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Pathophysiology of reduced forced vital capacity with airflow obstruction on spirometry: performance of two mathematical models in clinical practice

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TO THE EDITOR:

Spirometry has limitations when it comes to airflow obstruction (AO) associated with reduced FVC, a common situation in which the cause of this reduction needs to be clarified. FVC can be reduced due to associated ventilatory restriction, characterizing a mixed pattern (MP), or as a result of air trapping with increased RV, characterizing pure AO (PAO).[1]

In this context, it is recommended that pulmonary volumes (TLC and RV) be measured by available methods.[1-3] The problem with these methods is that they are costly and difficult to access through the public health care system. In order to gauge the cause of the FVC reduction in the presence of AO solely on the basis of spirometry data, several mathematical models have been created,[4-7] with the first ones being that by Pereira et al.[4] in 1991 and that by Lefante et al.[5] in 1996, which are herein referred to as Pereira's model and Lefante's model.

Pereira et al.[4] suggested that, in the presence of AO with a reduced FVC, the difference between percent predicted FVC (FVC%) and percent predicted FEV_1 (FEV_1%), that is, ▲%, should be calculated in the pre-bronchodilator phase (pre-BD). If ▲% is equal to or greater than 25%, the cause of the FVC reduction is hyperinflation, and it is a case of PAO. If ▲% is equal to or smaller than 12%, MP can be inferred. When ▲% is between 12% and 25%, the only option available is TLC measurement.[2,4]

Lefante et al.[5] proposed another solution: in the presence of AO with FEV_1/FVC equal to or less than 0.7, FVC% can be adjusted on the basis of the degree of obstruction (FEV_1/FVC) observed, by using the following formula: adjusted FVC% = observed FVC% + 76 − (105 × FEV_1/FVC). If the adjusted FVC% is equal to or above the lower limit of normal (LLN), it is a case of PAO. If the adjusted FVC% remains below the LLN, it is probably a case of MP.

Our objective was to evaluate the performance of these two mathematical models by measuring their sensibility, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR−) in determining the cause of the FVC reduction in patients with AO, using plethysmographic TLC values as the gold standard.

This was a cross-sectional analytical study of spirometry and plethysmography data. All tests were performed at the Laboratory of Pulmonary Function of the *Núcleo de Pesquisa em Asma e Inflamação das Vias Aéreas* (NUPAIVA, Center for Research on Asthma and Airway Inflammation) at the *Hospital Universitário Polydoro Ernani de São Thiago da Universidade Federal de Santa Catarina* (HU-UFSC, Polydoro Ernani de São Thiago University Hospital of the Federal University of Santa Catarina) with automated testing equipment (Vmax Autobox V62J; SensorMedics, Yorba Linda, CA, USA). The study was approved by the Research Ethics Committee of the HU-UFSC (Protocol no. 4.459.996).

Data collection extended from July of 2018 to May of 2022. The inclusion criteria were as follows: spirometry and plethysmography data from each patient who underwent both tests on the same occasion at NUPAIVA Laboratory of Pulmonary Function; pre-BD FEV_1/FVC ≤ 0.7; and reduced pre-BD FVC (below the LLN).

The selected tests were classified based on Pereira's and Lefante's models, and compared with the gold standard (i.e., plethysmographic TLC values), as either MP (TLC < LLN) or PAO (TLC ≥ LLN), the former being defined as a positive test result and the latter being defined as a negative test result.

Statistical descriptive analysis was performed for the variables sex, height, and weight of the patients, as well as for their pre-BD FEV_1%, pre-BD FVC%, pre-BD FEV_1/FVC, TLC%, ▲% and adjusted FVC% (Table 1).

Continuous data were analyzed by the Shapiro-Wilk test and were expressed as mean ± SD or median ± IQR. Differences between groups were assessed using the t test for independent samples or the Wilcoxon test, depending on data distribution. The R software, version 4.1.0 (The R Project for Statistical Computing, Vienna, Austria), was used.

The outcomes ▲% and adjusted FVC% were evaluated for accuracy, sensibility, specificity, PPV, NPV, LR+ and LR− in diagnosing MP, using plethysmographic TLC values as the gold standard (Table 1).

Of 277 tests, 76 met the inclusion criteria. Of those 76 tests, 68 were classified as PAO and 8 were classified as MP.

Lefante's model was more accurate in differentiating cases of PAO from cases of MP, reaching an accuracy of

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Table 1. Main characteristics of the participants as classified by spirometry and plethysmography and performance of Lefante's model vs. Pereira's model.[a,b]

	PAO	MP	p
Tests	68	8	
Male sex	37	6	
Female sex	31	2	
Age*	63.4 ± 13.9	58.1 ± 11.9	0.211
Height	160.2 ± 8.1	165.6 ± 12.7	0.100
Weight	69.3 ± 16.7	71.7 ± 17.3	0.696
Pre-BD FEV_1%	38.4 ± 12.2	48 ± 9.8	0.036
Pre-BD FVC%*	62.3 ± 10.5	63.4 ± 6.9	0.963
Pre-BD FEV_1/FVC†	0.5 ± 0.2	0.6 ± 0.1	0.012
TLC%*	116.9 ± 32.2	74 ± 9	0.000
▲%*	23.9 ± 10.3	15.4 ± 7	0.024
Adjusted FVC%†	89.5 ± 24.2	71.6 ± 11.1	0.041
Model	Lefante's	Pereira's[c]	
Performance parameters			
Sensitivity	63%	38%	
Specificity	72%	44%	
PPV	21%	23%	
NPV	94%	97%	
LR+	2.24	2.55	
LR−	0.52	0.28	
Accuracy	71%	43%	

PAO: pure airway obstruction; MP: mixed pattern; BD: bronchodilator; FEV_1%: percent predicted FEV_1; FVC%: percent predicted FVC; TLC%: percent predicted TLC; ▲%: pre-BD FVC% − pre-BD FEV_1%; adjusted FVC%: observed FVC% + 76 − (105 × FEV_1/FVC); PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, and LR−: negative likelihood ratio. [a]Values expressed as n or mean ± SD except where otherwise indicated. [b]Reference equations: Pereira et al.[8] for spirometry; Lessa et al.[9] for plethysmography. The LLN was defined as the 5th percentile of the predicted value. [c]Considering cases classified as undefined (25% > ▲% > 12%) by the model. *Variables showing parametric distribution after Box-Cox transformation. †Variables with non parametric distribution are expressed as median ± IQR.

71%, which contrasts with the accuracy of Pereira's model of only 43%. Pereira's model failed to classify 42.1% of the cases, considering 32 tests to be undefined. This high number of undefined cases is consistent with findings of the original study by Pereira et al.,[4] in which 50% of the tests were classified as undefined (30/60 cases), which has been an inherent limitation of Pereira's model since its proposal.

In our study, Pereira's model showed a PPV of only 23% in detecting MP, which contrasts with the 85% reported in the original study,[4] as well as a NPV of 97%, which is closer to the 95% reported in that study.[4] A possible explanation for the discrepancy in PPV may be the difference in the prevalence of MP between the two samples. In the study by Pereira et al.,[4] 30 patients with MP and 30 with PAO were artificially selected, that is, a MP prevalence of 50%, while in our consecutive sample we obtained a prevalence of 10.5%.

In 2019, Sadigursky et al.[10] also revisited Pereira's model, assessing its accuracy against plethysmographic measurement of lung volumes, and found that Pereira's model had a low PPV in detecting MP, which is consistent with our findings.

Considering that Pereira's model reliably classifies the cause of the FVC reduction only in patients with ▲% ≥ 25%, 45 (59.2%) of the patients in our sample (i.e., those with ▲% < 25%) would be referred for plethysmography accordingly. In contrast, if we consider that only cases classified as suspected MP by Lefante's model would have to undergo plethysmography, only 24 (31.6%) of the patients in our sample would need to undergo this test. Classifying all cases, including those classified as undefined by Pereira's model, Lefante's model maintained a high NPV of 94%, demonstrating the model's power to detect cases of PAO accurately. From these results, it is possible to envision the potential advantage of Lefante's model in terms of defining a greater number of cases regarding the pathophysiological diagnosis, saving costs and time.

This study has some limitations. First, it is a single-center study. Second, it was performed during the restrictions imposed by the COVID-19 pandemic. This limited the sample size.

We infer that Lefante's model has its greatest value in cases of negative test results, in which it has a high degree of accuracy in diagnosing PAO, identifying patients who would not require plethysmography and showing a significant gain in accuracy when compared with Pereira's model.

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AUTHOR CONTRIBUTIONS

BMSW and JTMJ: conception and planning of the study; interpretation of evidence; drafting and revision of the preliminary and final versions of the manuscript; and approval of the final version of the manuscript. AMS: planning of the study. RMS: conception and planning of the study.

CONFLICTS OF INTEREST

None declared.

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