6-minute walk distance was significantly reduced in COPD patients from GOLD stage III on, from BODE score 2 on, and from MMRC grade 1 on, when compared to 6-minute walk distance of patients with chronic bronchitis (fig. 2D; fig. 3D; fig. 4D). 6-minute walk distance decreased from patients with chronic bronchitis to patients in GOLD stage IV by 40 percent (fig. 2D).

Steps per day and the physical activity level were reduced on Sundays in patients with chronic bronchitis and in COPD patients with GOLD stage I- III. Minutes of at least moderate activity were reduced on Sundays in patients with chronic bronchitis, and in COPD patients with GOLD I and GOLD stage III (tables E2A-E2C of the online depository). Depending on the physical activity parameter, any 2 to 3 days was sufficient for a reliable measurement of physical activity in patients with GOLD stage IV, whereas up to 5 days of measurement was required in patients with GOLD stage I (fig. 7A-C).

The mean values for steps per day, minutes of moderate activity, and the physical activity level were nearly identical, either assessed by 5 or 6 days of measurement ( $r \geq 0.993$ ,  $P < 0.001$ ; fig. E1A-E1C of the online depository).

Moderate correlations were observed between clinical characteristics of patients with COPD and physical activity (table 3). When using the individual best day of every patient (defined as the highest number for steps per day, minutes of at least moderate activity, and the physical activity level) instead of the mean value correlations between clinical characteristics and parameters of physical activity were basically unchanged (table E3 of the online depository). The moderate correlations of 6-minute walk distance with parameters of physical activity did not significantly change, when patients with chronic bronchitis were included in the analysis (Figures E2A-E2C of the online depository). In patients with COPD GOLD staging system (GOLD stages III and IV) was the best predictor of very inactive patients (fig. 6; table

4). According to the area under curve, the predictive values, and the likelihood ratios GOLD staging system was superior to BODE score, FEV<sub>1</sub>, 6-minute walk distance, and MMRC in predicting very inactive patients (table 4).

## DISCUSSION

The main findings of our study are that significant limitations of physical activity are present in patients with COPD from GOLD stage II/BODE score 1 on, and that clinical characteristics commonly used to assess COPD severity do not completely reflect physical activity when a broad range of disease severity is evaluated.

Physical activity—measured by a pedometer or an accelerometer—has been shown before to be reduced in patients with severe COPD compared to healthy subjects [14;15]. Schönhofer and coworkers reported that the daily movement counts were 43% lower in 25 patients with severe COPD (mean FEV<sub>1</sub>, 47% pred.) than in 25 normal healthy subjects [14]. Pitta and coworkers reported that walking time was 46% lower and standing time was 35% lower in 50 patients with severe COPD (mean FEV<sub>1</sub>, 43% pred.) than in healthy subjects, whereas sitting time was 22% greater and lying-down time was 200% greater [15]. However, when comparing COPD patients with subjects without lung function limitations it was unclear at which clinical stage the reduction of physical activity occurs. In the present study, comparing patients with normal lung function but symptoms of chronic bronchitis with COPD patients, we found that steps per day and physical activity level were significantly reduced from GOLD stage II/BODE score 1 on and from GOLD stage III/BODE score 1 on, respectively. This indicates that limitations of physical activity show up first in patients with GOLD stage II/BODE score 1, but the limitations do not affect the physical activity level at that stage. We speculate that one possibility explaining this discrepancy might be the increased metabolic and ventilatory demands for activities

of daily living in patients with COPD compared to healthy subjects [35]. Another possibility might be that patients with COPD in GOLD stage II avoid walking-related activities first, while other activities are not affected at that stage. These speculations, however, are clearly subject to further research.

In the present study we had a physical activity level of 1.7 in patients with a normal lung function but symptoms of chronic bronchitis (mean age, 63 years; 79% males; 55 % retired). In a pooled analysis of physical activity levels of retired and elderly subjects physical activity levels ranged from 1.58 (n=27; women only, mean age 68 years) to 1.68 (n=20; men only; mean age, 69 years) [31]. In a recent study investigating the impact of physical activity on mortality in healthy older adults (n=302; mean age 75 years; 50 % males) the mean physical activity level was 1.7 [6]. These data indicate that the patients with chronic bronchitis in our cohort were within the range of physical activity levels commonly found in that age.

Another issue that has not been studied in detail is the difference in physical activity between the different clinical stages of COPD. Our patients in GOLD stage I and GOLD stage II had similar physical activity levels, whereas patients in GOLD stages III and IV differed markedly from patients in the earlier stages and from each other. Even though the absolute values for the physical activity levels did not significantly differ in patients in GOLD stage I and GOLD stage II compared to patients with chronic bronchitis, there was a remarkable shift from patients being active to patients being predominantly sedentary. This shift also occurred in COPD patients reported to suffer from dyspnea on exertion only or in COPD patients scored to have BODE 0.

There is a health recommendation published by the Centers for Disease Control and Prevention and the American College of Sports Medicine that every adult should perform 30 minutes of moderate-intensity physical activity on most, preferably all,

days of the week [36]. In fact, this recommendation means that 30 minutes of moderate physical activity (for example brisk walking) should be accumulated in bouts of at least 10 minutes on top what sedentary persons normally do [36]. We were unable to analyse our data with respect to this health guideline as no specific types of activities can be identified by the SenseWear Pro Armband. However, as shown previously, it is unlikely that patients with moderate to severe COPD are able to accumulate 30 minutes of brisk walking as they walk slowly for 44 minutes per day only [15].

Variability of physical activity, which is closely linked to reliability of the measurement, is an important issue in accelerometer studies. In our study, Sunday was a day of reduced physical activity in nearly all patients except those in GOLD stage IV. Former studies in healthy volunteers also found Sunday to be a day of reduced physical activity [33;34;37]. We demonstrate that the reliability of accelerometer findings depends on disease severity and on the number of days used for analysis. Assuming the worst consistency across days we found that up to 5 days of measurement was required to reliably measure physical activity in patients with COPD in GOLD stage I, which indicates that variability of physical activity is higher in less severe COPD. Two other accelerometer studies cited the intra-class correlation coefficient for accelerometer measurement over a period of time in patients with COPD before. Steele and coworkers had an intra-class correlation coefficient of 0.69 for statistical agreement of 3 days (Friday, Saturday, Sunday) in patients with severe COPD [8]. Pitta and coworkers showed that 2 days of measurement (weekdays only) was sufficient to obtain an intra-class correlation coefficient of  $\geq 0.7$  [15]. Recently, the number of days needed to reliably measure physical activity in healthy persons was the subject of a review article by Trost *et al.* [20], who recommended 3 to 5 days of accelerometer monitoring to obtain a reliable measure of physical activity. Our data

for patients with chronic bronchitis and patients with COPD are in line with this recommendation.

To our knowledge, MMRC dyspnea scale has never been evaluated as a measure of physical activity in patients with COPD. However, MRC grade 4 and 5 (equivalent to MMRC grade 3 and 4) has been shown categorize patients with COPD in terms of their disability [27]. In our study patients with COPD, who reported to be too breathless to leave the house (MMRC 4), had a physical activity level of 1.26, which is only slightly higher compared to a chair- or bed-bound patient [31] .

For physicians taking care of patients with COPD it would be ideal to reliably estimate physical activity by COPD-related clinical characteristics either assessed by lung function, a simple exercise test or by a dyspnea scale. Physical activity, however, is a complex multidimensional behaviour that is affected not only by physical attributes but also by psychosocial and environmental factors that are beyond the scope of those tests [38;39]. Overall, we found moderate relationships between the clinical characteristics of COPD patients and their physical activity. 6-minute walk distance showed closer associations with physical activity than airway obstruction, which has been found before [8;15;40]. However, when compared with the other clinical characteristics used in this study differences were very small. In our study 6-minute walk distance was inferior to airway obstruction and the clinical staging systems in the prediction of very inactive patients. One possibility for this observation might be that physical activity decreased to a greater extent than 6-minute walk distance. Furthermore, Pitta and coworkers showed previously that 6-minute walk distance is only of limited value as a surrogate marker of physical activity in patients with COPD, who walk more than 400 m [15]. In our study the mean 6-minute walk distance of all patients was 439 m. The mean 6-minute walk distance in GOLD stage III still was 414 m, which indicates that most of our patients walked

more than 400 m. In line with the findings of Pitta and coworkers we can conclude that 6-minute walk distance is unlikely to replace an objective measurement of physical activity, when the whole range of disease severity is investigated.

In our study GOLD stages III and IV showed to be the best predictors of very inactive patients. However, only half of the patients in GOLD stage III was very inactive at all. Therefore, even with the best predictor some level of uncertainty remains identifying very inactive patients.

Our study has limitations that need to be addressed. First, it is a single-centre study performed in patients, who were interested in this research project. This may limit applicability across different centres and different clinical settings. Second, we did not include a control group of never smokers in our study. Third, we did not perform an analysis of physical activity by season and winter time is not represented in the recruitment period. This, however, should not interfere with the conclusions of our study.

In summary, this study shows that physical activity is reduced in patients with COPD from GOLD stage II/BODE score 1 on, and that clinical characteristics reflecting COPD severity do not completely reflect physical activity in patients with COPD.

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## FIGURE LEGENDS

Figure 1.

Patients excluded from analysis.

**Figure 1.**

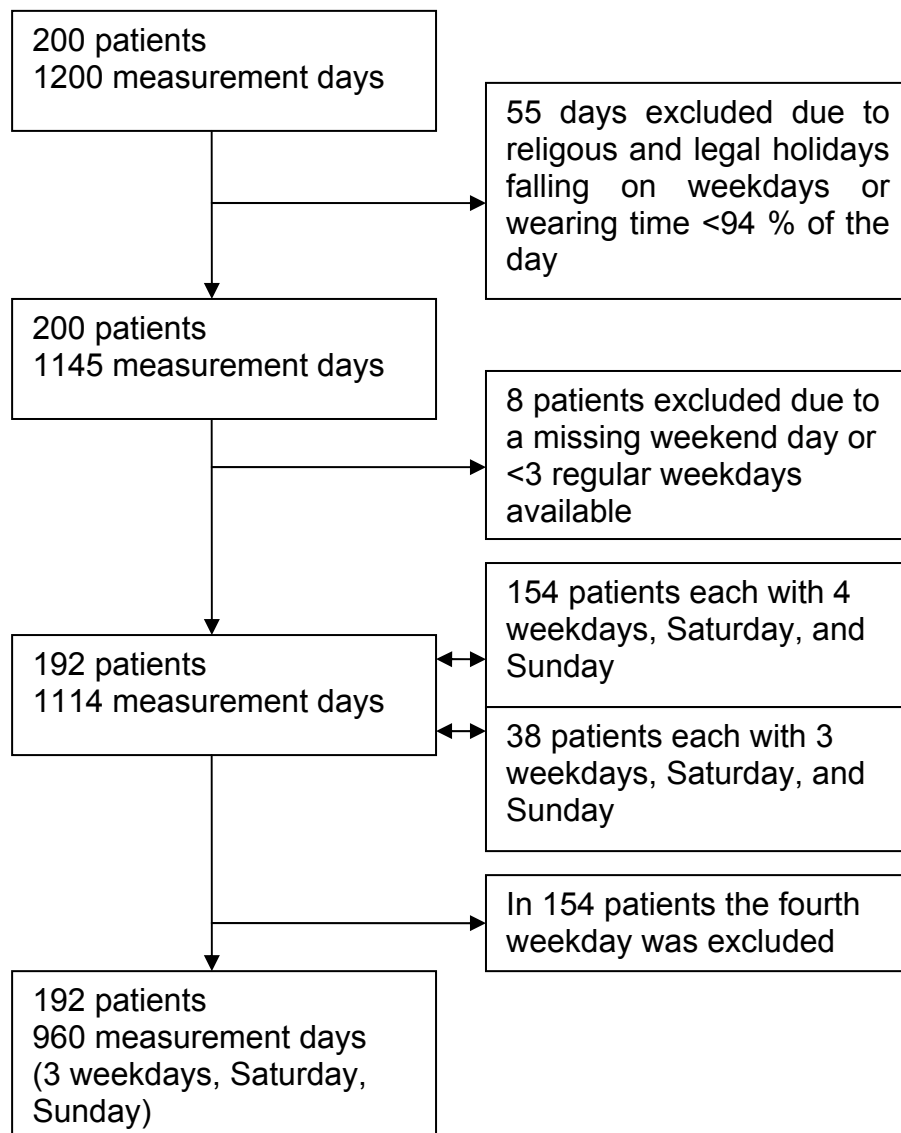


Figure 2.

Mean steps per day (A), mean minutes > 3 metabolic equivalents (METs) (B), mean physical activity level (C), and mean 6-minute walk distance (D) for patients with chronic bronchitis (CB) or COPD according to GOLD stages. Bars represent means, and horizontal lines represent 95% confidence interval (CI). Linear differences from CB to GOLD stage IV were tested by unweighted ANOVA for linear trend.

Differences between groups were tested by LSD post hoc analysis.

(A)  $P$  for linearity < 0.001. GOLD stage II, III, and IV were significantly reduced compared to CB ( $P = 0.02$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively). GOLD stage III was significantly reduced compared to GOLD stage I, and II ( $P < 0.001$ , and  $P = 0.001$ ). GOLD stage IV was significantly reduced compared to GOLD stage I, II, and III ( $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.003$ , respectively).

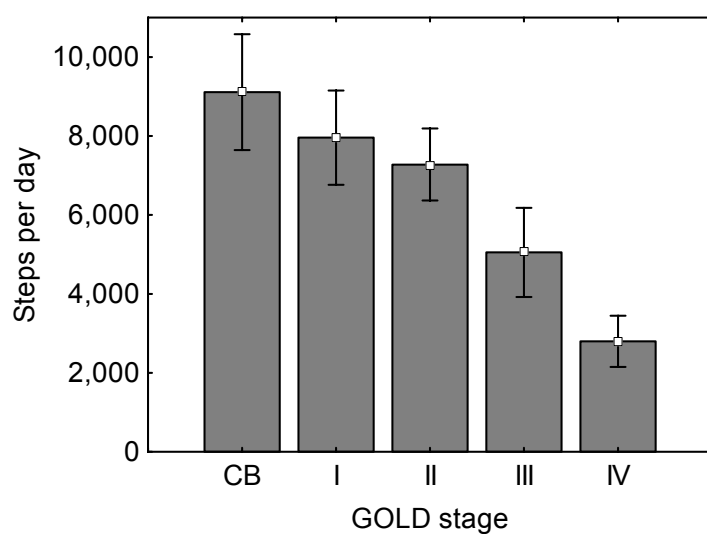
(B)  $P$  for linearity < 0.001. GOLD stage III, and IV were significantly reduced compared to CB ( $P = 0.002$ , and  $P < 0.001$ , respectively). GOLD stage III was significantly reduced compared to GOLD stage I, and II ( $P = 0.04$ , and  $P = 0.02$ ). GOLD stage IV was significantly reduced compared to GOLD stage I, II and III ( $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.002$ , respectively).

(C)  $P$  for linearity < 0.001. GOLD stage III, and IV were significantly reduced compared to CB ( $P < 0.001$ ). GOLD stage III was significantly reduced compared to GOLD stage I, and II ( $P < 0.001$ ). GOLD stage IV was significantly reduced

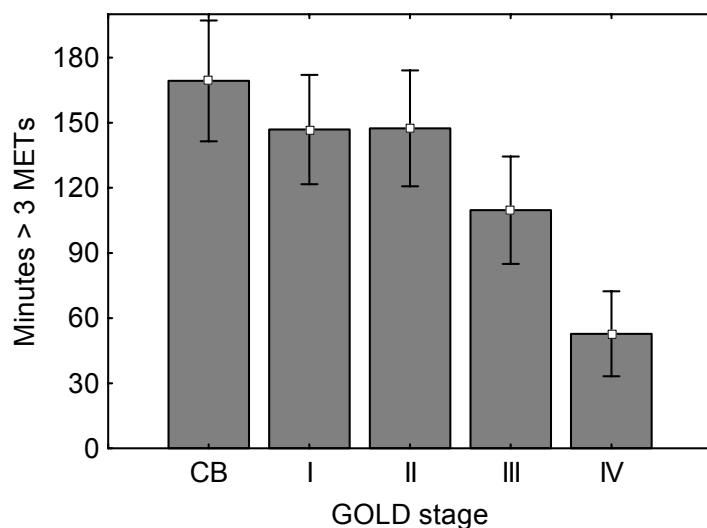
compared to GOLD stage I, II and III ( $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.006$ , respectively).

(D)  $P$  for linearity  $< 0.001$ . GOLD stage III, and IV were significantly reduced compared to CB ( $P < 0.001$ ). GOLD stage III was significantly reduced compared to GOLD stage I, and II ( $P < 0.001$ , and  $P = 0.009$ ). GOLD stage IV was significantly reduced compared to GOLD stage I, II and III ( $P < 0.001$ ).

**Figure 2A.**



**Figure 2B.**



**Figure 2C.**

**Figure 2D.**

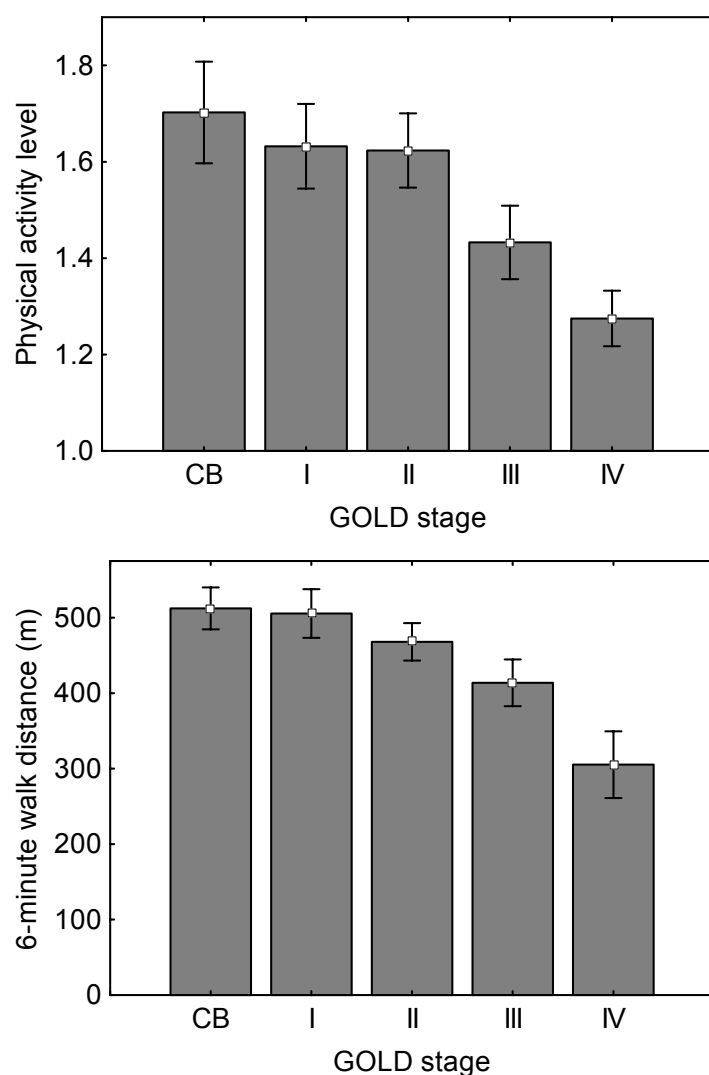


Figure 3.

Mean steps per day (A), mean minutes > 3 metabolic equivalents (METs) (B), mean physical activity level (C), and mean 6-minute walk distance (D) for patients with chronic bronchitis (CB) or COPD according to BODE quintiles, i.e. BODE score 0 (quintile 1, n = 39), BODE score 1 (quintile 2, n = 31), BODE score 2 (quintile 3, n = 29), BODE score 3–4 (quintile 4, n = 31), and BODE score 5–10 (quintile 5, n = 33). Bars represent means, and horizontal lines represent 95% confidence interval (CI). Linear differences from CB to BODE score 5–10 were tested by unweighted ANOVA for linear trend. Differences between groups were tested by LSD post hoc analysis.



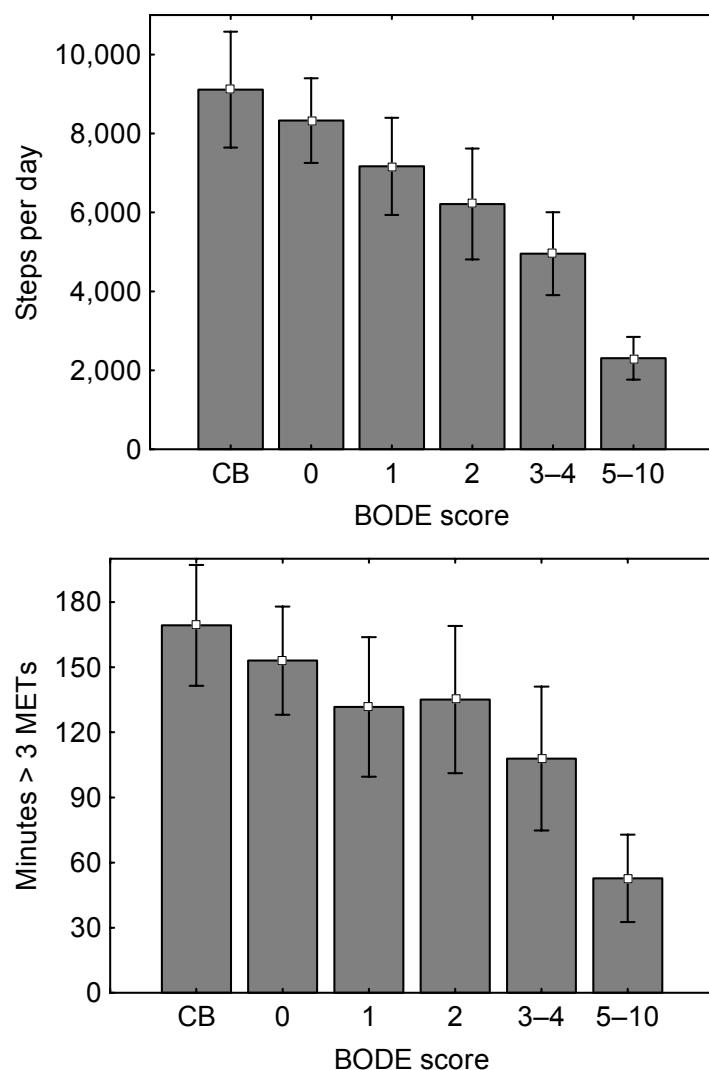
(A)  $P$  for linearity  $< 0.001$ . BODE score 1, 2, 3–4, and 5–10 were significantly reduced compared to CB ( $P = 0.02$ ,  $P = 0.001$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

(B)  $P$  for linearity  $< 0.001$ . BODE score 3–4, and 5–10 were significantly reduced compared to CB ( $P = 0.003$ , and  $P < 0.001$ , respectively).

(C)  $P$  for linearity  $< 0.001$ . BODE score 1, 2, 3–4, and 5–10 were significantly reduced compared to CB ( $P = 0.04$ ,  $P = 0.003$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

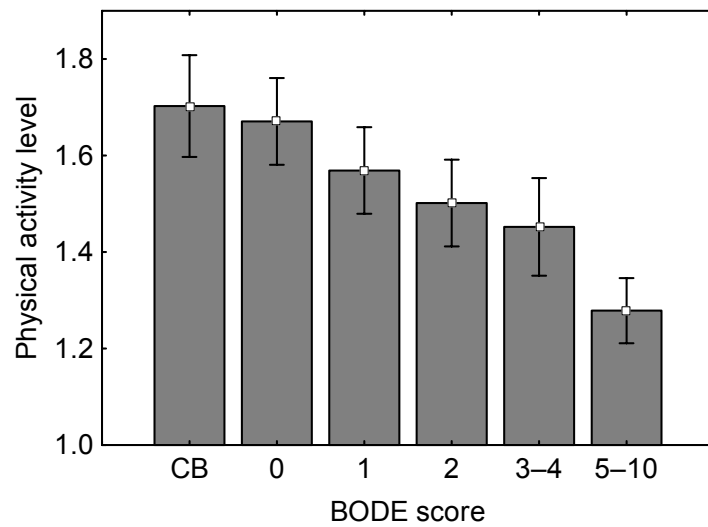
(D)  $P$  for linearity  $< 0.001$ . BODE score 2, 3–4, and 5–10 were significantly reduced compared to CB ( $P = 0.004$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

**Figure 3A.**

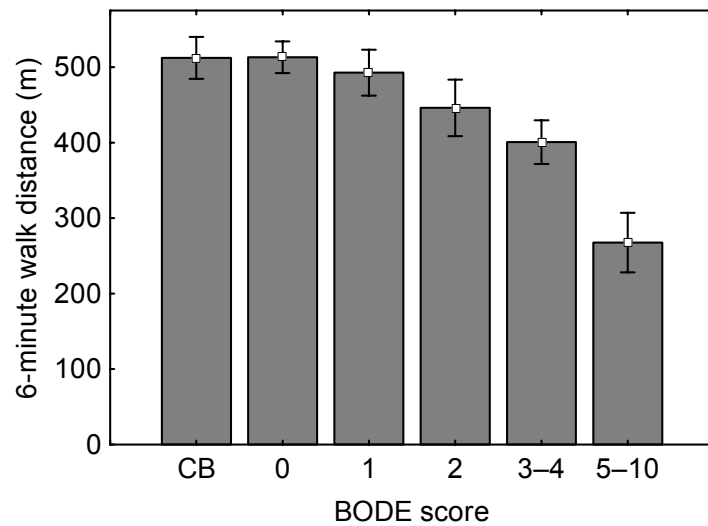


**Figure 3B.**

**Figure 3C.**



**Figure 3D.**



**Figure 4.**

Mean steps per day (A), mean minutes > 3 metabolic equivalents (METs) (B), mean physical activity level (C), and mean 6-minute walk distance (D) for patients with chronic bronchitis (CB) or COPD according to MMRC dyspnoea scale. Frequency of MMRC grade 0, 1, 2, 3, and 4 were  $n = 44, 55, 27, 28,$  and  $9$ . Bars represent means, and horizontal lines represent 95% confidence interval (CI). Linear differences from CB to MMRC grade 4 were tested by unweighted ANOVA for linear trend.

Differences between groups were tested by LSD post hoc analysis.

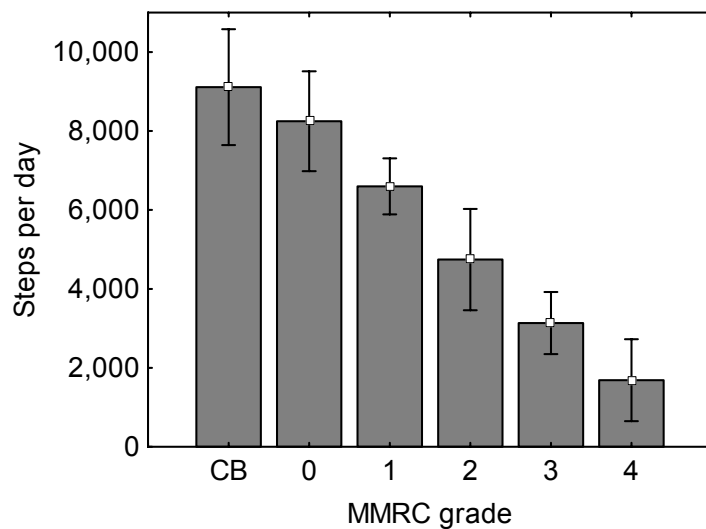
(A)  $P$  for linearity  $< 0.001$ . MMRC grade 1, 2, 3, and 4 were significantly reduced compared to CB ( $P < 0.001$ ).

(B)  $P$  for linearity  $< 0.001$ . MMRC grade 1, 2, 3, and 4 were significantly reduced compared to CB ( $P = 0.01$ ,  $P < 0.001$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

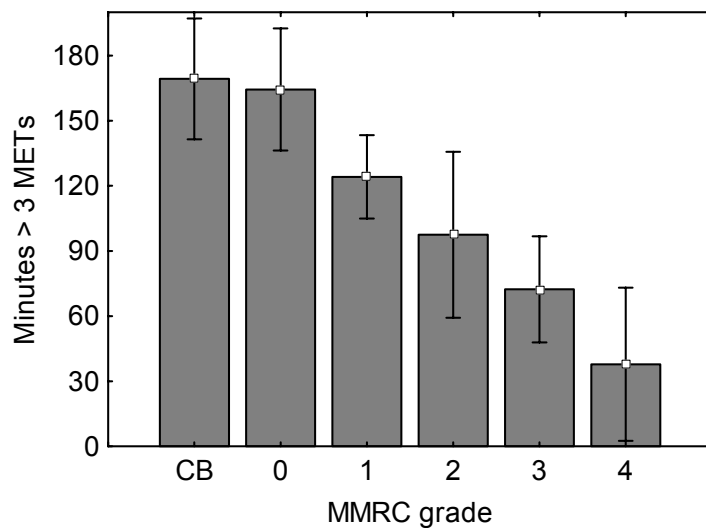
(C)  $P$  for linearity  $< 0.001$ . MMRC grade 1, 2, 3, and 4 were significantly reduced compared to CB ( $P = 0.008$ ,  $P < 0.001$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

(D)  $P$  for linearity  $< 0.001$ . MMRC grade 1, 2, 3, and 4 were significantly reduced compared to CB ( $P = 0.02$ ,  $P < 0.001$ ,  $P < 0.001$ , and  $P < 0.001$ , respectively).

**Figure 4A.**



**Figure 4B.**



**Figure 4C.**

**Figure 4D.**

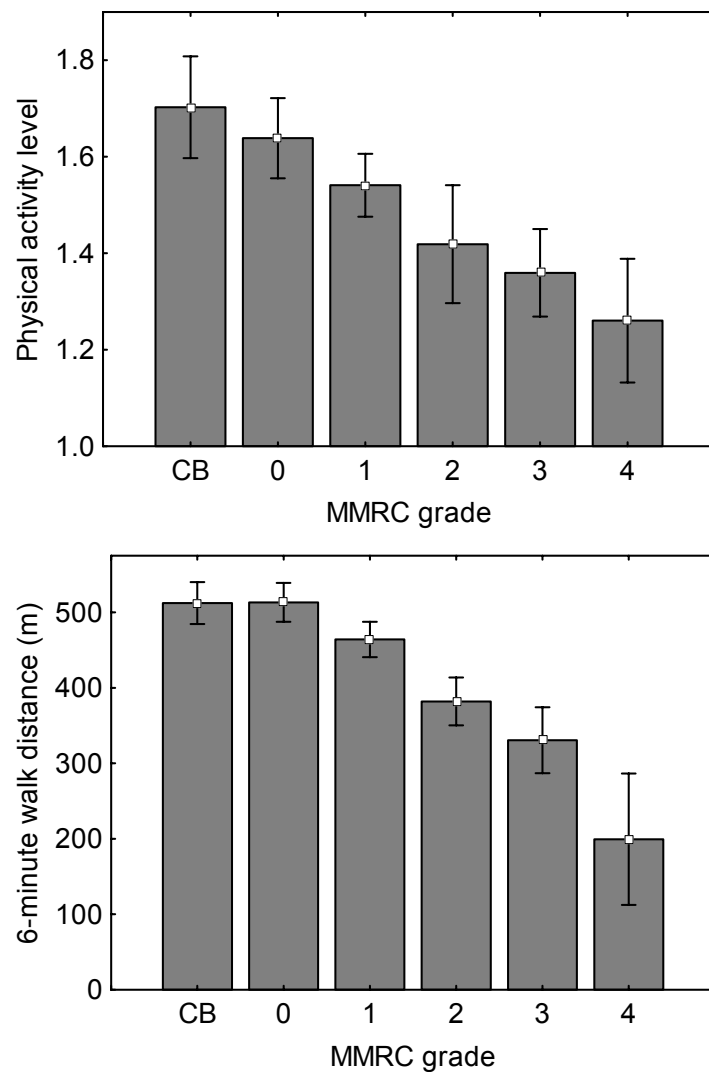
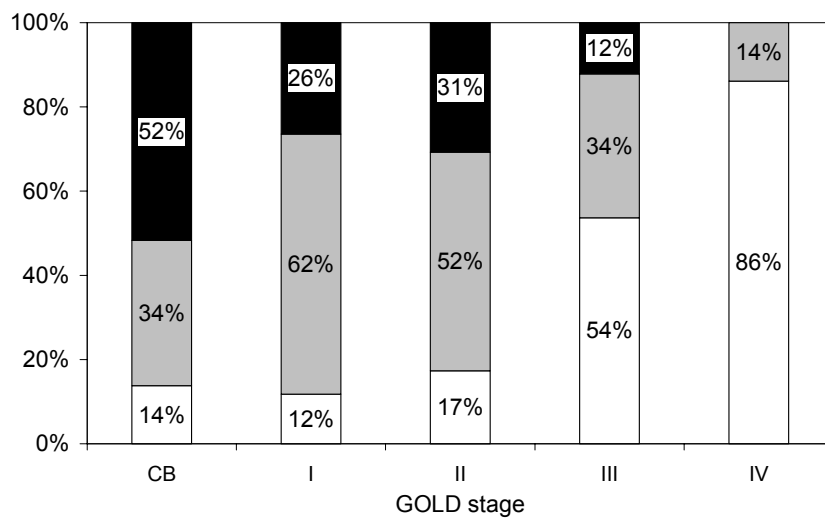


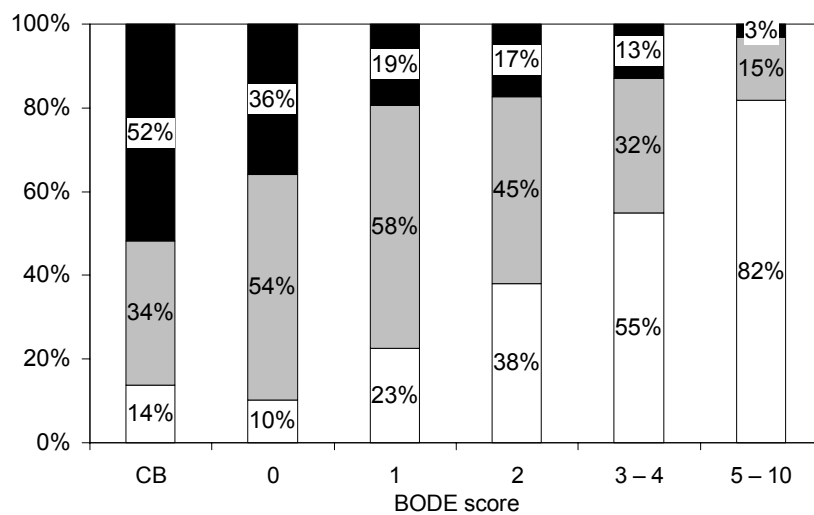
Figure 5.

Percentage of patients who were active (physical activity level  $>1.70$ ; solid bars), predominantly sedentary (physical activity level  $1.40$ - $1.69$ ; shaded bars), or very inactive (physical activity level  $<1.40$ ; open bars) according to GOLD stages (A), BODE score (B), and MMRC dyspnoea scale (C). CB, chronic bronchitis.

**Figure 5A.**



**Figure 5B.**



**Figure 5C.**

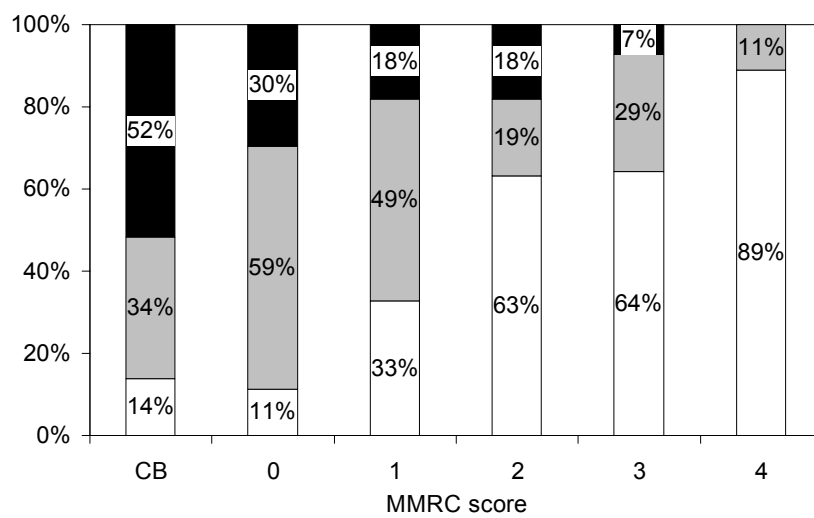


Figure 6.

Receiver operating characteristic curves for GOLD stages (dashed line) and 6-minute walk test (solid line) serving as predictors of very inactive patients with COPD (physical activity level  $<1.40$ ).

**Figure 6.**

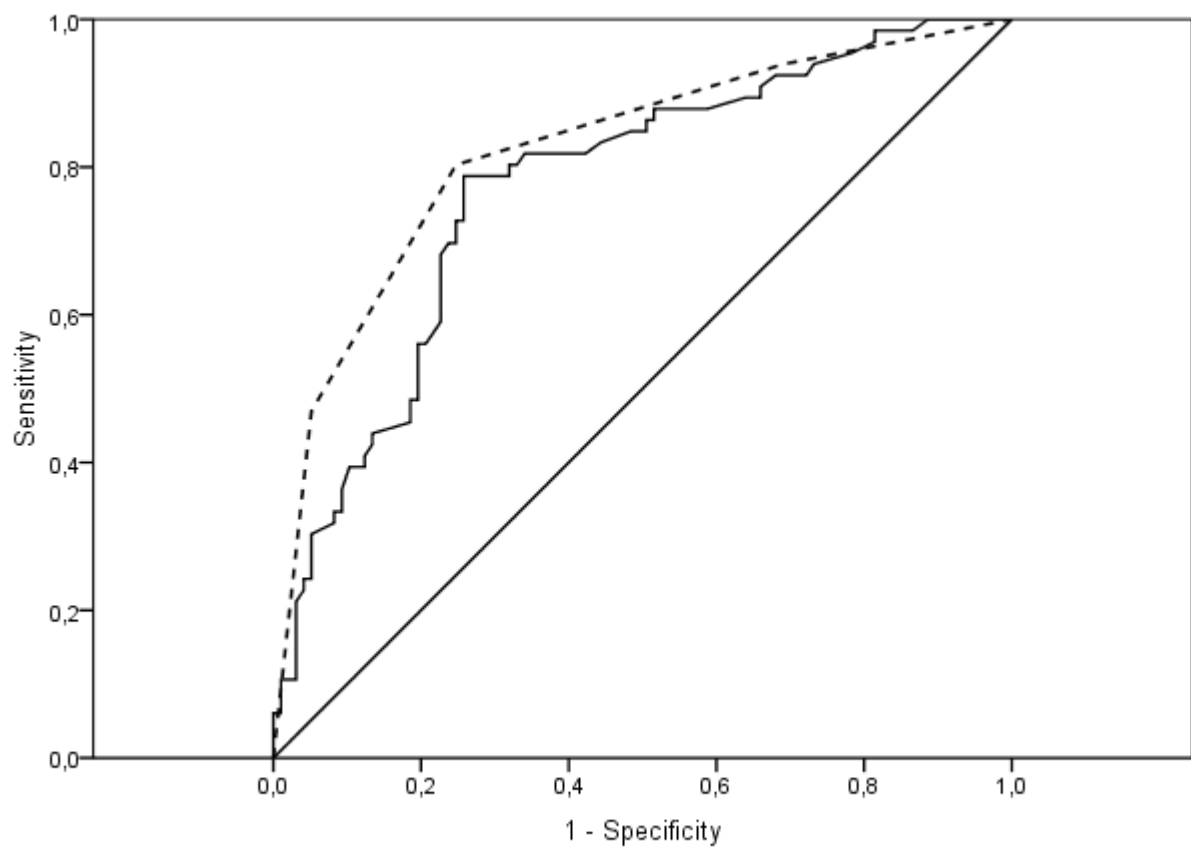


Figure 7.

Minimal intra-class correlation coefficient for consistency of steps per day (A), minutes > 3 metabolic equivalents (METs) (B), and the physical activity level (C) across the measured days. Intra-class correlation coefficients were calculated for every possible combination of days—10 combinations for 2 days, 10 combinations for 3 days, 5 combinations for 4 days, and 1 combination for 5 days.

Figure 7A.

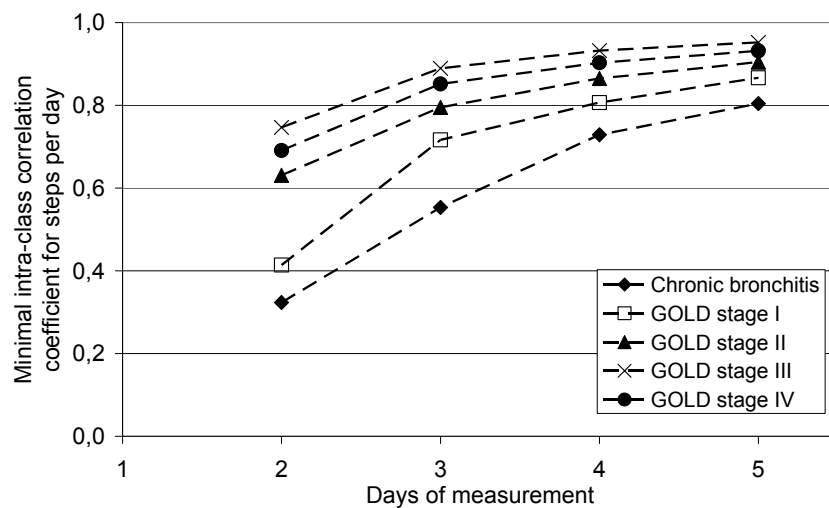


Figure 7B.

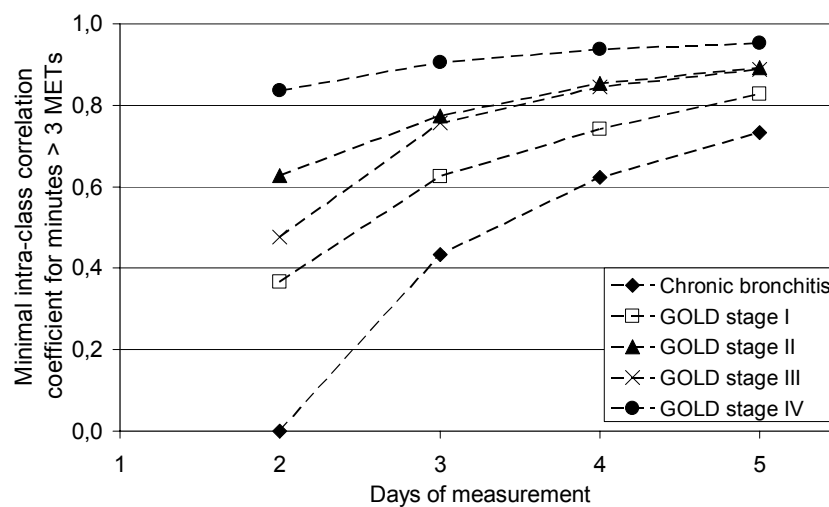
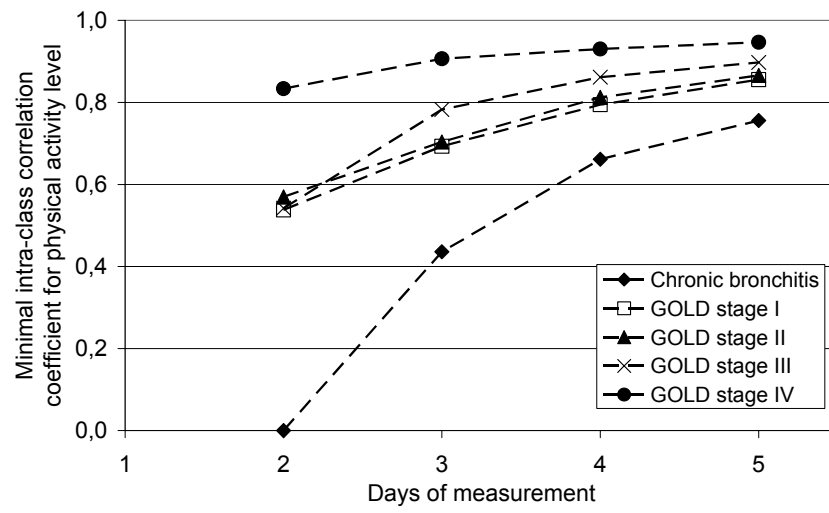


Figure 7C.





**TABLE 1. Patient Characteristics**

	Total	Chronic bronchitis	GOLD I	GOLD II	GOLD III	GOLD IV
Patients, n (%)	192 (100)	29 (15)	34 (18)	52 (27)	41 (21)	36 (19)
Age, years , mean (SD)	64 (6.4))	63 (5.9)	66 (5.6)	64 (6.4)	63 (7.4)	64 (6.2)
Males, n (%)	145 (76)	23 (79)	25 (74)	37 (71)	33 (80)	27 (75)
Body mass index, kg/m <sup>2</sup> , mean (SD)	26.3 (4.8)	27.2 (3.0)	27.0 (4.2)	27.3 (5.0)	25.1 (5.1)	24.6 (5.3)
Pack-years of smoking, mean (SD)	52 (25)	54 (22)	47 (27)	51 (28)	56 (24)	54 (20)
Regular drinkers, n (%)	91 (47)	17 (59)	17 (50)	25 (48)	21 (51)	11 (31)
Drinks per week of regular drinkers, median (IQR)	5 (2 –14 )	6 (2 – 17)	4 (2 – 7)	5 (2.5 – 10)	5 (2 – 14)	9.5 (3 – 14)
Retired or early retired, n (%)	145 (76)	16 (55)	27 (79)	38 (73)	31 (76)	33 (92)
Unemployed, n (%)	20 (10)	6 (21)	3 (9)	4 (8)	5 (12)	2 (6)
University entrance degree, n (%)	19 (10)	3 (10)	3 (9)	7 (14)	4 (10)	2 (6)

Definition of abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; IQR = interquartile range.

**TABLE 2. Lung function**

	Total	Chronic bronchitis	GOLD I	GOLD II	GOLD III	GOLD IV
FEV <sub>1</sub> , % pred., mean (SD)	62.8 (26.2) <sup>†</sup>	99.4 (10.3)	90.0 (8.7)	63.0 (8.1)	40.6 (5.1)	32.8 (11.4)
FVC, % pred., mean (SD)	94.1 (21.6)	105.7 (13.0)	114.2 (14.8)	97.0 (16.2)	84.3 (16.3)	72.8 (20.7)
FEV <sub>1</sub> /FVC, mean (SD)	51.9 (15.6)	74.9 (4.7)	62.9 (6.7)	52.7 (9.2)	39.4 (8.4)	36.2 (8.6)
Capillary Po <sub>2</sub> ,* mm Hg	69.9 (8.5)	76.2 (9.6)	71.0 (6.7)	71.2 (7.7)	69.7 (6.1)	60.4 (5.8)
Capillary Pco <sub>2</sub> ,* mm Hg	37.8 (4.8)	34.9 (3.8)	36.0 (3.8)	37.6 (3.9)	38.0 (3.3)	42.6 (6.1)

\* Data are missing for seven patients.

<sup>†</sup> Mean FEV<sub>1</sub>, % pred., for COPD patients only = 56.3 (22.6).

Definition of abbreviations: FVC = forced vital capacity; FEV<sub>1</sub> = forced expiratory volume in 1 s; Po<sub>2</sub> = partial pressure of oxygen; Pco<sub>2</sub> = partial pressure of carbon dioxide

**Table 3. Correlation coefficients between clinical characteristics and mean physical activity in patients with COPD (n = 163)**

	Steps per day	Minutes of at least moderate activity	Physical activity level
GOLD stages	– 0.58	– 0.46	– 0.52
6-minute walk test	0.63	0.47	0.46
FEV <sub>1</sub> , % pred.	0.46	0.31	0.42
MMRC	– 0.57	– 0.46	– 0.44
BODE score	– 0.62	– 0.44	– 0.49

Correlations are indicated by Pearson correlations coefficients (FEV<sub>1</sub> and 6-minute walk distance) and Spearman rank coefficients (GOLD stages, MMRC, and BODE score). *P* values for every correlation < 0.001. Definition of abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; FEV<sub>1</sub> = forced expiratory volume in 1 s; MMRC = modified medical research council dyspnoea scale; BODE = body mass index, airway obstruction, dyspnea, exercise capacity

**Table 4. Receiver operating characteristic curves for prediction of very inactive\* patients with COPD (n = 163)**

Predictors	Area	SE	P value	95% CI of area	Cutoff Point <sup>†</sup>	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Likelihood ratio of a positive test result	Likelihood ratio of a negative test result
GOLD stages	0.823	0.035	<0.001	0.76 to 0.89	III	0.80	0.75	0.69	0.85	3.25	0.26
BODE score	0.796	0.036	<0.001	0.73 to 0.87	3	0.67	0.79	0.69	0.78	3.23	0.42
FEV <sub>1</sub>	0.795	0.036	<0.001	0.73 to 0.87	54 % pred.	0.80	0.71	0.65	0.84	2.78	0.28
6-minute walk test	0.773	0.037	<0.001	0.70 to 0.85	445 m	0.79	0.74	0.68	0.84	3.06	0.29
MMRC	0.768	0.037	<0.001	0.70 to 0.84	grade 2	0.65	0.78	0.67	0.77	3.01	0.44

\* Very inactive is defined as a physical activity level <1.40, including 66 patients with COPD (40.5 % of all COPD patients).

<sup>†</sup> Equal or greater than. Definition of abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; BODE = body mass index, airflow obstruction, dyspnea, exercise capacity; FEV<sub>1</sub> = forced expiratory volume in 1 s; MMRC = modified medical research council dyspnoea scale;