



Scientific Letter

[Translated article] FEV1/FVC Cut-off Values for the Diagnosis of Airflow Obstruction in Pediatric Patients: The Pediatric Airflow Obstruction (PAO) Study



Valores de corte de FEV1/FVC para el diagnóstico de obstrucción al flujo aéreo en población pediátrica: estudio PAO (Pediatric Airflow Obstruction)

To the Director

Forced spirometry is a basic test in the study of lung function.¹ Different patterns are identified from the forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio and the FVC value.²

Although numerous equations have been proposed for the calculation of predicted values,³ many scientific societies currently use the equations developed by the Global Lung Function Initiative 2012 (GLI-2012) that have been validated in many countries.^{4,5} In Spain, these equations have been validated in preschool children.⁶ Among the results they provide are the lower limits of normal (LLN) of different parameters, any value below the LLN (z-score -1.64) being considered abnormal.⁴

An FEV1/FVC ratio $<LLN$ is defined as obstruction.² However, guidelines for the management of chronic obstructive pulmonary disease (COPD)⁷ or asthma^{8,9} continue to recommend the use of the fixed ratio as a discriminatory criterion, and this approach is widely used in routine clinical practice.

In children, there is currently no consensus on the value that defines the presence of obstruction, and the recommended lower values range between 85% and 90%.^{8,9}

We performed a cross-sectional observational study to assess the validity of different FEV1/FVC ratios for the diagnosis of obstruction in the pediatric population. Spirometries performed in pediatric patients (6–18 years) in our hospital between June and December 2016 were analyzed.

Forced spirometry was performed by experienced operators following ATS/ERS guidelines¹⁰ using the MEDGRAPHICS ULTIMA PF[®] lung function equipment from MGC DIAGNOSTICS. Predicted values were calculated using the GLI-2012 equations⁴ and spirometries that met validity and reproducibility criteria were included.¹

The gold standard for obstruction was defined as a FEV1/FVC ratio z-score of less than -1.64 (GLI-2012).

The statistical analysis was performed using Stata[®] version 15 software from StataCorp LLC. A descriptive analysis was performed

using frequency measures (%) and central tendency and dispersion measures (mean and standard deviation), according to the type of variable. A diagnostic analysis was performed between the different cut-off points of the FEV1/FVC ratio (between $<90\%$ and $<75\%$) versus the gold standard of a FEV1/FVC z-score of less than -1.64 . The study was approved by the reference ethics committee.

We included 324 Caucasian patients: 198 males (61.1%), mean age 10.0 ± 2.9 years, height 141.5 ± 16.0 cm, and weight 40.6 ± 15.6 kg. Mean FEV1, FVC, and FEV1/FVC \pm standard deviation were 1.98 ± 0.70 L, 2.28 ± 0.82 L, and $87.2 \pm 7.0\%$, and the FEV1, FVC, and FEV1/FVC z-scores were -0.63 ± 1.07 , -0.60 ± 1.04 , and -0.50 ± 1.16 , respectively.

The prevalence of obstruction in our series according to LLN was 8.0%. Table 1 shows prevalence, classification errors, sensitivity, specificity, negative predictive value, positive predictive value, and area under the curve of the cut-off points analyzed from the FEV1/FVC ratio in the whole series and in 2 different age ranges. These results were similar when analyzed by sex (data not shown).

The prevalence of obstruction in our study was comparable with other studies in the pediatric population.^{11,12}

Currently, there are 2 different approaches to the interpretation of spirometries. On the one hand, some authors advocate the use of the fixed ratio for its simplicity and applicability.^{7–9} This is based on studies that showed worse survival in patients with an FEV1/FVC ratio $<70\%$ and $>LLN$ compared with patients with FEV1/FVC $>70\%$.¹³ In contrast, other authors support the use of LLN and the z-score, based on studies showing that morbidity or all-cause mortality is not higher in patients with suspected COPD unless the FEV1/FVC ratio is $<LLN$.¹⁴

Our study shows that using cut-off points with high sensitivity and low specificity values (90% and 85%) overestimates the prevalence of obstruction, and can lead to overtreatment and higher costs. Thus, compared with the gold standard, the cut-off point of 90% recommended by GINA⁸ would overestimate obstruction in our patients by 57.4%, whereas the 85% recommended by GEMA⁹ would overestimate obstruction by 26.2%.

To our knowledge, no other studies have evaluated the validity of the fixed ratio using the GLI-2012 LLN as a gold standard. Our study, conducted in a Caucasian population, shows that a fixed value of 80% for the FEV1/FVC ratio has greater validity than higher cut-off points; however, this value still leads to an overdiagnosis of up to 3.7%. Lower cut-off points (78% and 79%) in our series showed lower rates of overdiagnosis, with no increase in the rate of underdiagnosis; comparable results were reported by Stanojevic et al. using an LLN of 78%.¹⁵

Our study has some limitations. Primarily, patients' symptoms and exacerbations were not analyzed, and it is not known whether

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Table 1

Prevalence and errors in classification with different cut-off points in 2 age ranges. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and ROC curve (area under the curve) of each parameter at the global level.

	<LLN		<90%		<85%		<80%		<79%		<78%	
Age, years	>6–≤11	>11–≤18	>6–≤11	>11–≤18	>6–≤11	>11–≤18	>6–≤11	>11–≤18	>6–≤11	>11–≤18	>6–≤11	>11–≤18
Obstruction, n	15	11	139	73	67	45	23	15	18	14	12	14
Prevalence ^a	7.1%	9.6%	66.2%	64.0%	31.9%	39.5%	11.0%	13.2%	8.6%	12.2%	5.7%	12.2%
Overdiagnosis, n (%)			124 (59.0%)	62 (54.4%)	52 (24.8%)	34 (29.8%)	8 (3.8%)	4 (3.5%)	3 (1.4%)	3 (2.6%)	0	3 (2.6%)
Underdiagnosis, n (%)			0	0	0	0	0	0	0	0	3 (1.4%)	0
Sensitivity			100%		100%		100%		100%			88.5%
Specificity			37.6%		71.1%		96.0%		98.0%			99.0%
PPV			12.3%		23.2%		68.4%		81.3%			88.5%
NPV			100%		100%		100%		100%			99.0%
ROC area			0.688		0.856		0.980		0.990			0.937

^a Calculated from total patients by age range: 210 patients in the range >6–≤11 and 114 patients in the age range >11–≤18.

the lower ratio was observed in the most symptomatic patients. However, Bacharier et al.¹⁶ showed that asthma severity correlated with the FEV1/FVC ratio, which decreased progressively as severity increased. Another weakness of our study is that obstruction was overestimated by 1.9% when the fixed value of 79% was used. However, this is clearly lower than the overestimation produced by the criteria recommended by GINA or GEMA,^{8,9} for which the rate of overdiagnosis was between 26.2 and 57.4%.

The study also has its strengths: it is the first to evaluate the validity of the fixed ratio using the GLI-2012 LLN as a gold standard. Our findings are important because the software of many spirometry devices used in both primary and specialized care does not include the GLI-2012 equations, and most clinicians do not have the time to use these equations to calculate predicted values in clinical practice. In its favor, the fixed criterion is simple, applicable, and supported by authors who advocate its use for its high degree of sensitivity, specificity, positive and negative predictive value, and the fact that it has an area under the curve close to 1 of the gold standard that is supported by those who prefer to use the LLN criterion.

In conclusion, we believe that the discriminative criterion for defining the presence of obstruction should be the LLN, rather than a fixed criterion. If a fixed limit must be used, our study shows that the best sensitivity and specificity values are obtained with an FEV1/FVC value of less than 79%. This improves diagnostic accuracy compared to the criteria previously used and is easily applied in routine clinical practice.

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