# Journal Pre-proof


FEV1Q as a Predictive Metric for Asthma Outcomes

Betancor D Olaguibel JM del Pozo V Alvarez Puebla MJ Arismendi E Barroso B Bobolea I Cárdaba B Cañas JA Domínguez-Ortega J Cruz MJ Curto E Garcia de la Fuente A González-Barcala FJ Luna-Porta JA Martínez-Rivera C Mullol J Muñoz X Picado C Plaza V Quirce S Rial MJ Soto-Retes L Valverde-Monge M Mahíllo-Fernández I Sastre J

PII: S0300-2896(25)00072-9

DOI: https://doi.org/doi:10.1016/j.arbres.2025.02.011

Reference: ARBRES 3750

To appear in: *Archivos de Bronconeumologia*

Received Date: 28 January 2025

Accepted Date: 20 February 2025

Please cite this article as: Betancor D, Olaguibel J, del Pozo V, Alvarez Puebla M, Arismendi E, Barroso B, Bobolea I, Cárdaba B, Cañas J, Domínguez-Ortega J, Cruz M, Curto E, Garcia de la Fuente A, González-Barcala F, Luna-Porta J, Martínez-Rivera C, Mullol J, Muñoz X, Picado C, Plaza V, Quirce S, Rial M, Soto-Retes L, Valverde-Monge M, Mahíllo-Fernández I, Sastre J, FEV1Q as a Predictive Metric for Asthma Outcomes, *Archivos de Bronconeumología* (2025), doi: https://doi.org/10.1016/j.arbres.2025.02.011

**Type or article: scientific letter**

**Title: FEV1Q as a Predictive Metric for Asthma Outcomes**
**Short Title: FEV1Q in Asthma**

Authors: Betancor D[1], Olaguibel JM [2,3], del Pozo V[3,4], Alvarez Puebla MJ [2,3], Arismendi E[3,5], Barroso B[1,3], Bobolea I [3,5], Cárdaba B [3,4], Cañas JA[3,4], Domínguez-Ortega J [3,6,] Cruz MJ [3,7], Curto E [8], Garcia de la Fuente A [3,5], González-Barcala FJ [9], Luna-Porta JA [3,6], Martínez-Rivera C [3,10], Mullol J [3,11], Muñoz X [3,7,12], Picado C [5] , Plaza V [8] , Quirce S [3,6], Rial MJ [3,13], Soto-Retes L [8] , Valverde-Monge M [1,3], Mahíllo-Fernández I [14] , Sastre J [1,3]

1 Servicio de Alergología, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

2 Servicio de Alergología, Hospital Universitario de Navarra, Pamplona, Spain

3 CIBER de Enfermedades Respiratorias (CIBERES), Madrid, Spain

4 Instituto de Investigación Sanitaria Fundación Jiménez Díaz (IIS-FJD, UAM), 28040 Madrid, España.

5 Pulmonology and Allergy Department, Hospital Clínic Universitat de Barcelona, Spain

6 Servicio de Alergia, Hospital Universitario La Paz, Madrid, Spain

7 Servicio de Neumología, Hospital Vall d'Hebron, Barcelona, Spain

8 Servicio de Neumología y Alergia, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

9 Department of Respiratory Medicine, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain.

10 Servicio de Neumología, Hospital Germans Trias i Pujol, Badalona, Spain

11 Rhinology Unit & Smell Clinic, ENT Department, Hospital Clínic Barcelona, FRCB-IDIBAPS, Universitat de Barcelona, Barcelona, Spain

12 Departamento de Biología Celular, Fisiología e Inmunología, Universitat Autónoma de Barcelona, Barcelona, Spain

13 Servicio de Alergología, Complexo Hospitalario Universitario A Coruña, A Coruña, Spain

14 Unidad de Bioestadística y Epidemiología, Instituto de Investigación Sanitaria Fundación Jimenez Diaz, Madrid, Spain

Corresponding Author:
Diana Betancor
Allergy Department, Hospital Universitario Fundación Jiménez Díaz, Avda. Reyes Católicos, 2, 28040 Madrid, Spain
E-mail: diana13_b@hotmail.com

**Text:**

The Forced Expiratory Volume in 1 Second Quotient (FEV1Q) offers a novel and straightforward spirometric approach to predict lung function decline and all-cause mortality in both healthy and diseased populations[1-5.] FEV1Q is calculated by dividing FEV1 by sex-specific baseline thresholds: 0.4 L for women and 0.5 L for men. FEV1Q decreases by one unit every 18 years, with an accelerated decline observed in smokers and elderly individuals[1-4]. However, thresholds for clinically significant changes in FEV1Q remain undefined. Lower FEV1Q values have been linked to increased mortality risk[1] and have shown predictive power for hospitalization and functional status in chronic obstructive pulmonary disease (COPD) and healthy individuals[6-8]. Nevertheless, its relationship with asthma-specific outcomes has not been explored.

This study primarily investigates correlations between FEV1Q and demographic, clinical, and inflammatory characteristics in asthma patients. Secondary objectives include assessing the predictive value and diagnostic accuracy of FEV1Q for asthma severity, control, and exacerbations, as well as comparing FEV1Q to FEV1% predicted (FEV1%) and FEV1 z-scores.

The MEGA cohort is a multicenter, real-life cohort of asthma patients with varying severity levels. A retrospective review identified 445 patients with complete lung function data. Asthma was diagnosed following GINA guidelines as our previous MEGA studies[9,10]. Patient demographics, asthma severity (per GINA guidelines), control (Asthma Control Test [ACT]), exacerbation frequency, lung function, and biomarker levels were analyzed. Lung function was categorized into quartiles for three metrics: FEV1Q, FEV1%, and FEV1 z-scores. Receiver-operating characteristic (ROC) curves were used to evaluate the predictive capability of these metrics for asthma severity and control. Adjustments were made for age, sex, body mass index (BMI), and smoking status. Diagnostic accuracy was assessed through spirometric evidence of airway obstruction (defined by FEV1/FVC ratio $\leq$ 70% and FEV1/FVC z-score $\leq$ -1.64), bronchial hyperresponsiveness (assessed by a methacholine challenge with a PC20 < 4 mg/dL), poor asthma control (an ACT score $\leq$ 19), and exacerbation history in the predicting year.

Quantitative variables were summarized using means and standard deviations, while qualitative variables were reported as absolute and relative frequencies. Correlations were analyzed using Pearson's or Spearman's methods. The area under the curve (AUC) with a 95% confidence interval (CI) was calculated, and thresholds were determined to maximize the Youden index. Sensitivity and specificity values for the thresholds were also calculated. Odds ratios were derived using logistic regression models, adjusted for confounders (severe asthma, last year exacerbation or severe exacerbation, Emergency-room (ER) visit, hospital admission and control). Statistical analyses were performed with GraphPad Instat 6 and R software. The significance level was set at 0.05.

The mean patient age was 48.5 years, with 66.2% being female. Lung function patterns indicated normal function in 56.8%, obstruction in 23.6%, and air trapping in 19.5% that corresponded to a mean (standard deviation) FEV1Q value of 6.63 (1.5), 4.52 (1.58) and 5.86 (2.13), respectively. Severe asthma was diagnosed in 37.7%, moderate in 33.1%,

mild in 17.7%, and intermittent in 4.9%. Demographic and clinical characteristics from our patients were previously published[9,10].

Results showed significant but weak correlations between FEV1Q and all measured demographic and clinical characteristics (r values between -0.35 and 0.35), except for a moderate correlation with age ($r = -0.53$, $p < 0.001$). No significant correlations were found between FEV1Q and inflammatory biomarkers (Table 1). Lower FEV1Q values, represented by the first quartile, were significantly associated with increased risks of severe asthma, exacerbations, emergency room visits, hospital admissions, and poor asthma control. Multivariate logistic regression confirmed that these significant associations were independent of age, sex, BMI, and smoking status (Table 2).. Moreover, the odds ratios for the first quartile of FEV1Q were higher to those for the same quartile of FEV1% and the FEV1 z-score across all outcomes. This finding indicates that lower FEV1Q values were associated with a greater risk of all previously mentioned outcomes than lower values of FEV1% and FEV1 z-score

The diagnostic accuracy of FEV1Q for asthma control and exacerbations was modest, with AUC values of 0.67 and 0.69, respectively. Optimal thresholds yielded sensitivities of 60% and 59%, and specificities of 70% and 100%, for asthma control and exacerbations, respectively with FEV1Q cut-off values of <5.23 for asthma control and <5.60 for exacerbations. The AUC values for bronchial hyperresponsiveness (0.63, 95% CI: 0.53–0.72) and airway obstruction (FEV1/FVC ratio: 0.49, 95% CI: 0.44–0.54; FEV1/FVC z-score: 0.60, 95% CI: 0.55–0.65) were also assessed with similar results. See Table 1S and figure 1 Supplement.

This study supports that FEV1Q is a predictor of asthma severity, exacerbations, hospital admissions, and poor control even more than FEV1% and FEV1 z-score, in line with COPD studies[6-8] and healthy-aged subjects[11] , independently of patient's demographic characteristics. This finding can be explained by the fact that FEV1Q standardizes lung function using the relevant sex-specific lower limit, providing a measure of the remaining FEV1 capacity for the subject, in contrast to other assessments as FEV1% and FEV1 z-score that focus on the lung function that the individual may have already lost based on the deviation of an individual's measurements from a predicted and determined value (2). Nevertheless, while FEV1Q outperforms FEV1% and FEV1 z-score for most outcomes

in this study, its AUC (0.67-0.69) is modest and the undefined cut-offs limit its diagnostic accuracy.

Up to now, FEV1Q predictive involvement has been evaluated in different diseases[3,5] but not in asthma. In the Hegendörfer et al. study[8], just 14% of the population had respiratory diseases such as asthma or COPD. However, since both diseases were evaluated together, the ability to generalize the findings to each disease individually was limited. Huang et al.[7] evaluated FEV1Q´s role in COPD. They demonstrated that this parameter predicted severe COPD exacerbations, whereas in our study, FEV1Q was a significant predictor of exacerbations but not specifically of the severe ones ($p>0.05$). Differences in the clinical characteristics and lung function measurements between asthma and COPD can account for the discrepancies. These findings emphasize the value of assessing the influence of this parameter in each disease and for each outcome.

As described in some studies in asthma with FEV1 predicted[9], a correlation between inflammatory biomarkers and lung function tests, such as FEV1Q, is not always found.

We analyzed patient´s data retrospectively which could be one study limitation. Furthermore, as a methacholine challenge was an inclusion criterion for MEGA, not all patients from the MEGA cohort have data compiled about lung function which is required for our study and therefore, our study population is lower than the total MEGA cohort which can be another study limitation. However, with our criteria selection, we ensured the correct evaluation of the selected parameters even though the results could not represent all the studied patients.

In conclusion, this is the first study to evaluate FEV1Q's role in predicting asthma-specific outcomes. Despite its limitations, FEV1Q outperformed traditional lung function metrics in predicting asthma severity, exacerbations, and hospitalizations. Future research is needed to establish clear thresholds and validate these findings across diverse populations.

Funding of the Research: This study was supported in part by an unrestricted research grant from Sanofi.

Authors' contributions

DB and JS contributed equally to the conception and design of the study, as well as the collection of data and writing of the manuscript. All other investigators contributed to data collection, analysis, and interpretation. All authors critically reviewed and approved the final manuscript

Conflicts of Interest: Dra. Betancor D was supported by a Rio Hortega Research Contract from Instituto Carlos III, Ministry of Science. Dra. Valverde has received lecture fees from GSK and is part of the advisory board for Organon. Dr. Rial reports personal fees from GSK, Allergy Therapeutics, and AstraZeneca, outside the submitted work. Dr. González-Barcala reports personal fees from ALK, AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Gebro Pharma, GlaxoSmithKline, Laboratorios Esteve, Menarini, Mundipharma, Novartis, Rovi, Roxall, Stallergenes-Greer, and Teva, and grants from Mundipharma, outside the submitted work. Dr. Quirce reports personal fees from AstraZeneca, Novartis, Sanofi, Boehringer Ingelheim, Teva, ALK, Mundipharma, GSK, Chiesi, and Leti, outside the submitted work. Dr. Soto-Retes reports non-financial support from CIBER de Enfermedades Respiratorias (CIBERES) during the conduct of the study and personal fees from Stallergenes-Greer, Menarini, Novartis, GSK, Hal Allergy, Allergy Therapeutics, and AstraZeneca, as well as grants from Sociedad Española de Alergología e Inmunología Clínica (SEAIC) and Sociedad Española de Neumología y Cirugía Torácica (SEPAR), outside the submitted work. Dr. Martínez-Rivera reports grants and personal fees from AstraZeneca, Teva, GSK, Novartis, and Mundipharma, outside the submitted work. Dr. Muñoz reports personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Teva, Mundifarma, Chiesi, and Faes, outside the submitted work. Dr. Sastre reports grants and personal fees from Sanofi, GSK, Novartis, AstraZeneca, Mundipharma, and Faes Farma, outside the submitted work. Dr. Olaguibel reports grants from Sanofi and/or personal fees from AstraZeneca and Mundipharma, outside the submitted work. Dr. Plaza reports grants and personal fees from AstraZeneca, Boehringer Ingelheim, Merck, Chiesi, Novartis, Menarini, and Sanofi,

outside the submitted work. Dr. Mullol reports personal fees and others from Sanofi-Genzyme & Regeneron, Novartis, Viatris (Mylan Pharma), Uriach Group, Mitsubishi-Tanabe, Menarini, UCB, AstraZeneca, GSK, and MSD, outside the submitted work. Dra. Del Pozo reports personal fees and others from Sanofi, AstraZeneca, and GSK, outside the submitted work. Other authors have no conflicts of interest.

Artificial Intelligence Involvement: Artificial intelligence (ChatGPT 4.0) was used for English correction of the manuscript's final version.

Table 1: The correlation between FEV1q and demographic and clinical characteristics, laboratory parameters and respiratory function in asthmatic patients.

| Measurement | R | 95% IC | P |
|---|---|---|---|
| **Demographic characteristics** | | | |
| Age | - 0.53 | 0.59 to -0.46 | <0.001 |
| Body mass index | - 0.21 | 0.29 to -0.12 | <0.001 |
| **Clinical characteristics** | | | |
| Asthma control test (ACT) | 0.32 | 0.25 to 0.41 | <0.005 |
| Last year exacerbation | - 0.16 | -0.28 to -0.04 | 0.01 |
| ER visit las year | - 0.23 | - 0.31 to -0.15 | <0.001 |
| Hospital admission last year | - 0.19 | - 0.27 to -0.10 | <0.001 |
| **Lung function test** | | | |
| PC20 methacholine challenge | 0.24 | 0.09 to 0.36 | <0.001 |
| TLC | 0.24 | 0.12 to 0.36 | <0.001 |
| RV | - 0.25 | - 0.37 to -0.13 | <0.001 |
| DLCO | 0.13 | - 0.01 to 0.26 | 0.04 |
| **Inflammatory biomarkers** | | | |
| FeNO | -0.03 | - 0.14 to 0.07 | NS |

| | | | |
|---|---|---|---|
| PBE | -0.05 | 0.16 a 0.047 | NS |
| Sputum eosinophilia | -0.11 | - 0.27 to 0.04 | NS |
| Sputum neutrophilia | -0.14 | 0.29 to 0.01 | NS |

**Table 2:** Crude and adjusted odds ratios: risk factors of severe (following GINA guidelines), and poorly controlled asthma (ACT score ≤ 19), exacerbations rate and severity, emergency room (ER) visits and hospital admission due to asthma according to FEV1Q value, FEV1% predicted and FEV1 z-score. Logistic regression models were used and adjustment was made for age, sex, body mass index, a smoking status.

| Variable | Quartiles | OR | (95% CI) | P | OR | (95% CI) | P |
|---|---|---|---|---|---|---|---|
| | | | UNADJUSTED | | | ADJUSTED | |
| | | | **FEV1Q** | | | | |
| **Severe asthma [1]** | 1 (≤4.5) | 12.7 | (6.91, 24.1) | <0.01 | 13.0 | (6.28, 28.1) | <0.01 |
| | 2 (>4.5 to ≤5.7) | 6.11 | (3.45, 11.2) | <0.01 | 6.57 | (3.53, 12.6) | <0.01 |
| | 3 (>5.7 to ≤7.1) | 2.43 | (1.33, 4.56) | <0.01 | 2.34 | (1.25, 4.46) | <0.01 |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| **Last year exacerbation** | 1 (≤4.5) | 4.94 | (2.89, 8.60) | <0.01 | 4.42 | (2.29, 8.68) | <0.01 |
| | 2 (>4.5 to ≤5.7) | 1.87 | (1.13, 3.11) | 0.01 | 1.83 | (1.06, 3.20) | 0.03 |
| | 3 (>5.7 to ≤7.1) | 1.79 | (1.07, 3.01) | 0.02 | 1.68 | (0.99, 2.89) | NS |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| **Last year severe exacerbation** | 1 (≤4.5) | 1.54 | (0.69, 3.62) | NS | 2.96 | (1.09, 8.45) | 0.04 |
| | 2 (>4.5 to ≤5.7) | 1.31 | (0.56, 3.20) | NS | 1.87 | (0.74, 4.97) | NS |
| | 3 (>5.7 to ≤7.1) | 1.23 | (0.51, 3.06) | NS | 1.48 | (0.59, 3.82) | NS |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| **ER visit** | 1 (≤4.5) | 4.23 | (2.38, 7.72) | <0.01 | 3.57 | (1.76, 7.39) | <0.01 |
| | 2 (>4.5 to ≤5.7) | 2.00 | (1.12, 3.66) | 0.02 | 1.79 | (0.95, 3.42) | NS |
| | 3 (>5.7 to ≤7.1) | 1.81 | (0.99, 3.37) | NS | 1.56 | (0.83, 2.96) | NS |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| **Hospital admission** | 1 (≤4.5) | 28.1 | (5.73, 509) | <0.01 | 26.2 | (4.59, 499) | <0.01 |
| | 2 (>4.5 to ≤5.7) | 13.8 | (2.68, 252) | 0.01 | 13.2 | (2.43, 246) | 0.01 |
| | 3 (>5.7 to ≤7.1) | 12.8 | (2.44, 236) | 0.01 | 11.5 | (2.11, 214) | 0.02 |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| **Uncontrolled asthma [2]** | 1 (≤4.5) | 4.68 | (2.67, 8.38) | <0.01 | 4.71 | (2.34, 9.7) | <0.01 |
| | 2 (>4.5 to ≤5.7) | 2.33 | (1.33, 4.12) | <0.01 | 2.41 | (1.32, 4.50) | <0.01 |
| | 3 (>5.7 to ≤7.1) | 0.98 | (0.53, 1.83) | NS | 0.93 | (0.49, 1.76) | NS |
| | 4 (>7.1) | 1.00 | | | 1.00 | | |
| | | | **FEV1%** | | | | |
| **Severe asthma [1]** | 1 (≤71) | 12.0 | (6.70, 22.3) | <0.01 | 11.5 | (6.23, 22.0) | <0.01 |
| | 2 (>71 to ≤85) | 4.29 | (2.44, 7.74) | <0.01 | 4.43 | (2.47, 8.15) | <0.01 |
| | 3 (>85 to ≤99) | 1.88 | (1.04, 3.45) | 0.04 | 1.78 | (0.97, 3.32) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| | 1 (≤71) | 3.82 | (2.28, 6.47) | <0.01 | 3.41 | (1.99, 5.94) | <0.01 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Last year exacerbation** | 2 (>71 to ≤85) | 1.74 | (1.04, 2.91) | 0.03 | 1.70 | (1.01, 2.90) | 0.04 |
| | 3 (>85 to ≤99) | 1.58 | (0.95, 2.63) | NS | 1.56 | (0.93, 2.64) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| **Last year severe exacerbation** | 1 (≤71) | 2.00 | (0.91, 4.64) | NS | 2.53 | (1.10, 6.19) | 0.03 |
| | 2 (>71 to ≤85) | 1.35 | (0.57, 3.33) | NS | 1.52 | (0.62, 3.83) | NS |
| | 3 (>85 to ≤99) | 1.00 | (0.40, 2.53) | NS | 1.06 | (0.42, 2.74) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| **ER visit** | 1 (≤71) | 3.63 | (2.09, 6.43) | <0.01 | 3.12 | (1.75, 5.67) | <0.01 |
| | 2 (>71 to ≤85) | 1.55 | (0.86, 2.81) | NS | 1.45 | (0.79, 2.67) | NS |
| | 3 (>85 to ≤99) | 1.40 | (0.77, 2.57) | NS | 1.26 | (0.68, 2.34) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| **Hospital admission** | 1 (≤71) | 4.78 | (2.00, 13.3) | 0.01 | 3.61 | (1.45, 10.3) | 0.01 |
| | 2 (>71 to ≤85) | 1.63 | (0.57, 5.01) | NS | 1.43 | (0.49, 4.44) | NS |
| | 3 (>85 to ≤99) | 1.25 | (0.40, 3.98) | NS | 1.00 | (0.30, 3.29) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| **Uncontrolled asthma [2]** | 1 (≤71) | 3.61 | (2.09, 6.36) | <0.01 | 3.50 | (1.96, 6.39) | <0.01 |
| | 2 (>71 to ≤85) | 2.32 | (1.33, 4.12) | 0.01 | 2.32 | (1.30, 4.19) | 0.01 |
| | 3 (>85 to ≤99) | 1.14 | (0.63, 2.10) | NS | 1.10 | (0.59, 2.04) | NS |
| | 4 (>99) | 1.00 | | | 1.00 | | |
| **FEV1 z-score** | | | | | | | |
| **Severe asthma [1]** | 1 (≤ -2.32) | 7.23 | (3.89, 13.8) | <0.01 | 7.43 | (3.93, 14.5) | <0.01 |
| | 2 (>-2.32 to ≤1.11) | 3.19 | (1.84, 5.63) | <0.01 | 3.14 | (1.78, 5.64) | <0.01 |
| | 3 (>-1.11 to ≤0.25) | 1.32 | (0.71, 2.47) | NS | 1.32 | (0.70, 2.49) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |
| **Last year exacerbation** | 1 (≤ -2.32) | 3.41 | (1.92, 6.19) | <0.01 | 3.21 | (1.78, 5.90) | <0.01 |
| | 2 (>-2.32 to ≤1.11) | 1.71 | (1.02, 2.90) | 0.04 | 1.55 | (0.91, 2.64) | NS |
| | 3 (>-1.11 to ≤0.25) | 1.68 | (0.97, 2.94) | NS | 1.64 | (0.94, 2.89) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |
| **Last year severe exacerbation** | 1 (≤ -2.32) | 2.01 | (0.87, 4.74) | NS | 2.40 | (1.02, 5.87) | 0.04 |
| | 2 (>-2.32 to ≤1.11) | 1.28 | (0.56, 3.03) | NS | 1.52 | (0.64, 3.74) | NS |
| | 3 (>-1.11 to ≤0.25) | 0.78 | (0.31, 1.99) | NS | 0.76 | (0.29, 1.95) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |
| **ER visit** | 1 (≤ -2.32) | 3.07 | (1.70, 5.63) | <0.01 | 2.82 | (1.54, 5.24) | 0.01 |
| | 2 (>-2.32 to ≤1.11) | 1.11 | (0.62, 1.99) | NS | 0.95 | (0.52, 1.73) | NS |
| | 3 (>-1.11 to ≤0.25) | 0.99 | (0.52, 1.85) | NS | 0.95 | (0.50, 1.80) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |
| **Hospital admission** | 1 (≤ -2.32) | 4.58 | (1.81, 13.2) | 0.01 | 3.89 | (1.50, 11.4) | 0.01 |
| | 2 (>-2.32 to ≤1.11) | 2.21 | (0.84, 6.48) | NS | 1.68 | (0.61, 5.05) | NS |
| | 3 (>-1.11 to ≤0.25) | 1.26 | (0.38, 4.17) | NS | 1.22 | (0.37, 4.08) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |
| **Uncontrolled asthma [2]** | 1 (≤ -2.32) | 3.23 | (1.76, 6.03) | <0.01 | 3.30 | (1.76, 6.32) | <0.01 |
| | 2 (>-2.32 to ≤1.11) | 2.16 | (1.23, 3.86) | 0.01 | 2.20 | (1.23, 4.02) | 0.01 |
| | 3 (>-1.11 to ≤0.25) | 1.01 | (0.52, 1.94) | NS | 0.96 | (0.49, 1.86) | NS |
| | 4 (> -0.25) | 1.00 | | | 1.00 | | |

1 Measured following GINA guidelines; 2 Uncontrolled asthma was considered when ACT ≤ 19

Footnote:

Number of patients in each quartil: for FEV1Q Q1 (FEV1Q ≤ 4.5) n=104, Q2 (FEV1Q >4.5 and ≤5.7) n=117, Q3 (FEV1Q >5.7 and ≤7.1) n=106 and Q4 (FEV1Q > 7.1) n=118; for FEV1% Q1 (FEV1% ≤71) n=110, Q2 (FEV1% >71 to ≤85) n=107, Q3 (FEV1% >85 to ≤99) n=110 and Q4 (FEV1%>99) n= 118 and for FEV1 zscore Q1 (FEV1 zscore ≤ -2.32) n=91, Q2 (FEV1 zscore >-2.32 to ≤1.11) n= 131, Q3 (FEV1 zscore >-1.11 to ≤0.25) n=110, Q4 (FEV1 zscore > -0.25) n=113.

**References:**

[1] .- Stanojevic S, Kaminsky DA, Miller MR, Thompson B, Aliverti A, Barjaktarevic I, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. Eur Respir J. 2022;13;60(1):2101499.

[2] .- Miller MR, Pedersen OF. New concepts for expressing forced expiratory volume in 1 s arising from survival analysis. Eur Respir J. 2010;35(4):873-882.

[3] .- da Silva Alves C, Barroso T, Gerardo A, Almeida T, Maduro S, Boléo-Tomé JP, et al. Forced Expiratory Volume in One Second Quotient (FEV1Q) as a Prognostic Factor in Amyotrophic Lateral Sclerosis Patients: Comparing Its Predictive Value to Other Lung Function Measurements. Cureus. 2024;14;16(2):e54176.

[4] .- Luoto J, Pihlsgård M, Wollmer P, Elmståhl S et al. Relative and absolute lung function change in a general population aged 60-102 years. Eur Respir J. 2019;14;53(3):1701812.

[5] .- Costanzo S, Magnacca S, Bonaccio M, Di Castelnuovo A, Piraino A, Cerletti C, et al. Reduced pulmonary function, low-grade inflammation and increased risk of total and

cardiovascular mortality in a general adult population: Prospective results from the Molisani study. Respir Med. 2021;184:106441.

[6] .- Bhatta L, Leivseth L, Mai XM, Henriksen AH, Carslake D, Chen Y, et al. Spirometric Classifications of Chronic Obstructive Pulmonary Disease Severity as Predictive Markers for Clinical Outcomes: The HUNT Study. Am J Respir Crit Care Med. 2021;15;203(8):1033-1037.

[7] Huang TH, Hsiue TR, Lin SH, Liao XM, Su PL, Chen CZ. Comparison of different staging methods for COPD in predicting outcomes. Eur Respir J. 2018;15;51(3):1700577.

[8] .- Hegendörfer E, Vaes B, Andreeva E, Matheï C, Van Pottelbergh G, Degryse JM. Predictive Value of Different Expressions of Forced Expiratory Volume in 1 Second (FEV1) for Adverse Outcomes in a Cohort of Adults Aged 80 and Older. J Am Med Dir Assoc. 2017;18:123–130.

[9] .- Betancor D, Olaguibel JM, Rodrigo-Muñoz JM, Alvarez Puebla MJ, Arismendi E, Barranco P et al. Lung Function Abnormalities and Their Correlation With Clinical Characteristics and Inflammatory Markers in Adult Asthma. J Investig Allergol Clin Immunol. 2023;27;33(4):294-296.

[10] .- Rial MJ, Álvarez-Puebla MJ, Arismendi E, Caballero ML, Cañas JA, Cruz MJ, et al. Clinical and inflammatory characteristics of patients with asthma in the Spanish MEGA project cohort. Clin Transl Allergy. 2021;11(1):e12001.

[11] .- Balasubramanian A, Wise RA, Stanojevic S, Miller MR, McCormack MC. $FEV_1Q$: a race-neutral approach to assessing lung function. Eur Respir J. 2024;4;63(4):2301622.