# Maximum Voluntary Ventilation and Its Relationship With Clinical Outcomes in Subjects With COPD

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BACKGROUND: Previous studies have reported that maximum voluntary ventilation (MVV) may be better associated with commonly used outcomes in COPD than FEV<sub>1</sub> and may provide information on respiratory mechanics. In this study, we aimed to investigate the relationship between MVV and clinical outcomes in COPD and to verify whether MVV predicts these outcomes better than FEV<sub>1</sub>. METHODS: We conducted a cross-sectional study involving individuals with COPD. Lung function was assessed with spirometry; maximum inspiratory and expiratory pressures (P<sub>Imax</sub> and P<sub>Emax</sub>, respectively) were assessed with manuvacuometry; and functional exercise capacity was assessed with the 6-min-walk test (6MWT). Dyspnea was assessed with the modified Medical Research Council (mMRC) scale; functional status was assessed with the modified Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ-m); and health status was assessed with the COPD Assessment Test (CAT). Correlations were verified with the Spearman coefficient, and stepwise multiple linear regression models investigated the predictors of clinical outcomes. RESULTS: Our study included 157 subjects: 82 males; median (interquartile range) age 66 (61-73) y; FEV<sub>1</sub> 46 (33-57) % predicted; 6MWT 86 (76-96) % predicted; PFSDQ-m total score 34 (14-57); and CAT total score 13 (7-19). Moderate correlations were found between MVV and  $P_{Imax}$  (r = 0.40), 6MWT (r = 0.50), mMRC (r = -0.56), and total scores on the PFSDQ-m (r = -0.40) and the CAT (r = -0.54). In the regression models, MVV was a predictor of almost all clinical outcomes, unlike FEV<sub>1</sub>. CONCLUSIONS: MVV correlates moderately with clinical outcomes commonly used in the evaluation of individuals with COPD, and MVV is a better predictor of respiratory muscle strength, functional exercise capacity, and patient-reported **outcomes than FEV<sub>1</sub>.** Key words: COPD; pulmonary function tests; spirometry; maximum voluntary ventilation; health status; exercise. [Respir Care 2021;66(1):79-86. © 2021 Daedalus Enterprises]

## Introduction

COPD is a systemic disease caused primarily by prolonged exposure to tobacco and other harmful particles.

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COPD deeply affects the health and quality of life of patients and is the third leading cause of death worldwide. <sup>1-5</sup> The main pulmonary symptoms of the disease are dyspnea, chronic cough, and increased sputum production, along with extrapulmonary manifestations such as fatigue,

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muscle dysfunction, reduction in functional exercise capacity, and sedentary lifestyle. <sup>2,3,6,7</sup>

The diagnostic confirmation of COPD is given by the clinical history along with spirometry, which quantifies FVC and FEV<sub>1</sub>. FEV<sub>1</sub> is the variable most widely used in research and clinical practice to classify the degree of airflow obstruction in COPD, in addition to its use as a prognostic factor and in therapeutic drug response.<sup>3-5</sup> However, there is limited correlation of FEV<sub>1</sub> with important patient-reported outcomes in COPD.<sup>8-10</sup> Furthermore, only a few studies have called attention to other disease markers that correlate better with these outcomes.<sup>11-14</sup>

Maximum voluntary ventilation (MVV) is a spirometric parameter that is not commonly explored in the scientific literature. Recently, with the emergence of new methods of lung function assessment, it has been explored even less. MVV evaluates the maximum amount of air a person can inhale and exhale voluntarily in a given period of time. This measure provides information on respiratory muscle mechanics and endurance, which are involved in the mechanism of dyspnea and exercise limitation. <sup>15-18</sup>

The hypothesis tested in this study is that MVV can predict better than  $\text{FEV}_1$  the overall impairment of subjects with COPD because it reflects the overall function of the respiratory system and not just the air-flow obstruction. In this context, the objective of this study was to investigate the relationship of MVV with clinical outcomes in this population and, additionally, to verify whether MVV is a better predictor of patient-reported outcomes than  $\text{FEV}_1$ .

# Methods

This was a retrospective analysis of baseline-only data from a convenience sample recruited between 2016 and 2018 for inclusion in a high-intensity exercise training program at the out-patient clinics of Respiratory Therapy and Pulmonology of the State University of Londrina in Brazil. Inclusion criteria were the diagnosis of COPD according to GOLD criteria,<sup>3</sup> clinical stability in the last 3 months before inclusion, not having participated in any rehabilitation program in the last year, and not presenting with any severe cardiovascular disease or musculoskeletal impairment that could potentially limit the tests. Exclusion criteria were the inability to perform the proposed tests or exacerbation that occurred during the evaluation protocol. The study was approved by the institution's ethics committee, and all subjects signed an informed consent form prior to any data collection.

## Assessments

At the first meeting, demographic and anthropometric data were collected, as well as information on comorbidities and history of exacerbations. Additionally, subjects

# **QUICK LOOK**

# Current knowledge

Research and clinical practice commonly use  $FEV_1$  to classify the degree of air-flow obstruction in patients with COPD, to serve as prognostic factor, and to evaluate therapeutic drug response. However, there is limited correlation of  $FEV_1$  with important outcomes in COPD such as dyspnea, functional exercise capacity, and quality of life. Only a few studies have called attention to other disease markers that correlate better with these outcomes.

# What this paper contributes to our knowledge

MVV correlates equally or better than  $FEV_1$  with functional and patient-reported outcomes in subjects with COPD. Additionally, MVV can reflect the ventilatory reserve available to respond to the increase in physiological demands during exertion. The results of this study reinforce the importance of this test in the comprehensive evaluation of lung function to assess the impact of physical and functional limitation in COPD.

were assessed regarding pulmonary function before and after bronchodilator use with a portable spirometer (SpirobankG, MIR, Rome, Italy) in the first 120 subjects, and plethysmography equipment (Vmax, Carefusion, Hoechberg, Germany) replaced the portable spirometer with the last 37 subjects. The protocol followed the American Thoracic Society/European Respiratory Society guidelines. <sup>15-19</sup> Reference values were those from Pereira and Rodrigues<sup>20</sup> for the Brazilian population. Measurements made after bronchodilator use were used for the analysis. It was not possible to perform plethysmography in the complete sample due to the unavailability of the equipment for a period of time.

The MVV maneuver was performed using the same portable spirometer or plethysmography equipment, as mentioned above. The test requires collaboration and maximum effort from the subject, which are encouraged through strong verbal encouragement. The maneuver is composed of deep, fast, and forced breathing for 12 s and maintaining a breathing frequency of 90–110 breaths/min, as established by guidelines. <sup>15-19,23</sup> Reference values were those specific for the Brazilian population according to Neder et al. <sup>24</sup> The estimated MVV was calculated as [(FEV<sub>1</sub> × 37.5) + 15]. The MVV index was calculated as [measured MVV/(FEV<sub>1</sub> × 40)]. This index is recommended by guidelines as an indicator of adequate effort as compared with the FEV<sub>1</sub>. An MVV index < 0.80 indicates disturbance or poor effort of the individual. <sup>15</sup>

Respiratory muscle strength was also assessed during the first visit through maximum inspiratory and expiratory pressures ( $P_{Imax}$  and  $P_{Emax}$ , respectively) with a digital manometer (MVD300, Globalmed, Porto Alegre, Brazil). Assessment was performed according to the technique described by Black and Hyatt<sup>22</sup> and Brazilian guidelines. <sup>23</sup> Brazilian reference values reported by Neder et al<sup>24</sup> were used.

All tests regarding pulmonary function and respiratory muscle strength were performed with the subjects in the seated position, using a nose clip, and oriented to keep the lips well coupled to avoid leakage. Subjects kept feet supported, with hands resting on the thighs, and maintained upright posture without compensations during the execution of the maneuvers. For all tests, individuals received detailed instructions with practical demonstration and standardized verbal encouragement.

In the second visit, functional exercise capacity was assessed with the 6-min-walk test (6MWT) according to international guidelines<sup>25</sup> and using reference values reported by Britto et al<sup>26</sup> for the Brazilian population. Subjects were instructed to walk the farthest possible distance (without running) on a flat corridor that was 30 m long for 6 min; subjects received standardized verbal encouragement every minute. Due to the learning effect, 2 tests were performed, with a minimum interval of 30 min between them, or until the vital signs returned to baseline.<sup>25</sup> The test with the greatest distance was used for analysis.

The modified Medical Research Council scale  $(mMRC)^{27,28}$  was used to assess limitation by dyspnea in daily life. The scale consists of 5 items that describe the sensation of dyspnea in daily activities and uses a scale of 0–4, where 0 = dyspnea triggered only in strenuous activities and <math>4 = limiting dyspnea on minimal exertion or at rest.

The modified version of the Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ-m) was applied to assess functional status. The questionnaire assesses 3 domains: influence of dyspnea on activities of daily living (ADL), influence of fatigue on ADL, and change in ADL in comparison to the period prior to the disease. A partial score is calculated for each domain, ranging from 0 to 100, and a total score sums up the 3 domains for a maximum score of 300, with higher values indicating worse functional status.<sup>27,29,30</sup>

The COPD Assessment Test (CAT) is composed of 8 items scored from 0 to 5 and is used to assess the impact of the disease on health status. Scores of 0–10 represented no impact, 11–20 mild impact, 21–30 moderate impact, and 31–40 high impact. The total score varies ranges from 0 to 40, with higher values indicating worse health status.<sup>30-32</sup>

# **Statistical Analysis**

Normality in data distribution was verified with the Shapiro-Wilk test, and results were described as mean  $\pm$  SD or median and interquartile range. All variables were

correlated with MVV and FEV<sub>1</sub> with using the Spearman correlation coefficient and, for the variables that presented significant correlations, multivariate linear regression models were used to verify the predictors of each clinical outcome, taking into consideration MVV, FEV<sub>1</sub>, and the anthropometric variables of age, gender, weight, and height (as a way to take into account possible confounding factors).<sup>33</sup> The software used for analysis were SPSS 22.0 (IBM, Armonk, New York) and GraphPad Prism 6.0 (GraphPad, La Jolla, California). Statistical significance was set as P < .05.

## Results

The analysis included data from 157 subjects who, in general, were normal weight to overweight and had moderate to severe air-flow obstruction, decreased inspiratory muscle strength, relatively preserved functional exercise capacity, good functional status, and moderate clinical impact on health status (Table 1). A sub-analysis was performed with data available from 37 individuals regarding static lung volumes evaluated with body plethysmography. The characterization of this sample is also found in Table 1.

Table 2 shows the correlations of MVV and  $FEV_1$  with weight, height, comorbidities, BODE index,  $P_{Imax}$ ,  $P_{Emax}$ , 6MWT, lung volumes, dyspnea, functional status, and health status. There were weak to moderate and statistically significant correlations for both MVV and  $FEV_1$  with the majority of the outcomes analyzed; the exceptions were total lung capacity, residual volume, and the CAT domains for chest pressure and sleep.

Considering only the magnitude of the correlations, for most of the outcomes MVV was better associated than  $FEV_1$  (even if slightly) except for the BODE index and the CAT domains for cough and secretion, which presented slightly higher correlation coefficients with  $FEV_1$ .

Table 3 shows the results of the linear regressions for 6MWT,  $P_{Imax}$ , and  $P_{Emax}$ . In Table 4, the results of the regression models for mMRC, PFSDQ-m, and CAT are presented. These data indicate that MVV appears to be an independent predictor of almost all of the analyzed outcomes, unlike FEV<sub>1</sub>.

# Discussion

Both traditionally and currently,  $FEV_1$  is the most commonly used pulmonary function variable for classification of disease severity and as a predictor of prognosis in patients with COPD. Our results indicate that MVV correlates equally or better than  $FEV_1$  with outcomes of dyspnea, exercise capacity, functional status, and health status in subjects with COPD, and MVV is a predictor of variation in most of these outcomes in regression models. The explanation for these results may be related to the fact

Table 1. Subject Characteristics

| Variables                          | Values           | Variables                               | Values        |  |
|------------------------------------|------------------|---|---------------|--|
| Male/female, n (%)                 | 82 (52)/75 (48)  | RV, % predicted                         | 156 (129–220) |  |
| Age, y                             | 66 (61–73)       | Inspiratory capacity/TLC ( $n = 37$ )   | 38 (32–44)    |  |
| Weight, kg                         | 69 (55–79)       | RV/TLC ( $n = 37$ )                     | 52 (46-60)    |  |
| Height, m                          | 1.5 (1.53–1.67)  | P <sub>Imax</sub> , cm H <sub>2</sub> O | 65 (50-80)    |  |
| Body mass index, kg/m <sup>2</sup> | 27 (22–31)       | P <sub>Imax</sub> , % predicted         | 75 (56–90)    |  |
| Comorbidities, $n (n = 144)$       | 1 (0–2)          | $P_{Emax}$ , cm $H_2O$                  | 95 (75–123)   |  |
| Comorbidities, S/N (%)             | 90 (62)/54 (38)  | P <sub>Emax</sub> , % predicted         | 103 (85–126)  |  |
| GOLD I/II/III/IV                   | 1/68/57/31       | 6MWD, m                                 | 465 (410–513) |  |
| BODE Index                         | 4 (2–5)          | 6MWD, % predicted                       | 86 (76–96)    |  |
| FVC, L                             | 2.2 (1.7–2.9)    | mMRC                                    | 3 (1–3)       |  |
| FVC, % predicted                   | 72 (55–84)       | PFSDQ-m Dyspnea                         | 11 (5–20)     |  |
| $FEV_1, L$                         | 1.10 (0.81–1.55) | PFSDQ-m Fatigue                         | 10 (3–8)      |  |
| FEV <sub>1</sub> , % predicted     | 46 (33–57)       | PFSDQ-m Activities                      | 10 (3-23)     |  |
| FEV <sub>1</sub> /FVC, %           | 52 (42–62)       | PFSDQ-m Total $(n = 65)$                | 34 (14–57)    |  |
| MVV, L/min                         | 42 (27–59)       | CAT Cough                               | 2 (1–3)       |  |
| MVV, % predicted                   | 42 (27–55)       | CAT Phlegm                              | 2 (1–4)       |  |
| Estimated MVV, L/min               | 57 (46–74)       | CAT Chest tightness                     | 0 (0-2)       |  |
| MVV index                          | 0.9 (0.8–1.1)    | CAT Breathlessness                      | 3 (2–5)       |  |
| TLC, L ( $n = 37$ )                | 6.85 (5.90–7.50) | CAT ADL Limitation                      | 2 (0-4)       |  |
| TLC, % predicted                   | 121 (110–135)    | CAT Confidence                          | 0 (0-3)       |  |
| Inspiratory capacity, L $(n = 37)$ | 2.62 (2.03–3.23) | CAT Sleep                               | 0 (0-2)       |  |
| Inspiratory capacity, % predicted  | 117 (94–129)     | CAT Energy                              | 2 (0–3)       |  |
| RV, L ( $n = 37$ )                 | 3.57 (2.62–4.59) | CAT Total $(n = 76)$                    | 13 (7–19)     |  |

Values are presented as median (interquartile range) unless otherwise noted. n = 157 unless otherwise noted.

GOLD = Global Initiative for Chronic Obstructive Lung Disease; BODE = body mass index, air-flow obstruction, dyspnea, exercise capacity; MVV = maximum voluntary ventilation;  $P_{Imax}$  = maximum inspiratory pressure;  $P_{Emax}$  = maximum expiratory pressure;  $P_{Emax}$  = maximum

that, while FEV<sub>1</sub> basically reflects air flow limitation, MVV also reflects the available ventilatory reserve to respond to an increasing physiological demand during exertion.<sup>7-9</sup>

A study by Rocha et al  $^{12}$  assessed the diaphragmatic mobility of 25 subjects with COPD and compared it with that of 25 matched controls. The authors reported reduced diaphragmatic mobility in subjects with COPD, as well as strong correlations of diaphragmatic mobility with inspiratory capacity (r = 0.81) and with MVV (r = 0.76). This suggests that the change in diaphragmatic mobility in patients with COPD is more associated with hyperinflation and with ventilatory capacity than with the obstruction itself, and consequently also more related to the sensation of dyspnea.

Our results also indicate moderate positive correlations between MVV and inspiratory capacity (r=0.67) and inspiratory capacity/total lung capacity (r=0.48), in addition to moderate negative correlations with the mMRC scale (r=-0.56) and the PFSDQ-m dyspnea domain (r=-0.44). These values reflect the association of better respiratory mechanics and endurance with lower hyperinflation and less dyspnea sensation.

Yamaguti et all<sup>14</sup> reported a stronger correlation between decreased diaphragmatic mobility and air trapping (ie, residual volume/total lung capacity; r=-0.76) than with hyperinflation (inspiratory capacity; r=0.63). Our results, in addition to showing a stronger association between hyperinflation and ventilatory capacity, also indicate a moderate negative correlation of MVV with the residual volume/total lung capacity ratio (r=-0.56), which reflects air trapping.

Pitta et al<sup>10</sup> reported that energy expenditure evaluated in daily life with a physical activity monitor correlates better with MVV (r=0.52) than with FEV<sub>1</sub> (r=0.37). In addition, Cavalheri et al<sup>11</sup> assessed the energy expenditure of individuals with COPD during ADL simulations and also reported a better correlation of this outcome with MVV (r=0.50) in comparison to FEV<sub>1</sub> (r=0.30) and FVC. These results indicate that MVV may reflect the capacity of response to increased respiratory demands and, consequently, also indicate its influence on the physical activity levels of these patients. Our results corroborate and complement these findings, presenting moderate and significant correlations of MVV with the 6MWT, which is already established as an independent predictor

Table 2. Correlations of Clinical Outcomes With MVV and FEV<sub>1</sub>

| Outcomes                                | MVV, L/min | Р      | FEV <sub>1</sub> , L | Р      | Outcomes            | MVV, L/min | Р      | FEV <sub>1</sub> , L | P      |
|---|------------|--------|----------------------|--------|---------------------|------------|--------|----------------------|--------|
| Weight, kg                              | 0.38       | < .001 | 0.38                 | < .001 | PFSDQ-m Dyspnea     | -0.44      | < .001 | -0.43                | < .001 |
| Height, m                               | 0.31       | < .001 | 0.31                 | < .001 | PFSDQ-m Fatigue     | -0.35      | .004   | -0.30                | .01    |
| BODE Index                              | -0.73      | < .001 | -0.75                | < .001 | PFSDQ-m Activities  | -0.30      | .01    | -0.25                | .044   |
| Comorbidities                           | -0.25      | .003   | -0.19                | .02    | PFSDQ-m Total       | -0.40      | .001   | -0.36                | .003   |
| P <sub>Imax</sub> , cm H <sub>2</sub> O | 0.40       | < .001 | 0.31                 | < .001 | CAT Cough           | -0.30      | .01    | -0.31                | .007   |
| P <sub>Emax</sub> , cm H <sub>2</sub> O | 0.34       | < .001 | 0.28                 | < .001 | CAT Phlegm          | -0.33      | .004   | -0.34                | .003   |
| 6MWD, m                                 | 0.50       | < .001 | 0.46                 | < .001 | CAT Chest tightness | -0.14      | .21    | -0.12                | .33    |
| TLC, L ( $n = 37$ )                     | 0.24       | .15    | 0.28                 | .09    | CAT Breathlessness  | -0.46      | < .001 | -0.41                | < .001 |
| Inspiratory capacity, L $(n = 37)$      | 0.67       | < .001 | 0.65                 | < .001 | CAT ADL limitation  | -0.50      | < .001 | -0.44                | < .001 |
| RV, L ( $n = 37$ )                      | -0.09      | .59    | -0.03                | .83    | CAT Confidence      | -0.47      | < .001 | -0.36                | .001   |
| Inspiratory capacity/TLC ( $n = 37$ )   | 0.48       | .02    | 0.45                 | .05    | CAT Sleep           | -0.07      | .52    | -0.09                | .042   |
| RV/TLC ( $n = 37$ )                     | -0.56      | < .001 | -0.53                | .01    | CAT Energy          | -0.29      | .01    | -0.28                | .02    |
| mMRC                                    | -0.56      | < .001 | -0.50                | < .001 | CAT Total           | -0.54      | < .001 | -0.49                | < .001 |

MVV = maximum voluntary ventilation; BODE = body mass index, air-flow obstruction, dyspnea, exercise capacity;  $P_{lmax} = maximum$  inspiratory pressure;  $P_{Emax} = maximum$  expiratory pressur

Table 3. Multiple Linear Regression Analysis for Respiratory Muscle Strength and Functional Exercise Capacity

|                                    | Nonstandardized Coefficient $\beta$ (95% CI) | P      | r <sup>2</sup> Adjusted, % | r <sup>2</sup> Adjusted, % |  |
|------------------------------------|--|--------|----------------------------|----------------------------|--|
| 6-min walk test                    |  |        |                            |                            |  |
| Constant                           | 662.35 (550–774)                             | < .001 |                            |                            |  |
| MVV, L/min                         | 2.06 (1.54–2.57)                             | < .001 | 23                         | 23                         |  |
| Age, y                             | -3.16 (-4.57 to -1.76)                       | < .001 | 30                         | 29                         |  |
| Body mass index, kg/m <sup>2</sup> | -3.41 (-5.35 to 1.45)                        | .001   | 35                         | 34                         |  |
| P <sub>Imax</sub>                  |  |        |                            |                            |  |
| Constant                           | 90.26 (61.35–119.18)                         | < .001 |                            |                            |  |
| MVV, L/min                         | 0.40 (0.25-0.56)                             | < .001 | 15                         | 14                         |  |
| Age, y                             | -0.64 (-1.06 to -0.21)                       | .003   | 20                         | 19                         |  |
| P <sub>Emax</sub>                  |  |        |                            |                            |  |
| Constant                           | 122.67 (78–167)                              | < .001 |                            |                            |  |
| MVV, L/min                         | 0.84 (0.41–1.27)                             | < .001 | 17                         | 17                         |  |
| Gender                             | 27.12 (17.31–36.43)                          | < .001 | 26                         | 25                         |  |
| Age, y                             | -1.20 (-1.76 to -0.63)                       | < .001 | 33                         | 32                         |  |
| Body mass index, kg/m <sup>2</sup> | 1.18 (0.41–1.95)                             | .003   | 37                         | 35                         |  |
| FEV <sub>1</sub> , L               | -22.47 (-41.83 to 3.11)                      | .02    | 39                         | 37                         |  |

 $P_{Imax} = maximum \ inspiratory \ pressure; \ P_{Emax} = maximum \ expiratory \ pressure; \ MVV = maximum \ voluntary \ ventilation.$ 

of mortality in COPD and is well associated with the levels of physical activity in daily life in this population. 34,35 Furthermore, the correlations with respiratory muscle strength reinforce MVV as a measure of the respiratory system broader than just the degree of air flow obstruction by FEV<sub>1</sub>. In this way, the associations described in this study support the usefulness of MVV as a possible marker of impairment caused by the disease. Thus, our results reinforce the importance of this test in the comprehensive evaluation of lung function to help assess the impact of physical and functional limitation caused by lung disease.

Dugan and Monroe<sup>32</sup> reported improvement in MVV after a pulmonary rehabilitation program composed of aerobic exercise and upper limb strength exercises, whereas FEV<sub>1</sub> did not improve significantly. Dugan and Monroe<sup>32</sup> also reported that, after pulmonary rehabilitation, there was no improvement in quality of life of subjects with COPD compared to a control group that received usual care, and the authors suggested the hypothesis that pulmonary rehabilitation promotes the improvement of respiratory muscle strength and endurance, leading to a greater sense of comfort for the individuals in the execution of their daily activities with consequent better perception of quality of life.

Table 4. Multiple Linear Regression Analysis for Dyspnea, Functional Status, and Health Status

|                         |            | Nonstandardized Coefficient $\beta$ (95% CI) | P     | r² Partial, % | r <sup>2</sup> Adjusted, % |
|-------------------------|------------|--|-------|---------------|----------------------------|
| mMRC                    | Constant   | 3.54 (3.18–3.90)                             | <.001 |               |                            |
|                         | MVV, L/min | -0.03 (-0.03 to -0.02)                       | <.001 | 28            | 28                         |
| PFSDQ-m Dyspnea         | Constant   | 59.43 (37.05–81.82)                          | <.001 |               |                            |
|                         | MVV, L/min | -0.19 (-0.31 to -0.07)                       | .002  | 27            | 24                         |
|                         | Age, y     | -0.55 (-0.88 to -0.23)                       | .001  | 14            | 12                         |
| PFSDQ-m Fatigue         | Constant   | 44.43 (19.86–69)                             | .001  |               |                            |
|                         | MVV, L/min | -0.15 (-0.28 to -0.03)                       | .02   | 8             | 7                          |
|                         | Age, y     | -0.37 (-0.73 to -0.02)                       | .039  | 14            | 11                         |
| PFSDQ-m Activities      | Constant   | 64.13 (32.02–96.25)                          | <.001 |               |                            |
|                         | MVV, L/min | -0.17 (-0.34 to -0.01)                       | .041  | 15            | 13                         |
|                         | Age, y     | -0.62 (-1.08 to -0.15)                       | .01   | 9             | 8                          |
| PFSDQ-m Total           | Constant   | 168 (94.77–241.24)                           | <.001 |               |                            |
|                         | MVV, L/min | -0.52 (-0.91 to -0.14)                       | .008  | 19            | 17                         |
|                         | Age, y     | -1.55 (-2.62 to -0.48)                       | .005  | 12            | 10                         |
| CAT Cough               | Constant   | 3.17 (2.40–3.93)                             | <.001 |               |                            |
|                         | MVV, L/min | -0.22 (-0.038 to -0.007)                     | .004  | 10            | 10                         |
| CAT Phlegm              | Constant   | 3.80 (2.77–4.85)                             | <.001 |               |                            |
|                         | MVV, L/min | -1.28 (-2.08 to -0.47)                       | .002  | 12            | 11                         |
| CAT Shortness of breath | Constant   | 9.39 (6.52–12.27)                            | <.001 |               |                            |
|                         | MVV, L/min | -0.32 (-0.47 to -0.02)                       | <.001 | 17            | 16                         |
|                         | Age, y     | -0.07 (-0.11 to -0.03)                       | .001  | 28            | 26                         |
| CAT ADL limitation      | Constant   | 8.58 (5.28–11.89)                            | <.001 |               |                            |
|                         | MVV, L/min | -0.04 (-0.06 to -0.02)                       | <.001 | 22            | 21                         |
|                         | Age, y     | -0.07 (-0.11 to -0.02)                       | .005  | 30            | 28                         |
| CAT Confidence          | Constant   | 7.08 (3.94–10.21)                            | .001  |               |                            |
|                         | MVV, L/min | -0.04 (-0.05 to -0.02)                       | <.001 | 19            | 18                         |
|                         | Age, y     | -0.06 (-0.11 to -0.02)                       | .006  | 27            | 25                         |
| CAT Energy              | Constant   | 2.78 (1.91–3.65)                             | <.001 |               |                            |
|                         | MVV, L/min | -0.02 (-0.04 to -0.01)                       | .02   | 8             | 7                          |
| CAT Total               | Constant   | 42.76 (28.15–57.37)                          | <.001 |               |                            |
|                         | MVV, L/min | -0.20 (-0.28 to -0.13)                       | <.001 | 26            | 25                         |
|                         | Age, y     | -0.28 (-0.49 to -0.07)                       | .01   | 33            | 31                         |

mMRC = modified version of the Medical Research Council scale; MVV = maximum voluntary ventilation; PFSDQ-m = Pulmonary Functional Status and Dyspnea Questionnaire, modified version; CAT = COPD Assessment Test; ADL = activities of daily living.

This study supports this hypothesis in that mMRC, PFSDQ-m, and CAT scores correlated better with MVV than with  $FEV_1$ .

The improvement of MVV (and not necessarily FEV<sub>1</sub>) in the study by Dugan and Monroe<sup>32</sup> may reflect a patient's improvement in their daily life after pulmonary rehabilitation, allowing less physical limitation due to dyspnea, greater functional reserve, improved performance on ADL and a better self-reported quality of life. These findings may contribute to the understanding of the disease complexity and promote improvement on the way the disease impacts patients with COPD. However, these assumptions are hypothetical and must be proven in longitudinal studies.

The use of 2 different devices to perform spirometry in this study could be considered a limitation. However, we believe that this does not influence the results because the technique used was the same for both groups, strictly following the test standardization proposed by international guidelines. Furthermore, an adequate effort by all subjects in the MVV maneuver can be ascertained by the very good MVV index in the whole sample (Table 1). Another limitation is the fact that the sample had only one GOLD I subject and, in general, the subjects presented preserved functional exercise capacity and good functional status. This may hinder the generalization of these results for patients with mild disease.

## **Conclusions**

Our results indicate that MVV correlates well with clinical outcomes in COPD, reflecting more widely the ventilatory dysfunction beyond chronic obstruction. In addition, MVV proved to be a better predictor of functional exercise

capacity, inspiratory muscle strength, dyspnea, functional status, and health status than  $FEV_1$  in this population. Therefore, it is recommended that this test must be integrated into clinical practice and research assessments, while the search for further evidence and standardization of the test should be encouraged.

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