Modified Medical Research Council and COPD Assessment Test Cutoff Points

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BACKGROUND: The modified Medical Research Council (mMRC) and COPD Assessment Test (CAT) are assessment instruments associated with level of physical activity of daily living (PADL) in patients with COPD. This study aimed to identify mMRC and CAT cutoff points to discriminate sedentary behavior and PADL level of subjects with COPD and verify whether these cutoff points differentiate pulmonary function, health-related quality of life (HRQOL), functional status, and mortality index in subjects with COPD. METHODS: Subjects (N = 131, FEV_1: 36.7 ± 16.1% predicted) were assessed for lung function, mMRC, CAT, HRQOL, functional status, and mortality index. PADL was monitored using a triaxial accelerometer, and subjects were classified as sedentary/nonsedentary (cutoff point of 8.5 h/d in PADL < 1.5 metabolic equivalent of task [MET]), physically active/inactive (cutoff point of 80 min/d in PADL ≥ 3 METs), and with/without severe physical inactivity (cutoff point of 4,580 steps/d), according to variables provided by accelerometer. RESULTS: ROC curve indicated mMRC cutoff point of ≥ 2 (P < .05) for physical inactivity (sensitivity = 66%, specificity = 56%, AUC = 0.62), severe physical inactivity (sensitivity = 81%, specificity = 66%, AUC = 0.76), and sedentary behavior (sensitivity = 61%, specificity = 70%, AUC = 0.65). The identified CAT cutoff points were ≥ 16 and ≥ 20, considering severe physical inactivity (sensitivity = 76%, specificity = 54%, AUC = 0.69, P < .001) and sedentary behavior (sensitivity = 51%, specificity = 90%, AUC = 0.71, P = .001), respectively. Subjects who had mMRC ≥ 2 and CAT ≥ 16 or ≥ 20 presented worse pulmonary function, HRQOL, functional status, and mortality index compared with those who scored mMRC < 2 and CAT <16 or < 20. CONCLUSIONS: mMRC cutoff point of ≥ 2 is recommended to discriminate PADL level and sedentary behavior, whereas CAT cutoff points of ≥ 16 and ≥ 20 discriminated severe physical inactivity and sedentary behavior, respectively. These cutoff points differentiated subjects with COPD regarding all the outcomes assessed in this study. *Key words: COPD; activities of daily living; functional status; exercise; sedentary behavior; symptom assessment; health status.* [Respir Care 2021;66(12):1876–1884. © 2021 Daedalus Enterprises]

Introduction

COPD is characterized by pulmonary and systemic manifestations that may lead to exertional dyspnea, a symptom associated with decreased health and functional status.[1-3] Functional status is multidimensional and comprises functional capacity, functional performance, functional reserve, and functional capacity utilization.[4] There is a growing interest in investigating functional performance[5] (ie, activities routinely performed by individuals)[6] since increased levels of physical activity in daily life (PADL) are widely recommended in pulmonary rehabilitation programs.[1] Also, low PADL levels reduce quality of life[7] and increase the risk of exacerbations and number of hospitalizations[8] and is considered the strongest predictor of mortality in patients with COPD.[9]

Although triaxial accelerometers are complex, high cost, and present low feasibility and clinical applicability, they provide objective data that cannot be provided by questionnaires and pedometers.[5] Pedometers, despite more accessible, are unreliable for detecting low-intensity movements, whereas questionnaires and scales are influenced by patient understanding and subjectivity.[5] Triaxial accelerometers are portable movement monitors that accurately measure time, number of steps, movement intensity, and energy expenditure in different postures and activities.[10] Cutoff

points capable of classifying sedentary behavior and PADL level of these patients have already been established.[11-13]

It is known that multiple symptoms experienced by patients with COPD, such as dyspnea, fatigue, anxiety, and depression, influence their physical activity.[14] The symptoms can be aggravated by physical inactivity, causing the disease spiral.[15] Previous studies[16-18] investigated relationships between PADL level and the multidimensional Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification. It complements spirometric classification, stratifies disease into 4 quadrants (considering symptoms and exacerbations in the last year),[3] and may reflect better COPD complexity.[16] However, symptoms are evaluated using the modified Medical Research Council (mMRC) scale or COPD Assessment Test (CAT) questionnaire and may lead to different distributions within the multidimensional classification.[19] Although 2 distinct CAT cutoff points are described for this population,[3,20] a significant discrepancy regarding disease severity[20] and symptoms is present when the score is applied to the same patient.[21] Munari et al[17] observed that mMRC was more strongly associated with functional status than CAT. Nevertheless, cutoff points of these instruments to discriminate sedentary behavior and PADL level have not yet been identified in COPD.

Therefore, this study aimed to confirm associations between CAT and mMRC and functional status classifications. Also, in case of confirmed significant association, (1) to determine mMRC and CAT cutoff points to discriminate sedentary behavior and PADL level of subjects with COPD and (2) to identify whether these cutoff points differentiate pulmonary function, health-related quality of life (HRQOL), functional status, and mortality index in subjects with COPD.

QUICK LOOK

Current knowledge

Multidimensional GOLD classification reflects the complexity of COPD better than spirometric classification. Despite this, evaluation by different instruments (modified Medical Research Council [mMRC] and COPD Assessment Test [CAT]) may lead to different distributions within the multidimensional classification. Also, disease severity and symptoms are discrepant when current CAT cutoff points are applied to the same patient. Furthermore, mMRC is more strongly associated with functional status than CAT.

What this paper contributes to our knowledge

An mMRC cutoff point of 2 is recommended to discriminate physical activity in daily life (PADL) level and sedentary behavior, whereas CAT cutoff points of 16 and 20 discriminated severe physical inactivity and sedentary behavior in subjects with COPD. These cutoff points also differentiated pulmonary function, health-related quality of life, functional and exercise capacity, PADL limitation, PADL level, and risk of death in subjects with COPD.

Methods

This is a cross-sectional study approved by the Human Research Ethics Committee of the Santa Catarina State University of (CAAE: 80831117.5.0000.0118). All subjects provided written informed consent prior to inclusion in the study. Subjects referred to the Center for Assistance, Teaching, and Research in Pulmonary Rehabilitation, with clinical diagnosis of COPD (GOLD II–IV), confirmed by spirometry,[3] age 40–80 y, and clinically stable in the month before the beginning of the protocol, were included. Exclusion criteria were disabling health conditions; other respiratory diseases; nonadherence to prescribed medications; exacerbation during study protocol; hospitalization in the previous 3 months; and current smokers, smoking cessation, or participation in pulmonary rehabilitation programs in the previous 6 months.

The protocol was conducted in 3 nonconsecutive visits and 2 consecutive days between March 2013 and December 2018. On the first visit, pulmonary function test, mMRC, London Chest Activity of Daily Living (LCADL), CAT, and modified St George Respiratory Questionnaire (mSGRQ) were performed. Two 6-min walk tests (6MWT) and 2

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Glittre-ADL (TGlittre) tests were performed on the second and third visits. Visits were interspersed for at least one day or as necessary to avoid influence of the previous evaluation. PADL was monitored in the fourth and fifth day.

Pulmonary function was assessed using an EasyOne portable spirometer (ndd Medical Technologies, Zürich, Switzerland), following the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations.[22] Predicted values for the Brazilian population were calculated.[23] CAT score was used to assess COPD impact on health status, and higher scores indicated worse health status.[24,25] mMRC was applied to stratify dyspnea severity during daily activities, and maximum scores reflected high degree of dyspnea. HRQOL was evaluated using mSGRQ and its domains: symptoms, activity, and impact. Each domain score and the total score (in percentage) were used for analysis.[26,27] ADL limitation due to dyspnea was evaluated using LCADL,[28,29] and both LCADL %total score[28] and cutoff point of 28%[30] were used in the analyses. 6MWT was performed in a 20-m corridor, following ATS/ERS[31] recommendations. The best distance covered in meters and percentage of predicted (% predicted)[32] and cutoff point of 82% predicted were included for data analysis.[33] TGlittre followed Skumlien et al[34] recommendations, and the test performed in the shortest time, % predicted,[35] and cutoff point of 3.5 min[36] were used for analysis. Body mass index, air flow obstruction, dyspnea, and exercise capacity (BODE) index were also calculated.[37]

PADLs were monitored using DynaPort MiniMod triaxial accelerometers (McRoberts BV, The Hague, the Netherlands) for 2 consecutive working days (12 h daily). Subjects received an instruction manual and verbal guidance for its use. Data were analyzed using the Dyrector software (McRoberts BV, The Hague, the Netherlands), and it was averaged for analysis, considering number of steps; time spent seated, lying down, standing, walking; and in PADL with metabolic equivalent of task (MET) ≥ 3 (PADL ≥ 3 METs) and < 1.5 MET (PADL < 1.5 MET). Sedentary time was considered the sum of sitting and lying times, whereas the sum of standing and walking times indicated active time.[38] Subjects were classified as (1) sedentary/nonsedentary, according to cutoff point of 8.5 h/d spent in PADL < 1.5 MET[11]; (2) physically active/inactive, according to cutoff point of 80 min/d spent in PADL ≥ 3 METs[12]; and (3) with/without severe physical inactivity, according to cutoff point of 4,580 steps/d.[13]

Statistical Analysis

Sample size was calculated using MedCalc 12.0 software (MedCalc, Ostend, Belgium), considering an area under the curve (AUC) of 0.7, bidirectional alpha of 0.05, and power of 80%. The optimal number was estimated as 105 subjects. SPSS Statistics (IBM, Armonk, New York) software version 20.0 was used for data analysis, adopting a significance level of 5%. Shapiro-Wilk test was used to verify data distribution. Correlations between CAT and mMRC scores, number of steps, and time spent in PADL > 3 METs and < 1.5 MET were performed using Pearson or Spearman correlation coefficients and classified as weak ($0.3 \leq r < 0.5$), moderate ($0.5 \leq r < 0.7$), strong ($0.7 \leq r < 1.0$), and perfect ($r = 1.0$).[39] Unpaired *t* test or Mann-Whitney *U* test compared CAT and mMRC scores between PADL classifications. If correlation coefficients between PADL and CAT and mMRC were ≥ 0.3, receiver operating characteristic (ROC) curves, AUC, and Youden Index verified discriminative capacity and determined the best CAT and mMRC cutoff points. The ROC curves were conducted with a nonparametric approach. Discriminative capacity was considered satisfactory when ≥ 0.70.[40] Sample was stratified according to identified mMRC and CAT cutoff points, whereas unpaired *t* test or Mann-Whitney *U* test compared pulmonary function, HRQOL, functional status, and mortality index. Associations between classifications based on CAT and mMRC cutoff points and PADL, 6MWT, TGlittre, and LCADL classifications were performed using chi-square test, whereas Cramer V coefficient verified the strength of associations, which varied from 0 (no association between the variables) to 1 (complete association). Binary logistic regression was performed considering classifications based on CAT and mMRC cutoff points as dependent variables and categorical variables that presented significant associations as independent variables. The model was adjusted to include variables with significant associations. Odds ratio and 95% CI were also reported.

Results

One hundred and thirty-eight patients were eligible for the study. Six were excluded due to exacerbation during the protocol, and one was unable to complete evaluations. Thus, 131 subjects (94 male) completed the study: 129 completed the mMRC and 121 the CAT. Of these, 31 (23.7%) presented moderate (GOLD II), 46 (35.1%) severe (GOLD III), and 54 (41.2%) very severe (GOLD IV) pulmonary function impairment. Seventy (53.4%) were physically inactive, 60 (45.8%) presented severe physical inactivity, and 108 (82.4%) sedentary behavior. Sample characteristics are described in Table 1.

CAT and mMRC scores correlated significantly with PADL variables (Table 2). Inactive subjects with severe physical inactivity and sedentary behavior presented higher mMRC and CAT scores than active subjects without severe physical inactivity and nonsedentary, respectively (Table 3).

mMRC and CAT Cutoff Points

The ROC curve indicated mMRC cutoff point of 2 in all classifications: physical inactivity level (sensitivity = 66%,

Table 1. Anthropometric Characteristics, Pulmonary Function, Dyspnea, Health Status, and Physical Activities of Daily Life of the Sample

Variables	Total Mean ± SD ($N = 131$)	mMRC < 2 Mean ± SD ($n = 57$)	mMRC ≥ 2 Mean ± SD ($n = 72$)	*P*	CAT < 16 Mean ± SD ($n = 48$)	CAT ≥ 16 Mean ± SD ($n = 73$)	*P*	CAT < 20 Mean ± SD ($n = 68$)	CAT ≥ 20 Mean ± SD ($n = 53$)	*P*
Age, y	66.5 ± 8.24	65.0 ± 8.52	67.6 ± 7.97	.07	66.2 ± 8.06	66.9 ± 8.57	.71	66.6 ± 8.20	66.7 ± 8.60	.95
Body weight, kg	69.8 ± 15.9	72.0 ± 16.3	68.0 ± 15.7	.17	70.9 ± 14.7	68.5 ± 17.2	.42	71.2 ± 15.1	67.2 ± 17.3	.17
Height, m	1.65 ± 0.09	1.66 ± 0.09	1.64 ± 0.09	.30	1.67 ± 0.10	1.64 ± 0.09	.08	1.67 ± 0.90	1.63 ± 0.09	.01
BMI, kg/m^2	25.4 ± 5.04	25.9 ± 5.08	25.1 ± 5.07	.37	25.3 ± 4.32	25.3 ± 5.56	.87	25.3 ± 4.38	25.3 ± 5.92	.82
FEV_1/FVC	0.44 ± 0.11	0.49 ± 0.11	0.39 ± 0.09	< .001	0.48 ± 0.10	0.41 ± 0.11	< .001	0.47 ± 0.10	0.39 ± 0.10	< .001
FEV_1, L	1.07 ± 0.50	1.33 ± 0.50	0.85 ± 0.38	< .001	1.29 ± 0.47	0.93 ± 0.48	< .001	1.28 ± 0.49	0.81 ± 0.40	< .001
FEV_1 ,% predicted	36.7 ± 16.1	44.9 ± 16.1	29.8 ± 12.3	< .001	43.2 ± 16.0	32.5 ± 14.8	< .001	42.5 ± 15.9	29.4 ± 13.3	< .001
FVC, L	2.39 ± 0.80	2.66 ± 0.81	2.16 ± 0.73	< .001	2.67 ± 0.80	2.20 ± 0.78	.001	2.68 ± 0.84	2.01 ± 0.63	< .001
FVC ,% predicted	63.6 ± 18.4	70.5 ± 17.1	57.9 ± 17.7	< .001	69.5 ± 17.7	59.7 ± 18.4	.003	69.3 ± 18.9	56.3 ± 15.8	< .001
mMRC*, score	2 [0–4]	–	–	–	1 [0–4]	3 [0–4]	< .001	1 [0–4]	3 [1–4]	< .001
CAT, total	17.9 ± 7.86	13.8 ± 6.34	21.1 ± 7.34	< .001	–	–	–	–	–	–
Time sitting, min	381 ± 104	363 ± 93.4	395 ± 110	.08	353 ± 101	400 ± 106	.02	371 ± 110	393 ± 101	.26
Time lying, min	105.0 ± 98.1	89.2 ± 91.4	115.0 ± 101.0	.08	106.0 ± 101.0	106.0 ± 97.4	.97	97.3 ± 95.4	117.0 ± 102.0	.31
Time standing, min	145 ± 57.4	157 ± 59.9	136 ± 54.6	.047	155 ± 66.1	138 ± 52.3	.24	149 ± 64.7	140 ± 49.8	.79
Time walking, min	65.4 ± 35.5	84.2 ± 33.4	50.7 ± 29.9	< .001	78.6 ± 34.8	54.4 ± 33.7	< .001	75.1 ± 37.3	49.8 ± 29.0	< .001
Time sedentary, min	486 ± 93.6	452 ± 90.8	511 ± 88.6	< .001	459 ± 101.0	505 ± 88.1	.01	468 ± 10.03	511 ± 79.9	.04
Time active, min	230 ± 89.6	266 ± 91.2	203 ± 79.0	< .001	258 ± 101.0	209 ± 79.0	.01	245 ± 100.0	206 ± 73.1	.06
MI walking, m/s^2	1.76 ± 0.50	1.89 ± 0.28	1.67 ± 0.60	< .001	1.85 ± 0.29	1.69 ± 0.61	< .001	1.80 ± 0.28	1.67 ± 0.70	< .001
Steps, no.	5,124 ± 2,977	6,797 ± 2,823	3,812 ± 2,381	< .001	6,317 ± 2,877	4,163 ± 2,790	< .001	5,949 ± 3,002	3,823 ± 2,578	< .001
PADL < 1.5 MET, min	573 ± 82.7	536 ± 80.7	601 ± 73.1	< .001	547 ± 85.9	597 ± 72.5	.001	555 ± 89.5	606 ± 59.2	.003
PADL ≥ 3 METs, min	90.3 ± 86.2	116.0 ± 119.0	69.2 ± 38.4	< .001	94.2 ± 46.2	76.0 ± 57.1	0.01	90.3 ± 47.9	74.2 ± 59.4	.02
6MWD, m	425 ± 93.0	463 ± 94.8	383 ± 70.4	< .001	468 ± 82.9	392 ± 90.3	< .001	453 ± 94.4	380 ± 75.9	.001
6MWT, % predicted	76.8 ± 14.7	82.4 ± 14.0	70.4 ± 12.8	< .001	83.9 ± 13.2	71.0 ± 13.8	< .001	80.8 ± 14.7	69.9 ± 12.9	.002
TGlittre, min	4.60 ± 2.10	3.70 ± 1.01	5.64 ± 2.53	< .001	3.85 ± 1.30	5.24 ± 2.42	.001	4.00 ± 1.43	5.57 ± 2.61	< .001
TGlittre, % predicted	153 ± 69.5	124 ± 31.4	188 ± 85.1	< .001	129 ± 44.0	174 ± 80.4	< .001	134 ± 47.0	185 ± 87.6	< .001
LCADL %total	33.6 ± 13.2	27.6 ± 7.7	39.9 ± 14.9	< .001	26.8 ± 6.0	39.9 ± 15.3	< .001	27.2 ± 6.3	46.0 ± 14.9	< .001
mSGRQ symptoms	37.8 ± 21.8	30.2 ± 18.6	45.8 ± 22.3	.001	27.5 ± 17.3	47.7 ± 20.0	< .001	30.2 ± 17.4	53.3 ± 19.6	< .001
mSGRQ activity	64.0 ± 20.4	54.4 ± 17.8	74.0 ± 18.2	< .001	51.5 ± 17.3	75.4 ± 17.0	< .001	54.3 ± 16.9	82.6 ± 13.5	< .001
mSGRQ impact	34.6 ± 20.5	25.0 ± 15.4	44.6 ± 20.5	< .001	22.8 ± 14.1	45.8 ± 19.5	< .001	25.5 ± 14.6	52.7 ± 18.4	< .001
mSGRQ total	44.2 ± 18.6	35.0 ± 13.7	53.7 ± 18.2	< .001	32.5 ± 12.8	55.2 ± 16.9	< .001	35.2 ± 12.6	62.0 ± 15.6	< .001
BODE index, score	3.33 ± 1.85	2.12 ± 1.12	4.67 ± 1.56	< .001	2.50 ± 1.46	4.00 ± 1.97	< .001	2.69 ± 1.61	4.43 ± 1.89	< .001

*Results are presented as median [interquartile range].
BMI = body mass index
mMRC = modified Medical Research Council
CAT = COPD Assessment Test
MI = movement intensity
PADL = physical activity in daily life
MET = metabolic equivalent of task
6MWT = 6-min walk test
6MWD = 6-min walk distance
TGlittre = Glittre-ADL test
LCADL = London Chest Activity of Daily Living
%total = percentage of total score
mSGRQ = modified St George Respiratory Questionnaire
BODE = body-mass index, air flow obstruction, dyspnea, and exercise capacity

Table 2. Correlations Between mMRC and CAT and Pulmonary Function and Physical Activities in Daily Life

Variables	mMRC		CAT	
	r	*P*	r	*P*
Time sitting, min	0.23	.01	0.20	.03
Time lying, min	0.08	.33	−0.002	.98
Time standing, min	−0.18	.03	−0.08	.40
Time walking, min	−0.52	< .001	−0.39	< .001
Time sedentary, min	0.34	< .001	0.24	.01
Time active, min	−0.36	< .001	−0.24	.01
MI walking, m/s^2	−0.51	< .001	−0.36	< .001
Steps, no.	−0.53	< .001	−0.40	< .001
PADL < 1.5 MET, min	0.47	< .001	0.31	.001
PADL ≥ 3 METs, min	−0.33	< .001	−0.29	.001

mMRC = modified Medical Research Council scale
CAT = COPD Assessment Test
MI = movement intensity
PADL = physical activity in daily life
MET = metabolic equivalent of task

specificity = 56%, $P = .01$), severe physical inactivity (sensitivity = 81%, specificity = 66%, $P < .001$), and sedentary behavior (sensitivity = 61%, specificity = 70%, $P = .02$), respectively. Regarding CAT, cutoff points were 16 and 20 for severe physical inactivity (sensitivity = 76%, specificity = 54%, $P < .001$) and sedentary behavior (sensitivity = 51%, specificity = 90%, $P = .001$), respectively (Fig. 1).

Subjects who scored mMRC ≥ 2 and CAT ≥ 16 and ≥ 20 presented worse pulmonary function; higher LCADL % total, BODE, mSGRQ (total and domain scores); worse 6MWT and TGlittre performances; and lower PADL level than those scoring mMRC < 2 and CAT < 16 and < 20. Also, CAT score was higher in subjects with mMRC ≥ 2, whereas mMRC score was higher in subjects with CAT ≥ 16 and ≥ 20 than those presenting mMRC < 2 and CAT < 16 and < 20, respectively (Table 1).

The mMRC cutoff point was associated with classification based on 6MWT, TGlittre, and LCADL %total (Cramer V = 0.32–0.48, $P < .05$ for all). Subjects with TGlittre ≥ 3.5 min and LCADL %total score ≥ 28% were 8.58-fold (95% CI 2.5–29.7, $P = .001$) and 6.36-fold (95% CI 1.7–20.6, $P = .002$) more likely to present mMRC ≥ 2, respectively. The CAT cutoff points were associated with 6MWT, TGlittre, and LCADL %total classifications (Cramer V = 0.33–0.57, $P < .05$ for all). Subjects with 6MWT < 82% predicted and LCADL %total score ≥ 28%

Table 3. Comparations of mMRC and CAT Between PADL ≥ 3METs, Severe Inactivity, PADL < 1.5 MET, 6MWT, TGlittre, and LCADL Classifications

Variables	mMRC Median [min–max]	*P*	CAT Mean ± SD	Mean Difference[#] 95% CI	*P*
PADL ≥ 3 METs					
≥ 80 min/d	1 [0–4]	.02	16.1 ± 7.54	3.12 (0.31–5.93)	.03
< 80 min/d	2 [0–4]		19.2 ± 7.89		
Severe inactivity					
≥4,580 steps/d	1 [0–4]	< .001	15.2 ± 7.05	5.62 (2.96–8.28)	< .001
<4,580 steps/d	3 [0–4]		20.8 ± 7.70		
PADL < 1.5 MET					
≥ 510 min/d	2 [0–4]	.02	18.8 ± 7.73	5.33 (1.71–8.96)	.004
< 510 min/d	1 [0–4]		13.5 ± 7.07		
6MWT					
≥ 82% predicted	1 [0–2]	.001	12.9 ± 5.79	6.37 (3.14–9.57)	< .001
< 82% predicted	2 [0–4]		19.3 ± 7.39		
TGlittre					
≥ 3.5 min	2 [0–4]	< .001	19.0 ± 7.65	5.48 (2.19–8.77)	.001
< 3.5 min	1 [0–3]		13.5 ± 5.96		
LCADL					
≥ 28% total	1 [0–3]	< .001	20.5 ± 6.68	8.27 (5.61–10.90)	< .001
< 28% total	2 [1–4]		12.2 ± 5.28		

mMRC = modified Medical Research Council
min–max = minimum–maximum
CAT = COPD Assessment Test
PADL = physical activity in daily life
MET = metabolic equivalent of task
6MWT = 6-min walk test
TGlittre = Glittre ADL-test
LCADL = London Chest Activity of Daily Living
[#] = mean difference between PADL, 6MWT, TGlittre, and LCADL classifications.

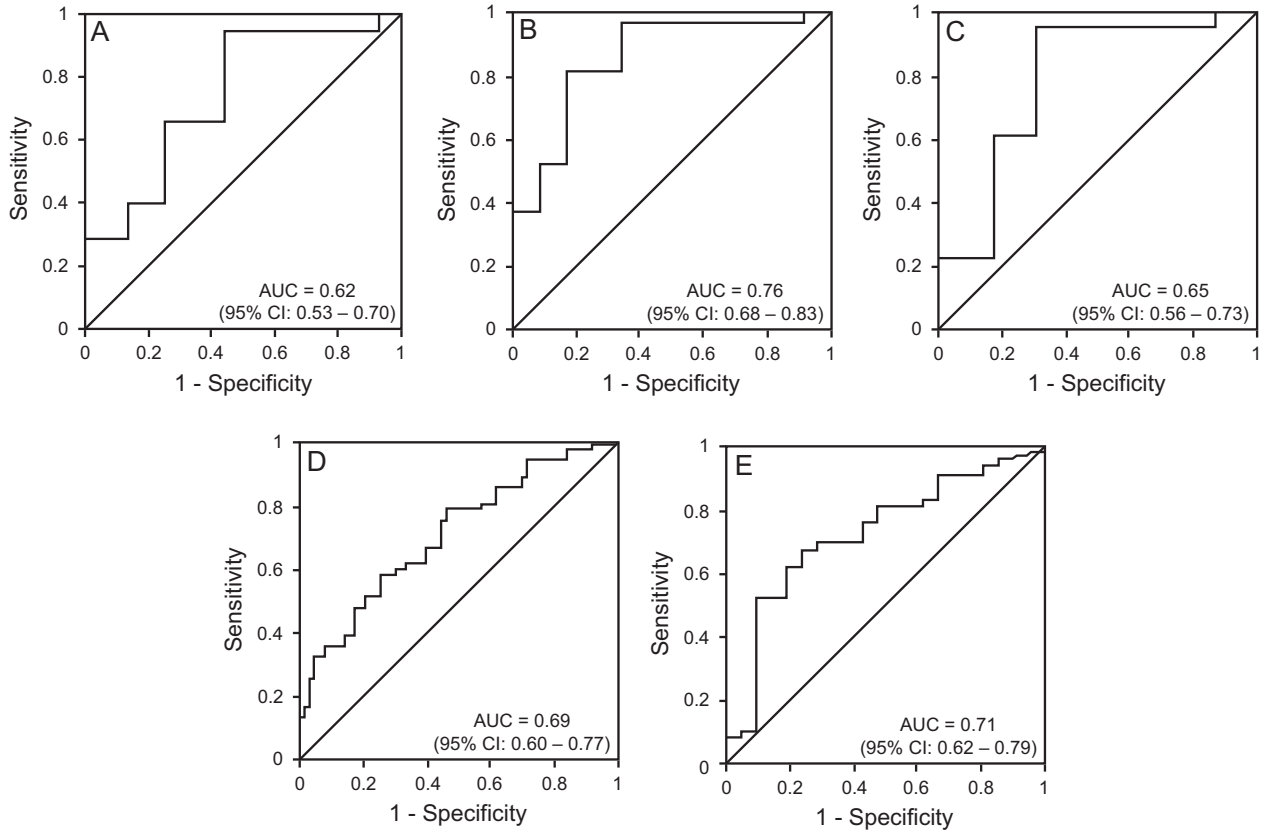

Fig. 1. Receiver operating characteristic curves for the modified Medical Research Council scale cutoff point (A, B, and C) to discriminate PADL level and sedentary behavior and for COPD Assessment Test (CAT) cutoff point (D and E) to discriminate severe physical inactivity and sedentary behavior in subjects with COPD. A: Physical inactivity level: cutoff point = 2, sensitivity = 66%, specificity = 56%, AUC = 0.62 (95% CI 0.53–0.70), $P = .01$. B: Severe physical inactivity: cutoff point = 2, sensitivity = 81%, specificity = 66%, AUC = 0.76 (95% CI 0.68–0.83), $P < .001$. C: Sedentary behavior: cutoff point = 2, sensitivity = 61%, specificity = 70%, AUC = 0.65 (95% CI 0.56–0.73), $P = .02$. D: Severe physical inactivity: cutoff point = 16, sensitivity = 76%, specificity = 54%, AUC = 0.69 (95% CI 0.60–0.77), $P < .001$. E: Sedentary behavior: cutoff point = 20, sensitivity = 51%, specificity = 90%, AUC = 0.71 (95% CI 0.62–0.79), $P = .001$.

were 5.44-fold (95% CI 1.7–17.0, $P = .004$) and 6.15-fold (95% CI 2.0–18.8, $P = .001$) more likely to present CAT $\geq$ 16 and 6.52-fold (95% CI 1.6–25.9, $P = .01$) and 22.8-fold (95% CI 4.5–115.0, $P < .001$) more likely to score CAT $\geq$ 20.

Discussion

This study identified cutoff points to interpret mMRC and CAT regarding PADL impairments and sedentary behavior in subjects with COPD. mMRC (2 points) and CAT (16 and 20 points) cutoff points were sensitive and specific to discriminate these outcomes in subjects with COPD. Those with mMRC $\geq$ 2 and CAT $\geq$ 16 and $\geq$ 20 presented worse pulmonary function, HRQOL, functional and exercise capacities, ADL limitation, lower PADL level, and higher risk of death according to the BODE index than those presenting mMRC $<$ 2 and CAT $<$ 16 and $<$ 20.

The instruments chosen to determine cutoff points were selected based on GOLD classification that quantifies future exacerbation risk and symptoms since 2011, allowing better clinical management of patients with COPD. Although PADL level and sedentary behavior are prognostic determinants, GOLD criteria do not consider them in the multidimensional classification.[3] Furthermore, no physical training strategies designed to address different quadrants of the multidimensional classification are present in the literature.[1] Despite GOLD criteria recommend physical activity for all patients with COPD, pulmonary rehabilitation programs are considered essential only for those classified in B, C, and D quadrants.[3] Therefore, PADL level and sedentary behavior monitoring may have equal or greater relevance than assessing exercise capacity since behavior change and adherence to active lifestyle are 2 of the greatest challenges and the primary focus of pulmonary rehabilitation programs.[1] In this sense, the present study may help design strategies for patients with different functional impairment levels, identified using instruments of easy clinical applicability and recommended by GOLD criteria. Another strength of this study is the objective PADL measurements provided by triaxial

accelerometers, differing from questionnaires reflecting subjective perception of physical activity.[5]

Previous studies preferred mMRC in the context of PADL since it better reflects PADL and differentiates patients in 4 multidimensional quadrants.[16,17] This is probably due to nonequivalence of cutoff points adopted by GOLD (ie, mMRC = 2 and CAT = 10), generating inconsistent classifications.[19] Smid et al[20] found that CAT cutoff point of 18 (using mMRC ≥ 2 as reference point) better distributed subjects in the multidimensional GOLD classification. This value is very close to cutoff points found in our study to discriminate severe physical inactivity and sedentary behavior. Casanova et al[41] identified that CAT cutoff point adopted by GOLD criteria was not associated with mortality, and the best predictive value for all-cause mortality (also using mMRC ≥ 2) was ≥ 17. mMRC ≥ 1 and CAT ≥ 10 cutoff points were equivalent in a study that determined low-symptom subjects.[42] However, our findings and previous studies[20,41] demonstrated that cutoff points higher than observed by Jones et al[42] provided valuable prognostic information and should be preferably used.

The current study also identified that the classification from mMRC and CAT cutoff points was able to discriminate subjects concerning the pulmonary function, HRQOL, functional and exercise capacities, ADL limitation, and higher risk of death according to the BODE index. These outcomes are complementary and are strongly associated to the prognosis of COPD.[1,37,43,44] The discriminatory power found can be considered clinically relevant since the differences between the groups presented higher values than the minimal important difference of the mSGRQ,[45] the 6MWT,[31] the TGlittre,[46] the LCADL,[47] and the number of steps.[48] Additionally, the BODE index was higher in subjects with scores mMRC ≥ 2 and CAT ≥ 16 and ≥ 20. It is relevant given that higher scores on the BODE index reflect an increased risk of death.[37]

The cutoff points were established based on variables of functional status and were associated with classifications from one scale and field tests related to functional status. Having cutoff points capable of discriminating functional status of patients can be quite useful for a better stratification of this outcome. In addition, it can help clinicians determine the urgency of the need to refer patients to centers with therapies more directed at improving functional status. Interestingly, TGlittre classification was associated with mMRC classification, whereas 6MWT was associated with CAT classification. TGlittre is a field test developed for subjects with COPD that encompasses tasks considered challenging in the subjects' routine[34] and is associated with other health outcomes.[49-51] Subjects performing TGlittre in ≥ 3.5 min were approximately 8-fold more likely to present mMRC ≥ 2, reinforcing the role of dyspnea in limiting ADLs and reflecting an important warning about PADL impairments in subjects with worse TGlittre performance.

The instruments used as anchors in this study present well-established cutoff points,[11-13] and their outcomes are predictors of mortality in subjects with COPD.[9,11] mMRC cutoff point of 2 was found for all anchors with AUC above or very close to the satisfactory threshold.[40] The same was observed for CAT but with different cutoff points to discriminate severe physical inactivity and sedentary behavior. In practice, these outcomes are confounded since one patient may be classified as physically active but still present sedentary behavior and perform activities with low energy expenditure throughout the day.[52] Therefore, the choice of using CAT cutoff points (16 and 20) must consider specific goals. Moreover, it was not possible to determine CAT cutoff point to discriminate physical inactivity level.

The time spent monitoring PADL probably influenced our results. However, previous studies demonstrated that data collected in 2 days produce reliable results.[17,53] Also, GOLD I patients were not included in this study; therefore, results should not be extrapolated to patients with mild pulmonary function impairment. This study will support health professionals to use mMRC and CAT to identify patients with low PADL levels and better guide nonpharmacologic strategies to reduce the effects of sedentary behavior and physical inactivity in this patient population. However, although valuable, mMRC and CAT scores and their cutoff points are not a surrogate for accelerometer data.

Conclusions

The mMRC cutoff point of 2 (< 2 and ≥ 2) is recommended to discriminate PADL level and sedentary behavior, whereas CAT cutoff points of 16 (< 16 and ≥ 16) and 20 (< 20 and ≥ 20) discriminated severe physical inactivity and sedentary behavior, respectively, in subjects with COPD with moderate to very severe pulmonary function impairment. These cutoff points also differentiated pulmonary function, HRQOL, functional and exercise capacity, ADL limitation, PADL level, and potential risk of death in subjects with COPD. Our study confirmed that mMRC and CAT could easily identify physical inactivity and sedentary behavior of subjects with COPD in routine clinical practice.

REFERENCES

1. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al; ATS/ERS Task Force on Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med 2013;188(8):e13-64-e64.
2. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest 2002;121(5):1434-1440.

3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2020 Report. Available at: http://www.goldcopd.org/. *Accessed November 4,2020*.
4. Leidy N. On functional status and the forward progress of merry-go-rounds: toward a coherent analytical framework. Nursing Research 1994;43(4):196-202.
5. Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, et al. An official European Respiratory Society statement on physical activity in COPD. Eur Respir J 2014;44(6):1521-1537.
6. Kocks JW, Asijee GM, Tsiligianni IG, Kerstjens HA, van der Molen T. Functional status measurement in COPD: a review of available methods and their feasibility in primary care. Prim Care Respir J 2011;20(3):269-275.
7. Durr S, Zogg S, Miedinger D, Steveling EH, Maier S, Leuppi JD. Daily physical activity, functional capacity, and quality of life in patients with COPD. COPD 2014;11(6):689-696.
8. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population-based cohort study. Thorax 2006;61(9):772-778.
9. Waschki B, Kirsten A, Holz O, Muller KC, Meyer T, Watz H, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. Chest 2011;140 (2):331-342.
10. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. Eur Respir J 2006;27(5):1040-1055.
11. Furlanetto KC, Donaria L, Schneider LP, Lopes JR, Ribeiro M, Fernandes KB, et al. Sedentary behavior is an independent predictor of mortality in subjects with COPD. Respir Care 2017;62(5):579-587.
12. van Remoortel H, Camillo CA, Langer D, Hornikx M, Demeyer H, Burtin C, et al. Moderate intense physical activity depends on selected metabolic equivalent of task (MET) cutoff and type of data analysis. PloS One 2013;8(12):e84365.
13. Depew ZS, Novotny PJ, Benzo RP. How many steps are enough to avoid severe physical inactivity in patients with chronic obstructive pulmonary disease? Respirology 2012;17(6):1026-1027.
14. Park SK, Meldrum CA, Larson JL. Subgroup analysis of symptoms and their effect on functioning, exercise capacity, and physical activity in patients with severe chronic obstructive pulmonary disease. Heart Lung 2013;42(6):465-472.
15. Polkey MI, Moxham J. Attacking the disease spiral in chronic obstructive pulmonary disease: an update. Clin Med (Lond) 2011;11(5):461-464.
16. Demeyer H, Gimeno-Santos E, Rabinovich RA, Hornikx M, Louvaris Z, de Boer WI, et al; PROactive consortium. Physical activity characteristics across GOLD quadrants depend on the questionnaire used. PloS One 2016;11(3):e0151255.
17. Munari AB, Gulart AA, Dos Santos K, Venancio RS, Karloh M, Mayer AF. Modified medical research council dyspnea scale in GOLD classification better reflects physical activities of daily living. Respir Care 2018;63(1):77-85.
18. Zogg S, Durr S, Miedinger D, Steveling EH, Maier S, Leuppi JD. Differences in classification of COPD patients into risk groups A-D: a cross-sectional study. BMC Res Notes 2014;7:562.
19. Karloh M, Fleig Mayer A, Maurici R, Pizzichini MM, Jones PW, Pizzichini E. The COPD assessment test: what do we know so far?: a systematic review and meta-analysis about clinical outcomes prediction and classification of patients into GOLD stages. Chest 2016;149 (2):413-425.
20. Smid DE, Franssen FME, Gonik M, Miravitlles M, Casanova C, Cosio BG, et al. Redefining cut-points for high symptom burden of the global initiative for chronic obstructive lung disease classification in 18,577 patients with chronic obstructive pulmonary disease. Journal of the American Medical Directors Association 2017;18(12):e1011-1097-1097.e24. 1097e1024.
21. Sillen MJ, Franssen FM, Delbressine JM, Uszko-Lencer NH, Vanfleteren LE, Rutten EP, et al. Heterogeneity in clinical characteristics and comorbidities in dyspneic individuals with COPD GOLD D: findings of the DICES trial. Respir Med 2013;107(8):1186-1194.
22. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al; ATS/ERS Task Force. Standardization of spirometry. Eur Respir J 2005;26(2):319-338.
23. Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol 2007;33(4):397-406.
24. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD assessment test. Eur Respir J 2009;34(3):648-654.
25. Silva GP, Morano MT, Viana CM, Magalhaes CB, Pereira ED. Portuguese-language version of the COPD assessment test: validation for use in Brazil. J Bras Pneumol 2013;39(4):402-408.
26. Jones PW, Quirk FH, Baveystock CM. The St George's respiratory questionnaire. Respir Med 1991;85 Suppl B(Suppl B):25-31, discussion 33–27.
27. Camelier A, Rosa FW, Salmi C, Nascimento OA, Cardoso F, Jardim JR. Using the Saint George's respiratory questionnaire to evaluate quality of life in patients with chronic obstructive pulmonary disease: validating a new version for use in Brazil. J Bras Pneumol 2006;32 (2):114-122.
28. Carpes MF, Mayer AF, Simon KM, Jardim JR, Garrod R. The Brazilian Portuguese version of the London chest activity of daily living scale for use in patients with chronic obstructive pulmonary disease. J Bras Pneumol 2008;34(3):143-151.
29. Garrod R, Bestall JC, Paul EA, Wedzicha JA, Jones PW. Development and validation of a standardized measure of activity of daily living in patients with severe COPD: the London chest activity of daily living scale (LCADL). Respir Med 2000;94(6):589-596.
30. Gulart AA, Munari AB, Klein SR, Venancio RS, Alexandre HF, Mayer AF. The London chest activity of daily living scale cutoff point to discriminate functional status in patients with chronic obstructive pulmonary disease. Braz J Phys Ther 2020 May-Jun;24(3):264-272.
31. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J 2014;44(6):1428-1446.
32. Britto RR, Probst VS, de Andrade AF, Samora GA, Hernandes NA, Marinho PE, et al. Reference equations for the 6-minute walk distance based on a Brazilian multicenter study. Braz J Phys Ther 2013;17 (6):556-563.
33. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J 1999;14(2):270-274.
34. Skumlien S, Hagelund T, Bjortuft O, Ryg MS. A field test of functional status as performance of activities of daily living in COPD patients. Respir Med 2006;100(2):316-323.
35. Reis CMD, Karloh M, Fonseca FR, Biscaro RRM, Mazo GZ, Mayer AF. Functional capacity measurement: reference equations for the Glittre activities of daily living test. J Bras Pneumol 2018;44(5):370-377.
36. Gulart AA, Munari AB, Klein SR, Santos da Silveira L, Mayer AF. The Glittre-ADL test cutoff point to discriminate abnormal functional capacity in patients with COPD. COPD 2018;15(1):73-78.
37. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. The. N Engl J Med 2004;350(10):1005-1012.

38. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2005;171(9):972-977.
39. Rumsey D. Statistics for Dummies. 2d ed. Wiley; 2016.
40. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol 2010;5(9):1315-1316.
41. Casanova C, Marin JM, Martinez-Gonzalez C, de Lucas-Ramos P, Mir-Viladrich I, Cosio B, et al. Differential effect of modified medical research council dyspnea, COPD assessment test, and clinical COPD questionnaire for symptoms evaluation within the new GOLD staging and mortality in COPD. Chest 2015;148(1):159-168.
42. Jones P, Adamek L, Nadeau G, Banik N. Comparisons of health status scores with MRC grades in a primary care COPD population: implications for the new GOLD 2011 classification. Eur Respir J 2013;42 (3):647-654.
43. Carone M, Antoniu S, Baiardi P, Digilio VS, Jones PW, Bertolotti G; QuESS Group. Predictors of mortality in patients with COPD and chronic respiratory failure: the quality-of-life evaluation and survival study (QuESS): A 3-Year Study. COPD 2016;13(2):130-138.
44. Dajczman E, Wardini R, Kasymjanova G, Prefontaine D, Baltzan MA, Wolkove N. Six-minute walk distance is a predictor of survival in patients with chronic obstructive pulmonary disease undergoing pulmonary rehabilitation. Canadian Respiratory Journal 2015;22(4):225-229.
45. Jones PW. St. George's respiratory questionnaire: MCID. COPD 2005;2(1):75-79.
46. Gulart AA, Araujo CLP, Munari AB, Santos KD, Karloh M, Foscarini BG, et al. The minimal important difference for Glittre-ADL test in patients with chronic obstructive pulmonary disease. Braz J Phys Ther 2020;24(1):54-60.
47. Almeida Gulart A, de Araujo CLP, Bauer Munari A, Schneider BF, Dal Lago P, Mayer AF. Minimal important difference for London chest activity of daily living scale in patients with chronic obstructive pulmonary disease. Physiotherapy 2020;107:28-35.
48. Demeyer H, Burtin C, Hornikx M, Camillo CA, Van Remoortel H, Langer D, et al. The minimal important difference in physical activity in patients with COPD. PloS One 2016;11(4):e0154587.
49. Gulart A, Santos K, Munari A, Karloh M, Cani K, Mayer A. Relationship between the functional capacity and perception of limitation on activities of daily life of patients with. COPD. Fisioter e Pesqui 2015;22(2).
50. Gulart AA, Munari AB, Queiroz APAD, Cani KC, Matte DL, Mayer AF. Does the COPD assessment test reflect functional status in patients with COPD? Chron Respir Dis 2017;14(1):37-44.
51. Karloh M, Araujo CL, Gulart AA, Reis CM, Steidle LJ, Mayer AF. The Glittre-ADL test reflects functional performance measured by physical activities of daily living in patients with chronic obstructive pulmonary disease. Braz J Phys Ther 2016;20(3):223-230.
52. Hill K, Gardiner PA, Cavalheri V, Jenkins SC, Healy GN. Physical activity and sedentary behavior: applying lessons to chronic obstructive pulmonary disease. Intern Med J 2015;45(5):474-482.
53. Gulart AA, Munari AB, Santos Silva IJC, Alexandre HF, Karloh M, Mayer AF. Baseline characteristics associated to improvement of patients with COPD in physical activity in daily life level after pulmonary rehabilitation. Respir Med 2019;151:142-147.