ORIGINAL RESEARCH

Measuring Restrictive Lung Disease Severity Using FEV_1 vs TLC

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Background: No clear parameters currently exist to grade severity in restrictive lung disease as for other ventilatory diseases. This article evaluates whether total lung capacity (TLC) or forced expiratory volume in 1 second (FEV_1) better correlates with the symptomatology of patients with restrictive lung disease.

Methods: A retrospective review of 6461 patient records at Veterans Affairs Caribbean Healthcare System in Puerto Rico was conducted, and 414 patients met the inclusion criteria. Pulmonary function test, Modified Medical Research Council Dyspnea Scale, FEV_1, and TLC data were collected for each patient.

Results: We identified a stronger correlation between FEV_1 ($r = 0.25$, $P < .001$) vs TLC ($r = 0.15$, $P < .001$) when related to the degree of dyspnea as measured with the Modified Medical Research Council Dyspnea Scale.

Conclusions: Results of this study suggest that compared with TLC, FEV_1 may provide a more accurate measure of restrictive lung disease severity. Further research should look for more accurate measures of patient dyspnea in restrictive lung disease.

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Respiratory diseases have varied clinical presentations and are classified as restrictive, obstructive, mixed, or normal. Restrictive lung diseases have reduced lung volumes, either due to an alteration in lung parenchyma or a disease of the pleura, chest wall, or neuromuscular apparatus. If caused by parenchymal lung disease, restrictive lung disorders are accompanied by reduced gas transfer, which may be portrayed clinically by desaturation after exercise. Based on anatomical structures, the causes of lung volume reduction may be intrinsic or extrinsic. Intrinsic causes correspond to diseases of the lung parenchyma, such as idiopathic fibrotic diseases, connective-tissue diseases, drug-induced lung diseases, and other primary diseases of the lungs. Extrinsic causes refer to disorders outside the lungs or extra-pulmonary diseases such as neuromuscular and non-muscular diseases of the chest wall.[1] For example, obesity and myasthenia gravis can cause restrictive lung diseases, one through mechanical interference of lung expansion and the other through neuromuscular impedance of thoracic cage expansion. All these diseases eventually result in lung restriction, impaired lung function, and respiratory failure. This heterogenicity of disease makes establishing a single severity criterion difficult.

Laboratory testing, imaging studies, and examinations are important for determining the pulmonary disease and its course and progression. The pulmonary function test (PFT), which consists of multiple procedures that are performed depending on the information needed, has been an essential tool in practice for the pulmonologist. The PFT includes spirometry, lung volume measurement, respiratory muscle strength, diffusion capacity, and a broncho-provocation test. Each test has a particular role in assisting the diagnosis and/or follow-up of the patient. Spirometry is frequently used due to its range of dynamic physiological parameters, ease of use, and accessibility. It is used for the diagnosis of pulmonary symptoms, in the assessment of disability, and preoperatory evaluation, including lung resection surgery, assisting in the diagnosis, monitoring, and therapy response of pulmonary diseases.

A systematic approach to PFT interpretation is recommended by several societies, such as the American Thoracic Society (ATS) and the European Respiratory Society (ERS).[2] The pulmonary function test results must be reproducible and meet established standards to ensure reliable and consistent clinical outcomes. A restrictive respiratory disease is defined by a decrease in total lung capacity (TLC) (< 5% of predicted value) and a normal forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio.[2] Although other findings—such as a

TABLE 1 Patient Demographics and Clinical Characteristics

Criteria	Total (N = 415)	mMRC 0 (n = 65)	mMRC 1 (n = 87)	mMRC 2 (n = 2)	mMRC 3 (n =146)	mMRC 4 (n = 115)	*P* value
Sex, No. (%)							.85
Male	409 (98.6)	65 (100)	86 (98.9)	2 (100)	143 (97.9)	113 (98.3)	
Female	6 (1.4)	0 (0)	1 (1.1)	0 (0)	3 (2.1)	2 (1.7)	
Race and ethnicity, No. (%)							.72
Hispanic	400 (96.4)	61 (93.8)	83 (95.4)	2 (100)	141 (96.6)	113 (98.3)	
Black	9 (2.2)	2 (3.1)	3 (3.4)	0 (0)	3 (2.1)	1 (0.9)	
White	6 (1.4)	2 (3.1)	1 (1.1)	0 (0)	2 (1.4)	1 (0.9)	
Age, mean (SD), y	72.1 (11.3)	73.9 (12.2)	71.8 (10.7)	76.5 (14.8)	71.5 (11.3)	71.9 (11.2)	.12
Height, mean (SD), in	68.0 (3.4)	67.9 (3.1)	68.4 (3.5)	66.0 (0.0)	67.9 (3.3)	67.9 (3.6)	.75
Weight, mean (SD), kg	86.5 (20.1)	83.0 (20.3)	84.3 (16.8)	66.9 (0.3)	86.8 (19.6)	90.0 (22.4)	.32
BMI, mean (SD)	29.0 (6.5)	27.8 (5.9)	28.0 (4.8)	24.5 (0.8)	29.0 (6.2)	30.6 (8.0)	.57
Smoking status, No. (%)							.18
Never	135 (32.5)	24 (36.9)	35 (40.2)	0 (0)	45 (30.8)	31 (27.0)	
Active	11 (2.7)	3 (4.6)	4 (4.6)	0 (0)	2 (1.4)	2 (1.7)	
Past	269 (64.8)	38 (58.5)	48 (55.2)	2 (100)	99 (67.8)	82 (71.3)	
Cigarette packs smoked/y, mean (SD)	22.9 (31.8)	22.3 (33.8)	19.0 (27.3)	35.0 (14.1)	20.8 (26.8)	28.6 (38.8)	.59
Years without smoking, mean (SD)	17.4 (17.6)	18.4 (19.8)	14.8 (15.5)	26.0 (8.5)	17.2 (17.8)	18.7 (17.5)	.20
Imaging studies conducted, No. (%)	286 (69.1)	43 (66.2)	62 (72.9)	2 (100)	89 (61.8)	90 (78.3)	.04
Etiology of restriction, No. (%)							
Interstitial lung disease	169 (41.4)	23 (35.4)	36 (42.4)	0 (0)	61 (42.7)	49 (43.4)	.71
Chest wall disorder	39 (9.6)	5 (7.7)	9 (10.6)	0 (0)	15 (10.5)	10 (8.8)	.94
Neuromuscular disorder	14 (3.4)	1 (1.5)	2 (2.4)	0 (0)	5 (3.5)	6 (5.3)	.67
Pneumonitis	25 (61.)	5 (7.7)	5 (5.9)	1 (50.0)	4 (2.8)	10 (8.8)	.05
Occupational exposure	29 (7.1)	4 (6.2)	8 (9.4)	1 (50.0)	5 (3.5)	11 (9.7)	.05
Environmental exposure	16 (3.9)	3 (4.6)	4 (4.7)	0 (0)	7 (4.9)	2 (1.8)	.58
Unknown	116 (28.4)	24 (36.9)	21 (24.7)	0 (0)	46 (32.2)	25 (22.1)	.15
Hospitalized	168 (40.5)	24 (36.9)	30 (34.5)	2 (100)	54 (37.0)	58 (50.4)	.04
Respiratory exacerbation	73 (17.6)	9 (13.8)	12 (13.8)	0 (0)	21 (14.4)	31 (27.0)	.06

Abbreviations: BMI, body mass index; mMRC, modified Medical Research Council score.

decrease in vital capacity—should prompt an investigation into whether the patient has a possible restrictive respiratory disease, the sole presence of this parameter is not definitive or diagnostic of a restrictive impairment.[2-4] The assessment of severity is typically determined by TLC. Unfortunately, the severity of a restrictive respiratory disease and the degree of patient discomfort do not always correlate when utilizing just TLC. Pulmonary sarcoidosis, for example, is a granulomatous lung disease with a restrictive PFT pattern and a disease burden that may vary over time. Having a more consistent method of grading the severity of the restrictive lung disease may help guide treatment. The modified Medical Research Council (mMRC) scale, a 5-point dyspnea scale, is widely used in assessing the severity of dyspnea in various respiratory conditions, including chronic obstructive pulmonary disease (COPD), where its scores have been associated with patient mortality.[1,5] The goal of this study was to document the associations between objective parameters obtained through PFT and other variables, with an established mea-

TABLE 2 Pulmonary Function Test Results and Clinical Variables

Criteria	Total (N = 415)	mMRC 0 (n = 65)	mMRC 1 (n = 87)	mMRC 2 (n = 2)	mMRC 3 (n = 146)	mMRC 4 (n = 115)	*P* value
TLC, mean (SD), %[a]	70.5 (33.0)	68.8 (7.2)	70.8 (5.8)	75.0 (1.4)	70.1 (7.2)	71.5 (62.1)	.10
FEV_1, mean (SD), %[a]	76.2 (18.9)	81.7 (19.3)	80.9 (18.0)	93.5 (34.6)	76.2 (17.1)	69.2 (19.4)	< .001
Lung restriction severity level, No. (%)							--
Using TLC							
Mild	232 (55.9)	35 (53.8)	57 (65.5)	2 (100)	86 (58.9)	52 (45.2)	
Moderate	128 (30.8)	23 (35.4)	28 (32.2)	0 (0)	44 (30.1)	33 (28.7)	
Moderate severe	44 (10.6)	6 (9.2)	2 (2.3)	0 (0)	15 (10.3)	21 (18.3)	
Severe	11 (2.7)	1 (1.5)	0 (0)	0 (0)	1 (0.7)	9 (7.8)	
Using FEV_1							
Mild	260 (62.7)	46 (70.8)	65 (74.7)	1 (50.0)	101 (69.2)	47 (40.9)	
Moderate	79 (19.0)	12 (18.5)	10 (11.5)	1 (50.0)	23 (15.8)	33 (28.7)	
Moderate severe	43 (10.4)	4 (6.2)	9 (10.3)	0 (0)	14 (9.6)	16 (13.9)	
Severe	33 (8.0)	3 (4.6)	3 (3.4)	0 (0)	8 (5.5)	19 (16.5)	
DLCO, mean (SD), mL/min/mm Hg	51.2 (22.5)	54.9 (24.2)	56.6 (19.1)	56.0 (7.1)	54.1 (20.8)	41.2 (23.1)	< .001
DLCO/VA, mean (SD), %[a]	79.3 (28.0)	82.4 (27.4)	86.0 (23.7)	80.0 (4.2)	83.7 (26.7)	66.9 (29.5)	< .001
FVC, mean (SD), %[a]	71.6 (16.5)	75.4 (17.6)	75.8 (15.4)	93.0 (21.2)	71.9 (14.1)	65.6 (17.6)	< .001
ERV, mean (SD), %[a]	58.8 (32.2)	64.5 (37.6)	62.7 (33.6)	86.5 (55.9)	60.7 (30.3)	49.7 (28.2)	.097
IVC, mean (SD), %[a]	61.5 (15.0)	61.6 (12.2)	64.3 (13.6)	70.5 (12.0)	62.6 (14.5)	57.9 (17.6)	.28
SVC, mean (SD), %[a]	60.3 (12.6)	62.2 (14.0)	63.6 (10.8)	74.0 (4.2)	61.0 (11.3)	55.7 (13.3)	.005
Best FVC, mean (SD), %[a]	71.9 (16.3)	76.0 (17.6)	75.8 (16.7)	93.0 (21.2)	72.5 (13.7)	65.7 (16.6)	< .001
Hemoglobin, mean (SD), %	14.0 (2.5)	14.0 (1.6)	14.2 (1.6)	12.1 (0.2)	13.7 (1.6)	14.3 (4.1)	.02
PaO_2, mean (SD), %	77.7 (15.5)	78.5 (18.1)	82.9 (15.2)	83.0 (4.2)	79.8 (12.0)	71.0 (16.0)	< .001
$PaCO_2$, mean (SD), %	41.1 (7.3)	41.6 (7.5)	40.7 (8.4)	36.5 (9.1)	40.8 (5.9)	41.5 (7.9)	.18
A-a gradient, mean (SD), mm Hg	19.4 (12.8)	15.5 (10.0)	15.1 (10.7)	21.2 (7.1)	18.9 (11.1)	25.4 (15.3)	.002
Heart failure, No. (%)							.11
Systolic heart failure	45 (10.8)	6 (9.2)	5 (5.7)	1 (50.0)	20 (13.7)	13 (11.3)	
Diastolic heart failure	91 (21.9)	10 (15.4)	17 (19.5)	1 (50.0)	35 (24.0)	28 (24.3)	
No history of heart failure	279 (67.2)	49 (75.4)	65 (74.7)	0 (0)	91 (62.3)	74 (64.3)	
LVEF, mean (SD), %	49.9 (14.8)	47.3 (14.9)	52.3 (15.6)	47.5 (9.2)	48.7 (15.8)	51.2 (13.5)	.30

Abbreviations: A-a gradient, alveolar-arterial gradient; DLCO, diffusing capacity of the lung for carbon monoxide; ERV, expiratory reserve volume; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; IVC, inspiratory vital capacity; LVEF, left ventricular ejection fraction; mMRC, modified Medical Research Council score; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; SVC, slow vital capacity; TLC, total lung capacity; VA, alveolar volume.
[a]Predicted percentage based on standardization for age, race, height, and weight.

surement of dyspnea to assess the severity grade of restrictive lung diseases.

METHODS

This retrospective record review at the Veterans Affairs Caribbean Healthcare System (VACHS) in San Juan, Puerto Rico, was conducted using the Veterans Health Information Systems and Technology Architecture to identify patients with a PFT, including spirometry, that indicated a restrictive ventilator pattern based on the current ATS/ERS Task Force on Lung Function Testing.[2] Patients were included if they were aged ≥ 21 years, PFT with TLC ≤ 80% predicted, mMRC score documented on PFT, and documented diffus-

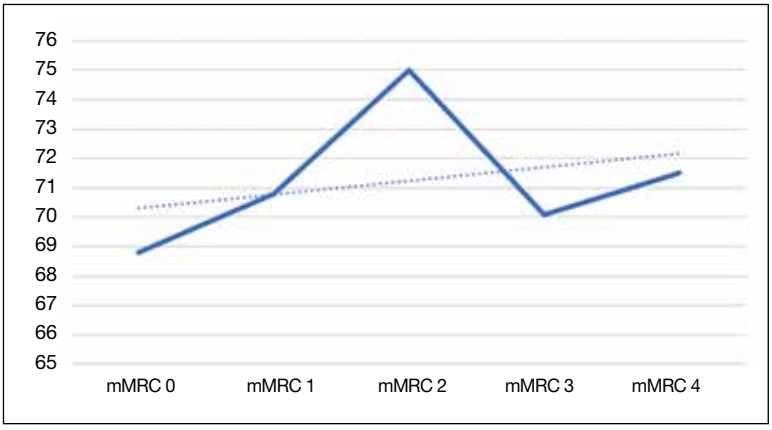
ing capacity of the lung for carbon monoxide (DLCO). Patients were excluded if their FEV_1/vital capacity (VC) was < 70% predicted using the largest VC, or no mMRC score was available. All patients meeting the inclusion criteria were considered regardless of comorbidities.

The PFT results of all adult patients, including those performed between June 1, 2013, and January 6, 2016, were submitted to spirometry, and lung volume measurements were analyzed. Sociodemographic information was collected, including sex, ethnicity, age, height, weight, and basal metabolic index. Other data found in PFTs, such as smoking status, smoking in packs/year, mMRC score, predicted TLC value, imaging present (chest X-ray, computed tomography), and hospitalizations and exacerbations within 1 year were collected. In addition, we examined the predicted values for FEV_1, DLCO, and DLCO/VA (calculated using the Ayer equation), FVC (calculated using the Knudson equation), expiratory reserve volume, inspiratory VC, and slow VC. PaO_2, $PaCO_2$, and Alveolar-arterial gradients also were collected.[6-9] Information about heart failure status was gathered through medical evaluation of notes and cardiac studies. All categorical variables were correlated with Spearman analysis and quantitative variables with average percentages. *P* values were calculated with analysis of variance.

RESULTS

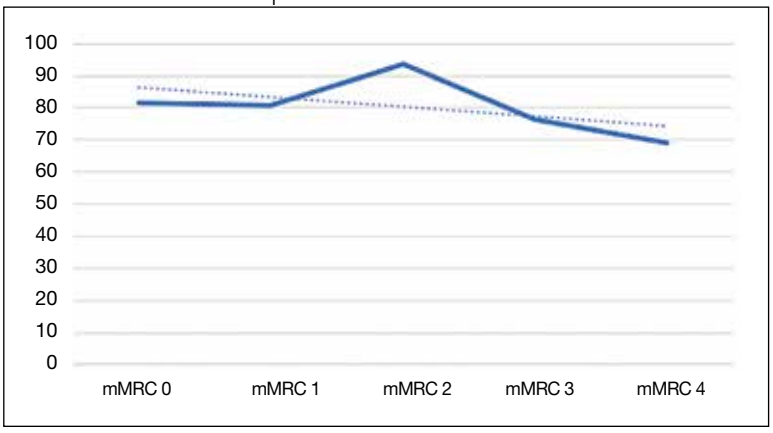
Of 6461 VACHS patient records reviewed, 415 met the inclusion criteria. Patients were divided according to their mMRC score: 65 had mMRC score of 0, 87 had an mMRC score of 1, 2 had an mMRC score of 2, 146 had an mMRC of 3, and 115 had an mMRC score of 4. The population was primarily male (98.6%) and of Hispanic ethnicity (96.4%), with a mean age of 72 years (Table 1). Most patients (n = 269, 64.0%) were prior smokers, while 135 patients (32.5%) had never smoked, and 11 (2.7%) were current smokers. At baseline, 169 patients (41.4%) had interstitial lung disease, 39 (9.6%) had chest wall disorders, 29 (7.1%) had occupational exposure, 25 (6.1%) had pneumonitis, and 14 (3.4%) had neuromuscular disorders.

FIGURE 1 Mean TLC vs mMRC



Abbreviations: mMRC, modified Medical Research Council score; TLC, total lung capacity.

FIGURE 2 Mean FEV_1 vs mMRC



Abbreviations: FEV_1, forced exhale volume in 1 sec; mMRC, modified Medical Research Council score.

There was a statistically significant relationship between mMRC score and hospitalization and FEV_1 but not TLC (Table 2). As mMRC increased, so did hospitalizations: a total of 168 patients (40.5%) were hospitalized; 24 patients (36.9%) had an mMRC score of 0, 30 patients (34.0%) had an mMRC score of 1, 2 patients (100%) had an mMRC score of 2, 54 patients (37.0%) had an mMRC score of 3, and 58 patients (50.0%) had an mMRC score of 4 (P = .04). Mean (SD) TLC values increased as mMRC scores increased. Mean (SD) TLC was 70.5% (33.0) for the entire population; 68.8% (7.2) for patients with an mMRC score of 0, 70.8% (5.8) for patients with an mMRC score of 1, 75.0% (1.4) for patients with an mMRC score of 2, 70.1% (7.2) for patients with an mMRC score of 3, and 71.5% (62.1)

for patients with an mMRC score of 4 (P = .10) (Figure 1). There was an associated decrease in mean (SD) FEV_1 with mMRC. Mean (SD) FEV_1 was 76.2% (18.9) for the entire population; 81.7% (19.3) for patients with an mMRC score of 0, 80.9% (18) for patients with an mMRC score of 1, 93.5% (34.6) for patients with an mMRC score of 2, 76.2% (17.1) for patients with an mMRC score of 3, and 69.2% (19.4) for patients with an mMRC score of 4; (P < .001) (Figure 2).

The correlation between mMRC and FEV_1 (r = 0.25, P < .001) was stronger than the correlation between mMRC and TLC (r = 0.15, P < .001). The correlations for DLCO (P < .001), DLCO/VA (P < .001), hemoglobin (P < .02), and PaO_2 (P < .001) were all statistically significant (P < .005), but with no strong identifiable trend.

DISCUSSION

The patient population of this study was primarily older males of Hispanic ethnicity with a history of smoking. There was no association between body mass index or smoking status with worsening dyspnea as measured with mMRC scores. We observed no significant correlation between mMRC scores and various factors such as comorbidities including heart conditions, and epidemiological factors like the etiology of lung disease, including both intrinsic and extrinsic causes. This lack of association was anticipated, as restrictive lung diseases in our study predominantly arose from intrinsic pulmonary etiologies, such as interstitial lung disease. A difference between more hospitalizations and worsening dyspnea was identified. There was a slightly higher correlation between FEV_1 and mMRC scores when compared with TLC and mMRC scores concerning worsening dyspnea, which could indicate that the use of FEV_1 should be preferred over previous recommendations to use TLC.[10] Other guidelines have utilized exercise capacity via the 6-minute walk test as a marker of severity with spirometry values and found that DLCO was correlated with severity.[11]

The latest ERS/ATS guidelines recommend z scores for grading the severity of obstructive lung diseases but do not recommend them for the diagnosis of restrictive lung diseases.[12] A z score encompasses diverse variables (eg, age, sex, and ethnicity) to provide more uniform and consistent results. Other studies have been done to relate z scores to other spirometry variables with restrictive lung disease. One such study indicates the potential benefit of using FVC alone to grade restrictive lung diseases.[13] There continues to be great diversity in the interpretation of pulmonary function tests, and we believe the information gathered can provide valuable insight for managing patients with restrictive lung diseases.

Limitations

Only 2 patients reported an mMRC score of 2 in our study. This may have affected statistical outcomes. It also may reveal possible deficits in the efficacy of patient education on the mMRC scale. This study was also limited by its small sample size, single center location, and the distribution of patients that reported an mMRC favored either low or high values. The patients in this study, who were all veterans, may not be representative of other patient populations.

CONCLUSIONS

There continue to be few factors associated with the physiological severity of the defective oxygen delivery and reported dyspnea of a patient with restrictive lung disease that allows for an accurate, repeatable grading of severity. Using FEV_1 instead of TLC to determine the severity of a restrictive lung disease should be reconsidered. We could not find any other strong correlation among other factors studied. Further research should be conducted to continue looking for variables that more accurately depict patient dyspnea in restrictive lung disease.

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Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner*, Frontline Medical Communications Inc., the US Government, or any of its agencies.

Ethics and consent

All documentation was approved by the Veterans Affairs Caribbean Healthcare System institutional review board. Appropriate waivers were obtained and there are no findings of incompliance present.

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