ORIGINAL ARTICLE

Dynamic Hyperinflation in Patients With Moderate-Severe Asthma: Relationship With Clinical Control and Small Airway Dysfunction

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Abstract

Background: Dynamic hyperinflation (DH), characterized by an abnormal increase in operative lung volumes during exercise, is associated with breathlessness and exercise intolerance. This study aimed to evaluate the relationship between DH and control of symptoms in patients with moderate-severe asthma.

Methods: A cross-sectional, multicenter, observational study was conducted in patients with moderate-severe asthma. DH was defined as a decrease in inspiratory capacity after a 6-minute walk test (6MWT), and asthma control was measured using the Asthma Control Test (ACT) and Spanish Guidelines for the Management of Asthma (GEMA). Secondary variables included sensitization to aeroallergens (prick test), quality of life (miniAQLQ), anxiety or depression, dyspnea (mMRC), fatigue (Borg scale), and small airway dysfunction (oscillometry).

Results: Among the 154 patients analyzed, 97 (63%) had DH. ACT scores did not differ significantly between patients with and without DH (20.8 [4.4] vs 21.7 [3.6]; *P*=.411). However, the percentage of patients with partially and poorly controlled asthma according to GEMA was significantly higher in the DH group than in those without DH (40.2% vs 24.6%; *P*=.048). Compared with patients without DH, patients with DH had higher dyspnea scores (0.9 [0.9] vs 0.5 [0.6]; *P*=.009), greater fatigue before the 6MWT (1.3 [1.9] vs 0.5 [1.1]; *P*=.004), higher respiratory reactance (0.7 [1.2] vs 0.4 [1.2] $cmH_2O/L/s$; *P*=.032), higher depression scores (4.2 [3.7] vs 2.1 [2.1], *P*=.002), and lower sensitization to aeroallergens (45.4% vs 68.4%; *P*=.014).

Conclusion: Although no relationship was found between DH and uncontrolled asthma via the ACT, the proportion of patients with uncontrolled asthma according to GEMA was significantly higher in the DH group.

Key words: Asthma control. Dynamic hyperinflation. Oscillometry. Dyspnea. Prevalence.

Resumen

Antecedentes: La hiperinflación dinámica (HD), caracterizada por un aumento anormal en los volúmenes pulmonares operativos durante el ejercicio, se asocia con disnea e intolerancia al ejercicio. Este estudio tuvo como objetivo evaluar la relación entre la HD y el control clínico en pacientes con asma moderada-severa.

Métodos: Se llevó a cabo un estudio observacional, transversal y multicéntrico en pacientes con asma moderada-severa. El objetivo principal fue determinar la relación entre la HD, definida como una reducción en la capacidad inspiratoria tras una prueba de caminata de 6 minutos (6MWT), y el control del asma, medido mediante el cuestionario de control del asma (ACT) y la Guía Española para el Manejo del Asma (GEMA). Las variables secundarias incluyeron sensibilización a aeroalérgenos (prueba de intradermorreacción), calidad de vida (MiniAQLQ), ansiedad o depresión, disnea (mMRC), fatiga (escala de Borg) y disfunción de las vías aéreas pequeñas (oscilometría).

Resultados: De los 154 pacientes analizados, 97 (63%) presentaron HD. No se observaron diferencias significativas en las puntuaciones de ACT entre los pacientes con y sin HD (20,8 ± 4,4 vs. 21,7 ± 3,6; p = 0,411). Sin embargo, la proporción de pacientes con asma parcialmente controlada o no controlada según GEMA fue significativamente mayor en el grupo con HD en comparación con aquellos sin HD (40,2% vs. 24,6%; p = 0,048). Los pacientes con HD presentaron puntuaciones más altas de disnea (0,9 ± 0,9 vs. 0,5 ± 0,6; p = 0,009), mayor fatiga antes del 6MWT (1,3 ± 1,9 vs. 0,5 ± 1,1; p = 0,004), mayor reactancia respiratoria (0,7 ± 1,2 vs. 0,4 ± 1,2 $cmH_2O/L/s$; p = 0,032), puntuaciones más elevadas de depresión (4,2 ± 3,7 vs. 2,1 ± 2,1; p = 0,002) y menor sensibilización a aeroalérgenos (45,4% vs. 68,4%; p = 0,014) en comparación con aquellos sin HD.

Conclusión: Aunque no se encontró una relación significativa entre la HD y el asma no controlada según las puntuaciones de ACT, la proporción de pacientes con asma no controlada según GEMA fue significativamente mayor en el grupo con HD.

Palabras clave: Control del asma. Hiperinflación dinámica. Oscilometría. Disnea. Prevalencia.

Summary box

- **What do we know about this topic?**
  Dynamic hyperinflation (DH) is highly prevalent among patients with moderate-severe asthma and is closely related to symptom control and small airway function.
- **How does this study impact our current understanding and/or clinical management of this topic?**
  This study emphasizes the significance of DH in the clinical management of moderate-severe asthma, illustrating its impact on symptom control, dyspnea, depression, physical activity, and small airway function. It further suggests that oscillometry parameters may provide a more effective means of assessing DH in these patients.

Introduction

Asthma is a common disease characterized by airway inflammation, bronchial hyperresponsiveness, and airflow limitation that affects the daily activities and quality of life of affected patients, particularly those with severe forms [1]. Prevalence ranges from 1% to 18% depending on the country, with more than 339 million people experiencing this condition worldwide [2]. Inhaled corticosteroids are the primary treatment for most patients, effectively reducing inflammation and improving lung function [1,3]. However, a subset of patients with uncontrolled asthma experience frequent exacerbations and a rapid decline in lung function despite optimal management. One of the complications of asthma is hyperinflation, which is characterized by air trapping due to expiratory flow limitation. Hyperinflation can be triggered both at rest and during exercise, leading to a decrease in inspiratory capacity [4].

Dynamic hyperinflation (DH) is characterized by an abnormal increase in operative lung volumes during exercise [5]. The limited evidence available to date suggests that the prevalence of DH in patients with moderate-severe asthma is high, with approximately 80% exhibiting this condition [6]. Factors such as elevated airway resistance due to increased airway smooth muscle contraction, edema, and hypersecretion, together with airway-parenchymal uncoupling, lead to premature airway closure and DH in affected patients. Those with the severe form usually develop DH during exercise to the same extent as patients with chronic obstructive pulmonary disease (COPD) [7,8]. DH has been reported in patients with asthma after provocation with methacholine or the exercise challenge test, probably reflecting induced bronchoconstriction [9,10].

Pulmonary hyperinflation, particularly alterations in lung volumes, has been proposed as a better predictor of respiratory failure and exertional dyspnea than changes in expiratory flow. It is also associated with limited functional and exercise capacity, thereby impacting patients' quality of life [6,11]. Studies have shown that obese patients with asthma experience higher DH during bronchoconstriction and that weight loss can improve this condition by reducing abdominal fat [10,12,13]. Additionally, it has been observed that distal airway function correlates better with clinical symptoms and asthma control [14]. The literature indicates that DH could be

related to a worsening of symptom control in patients with moderate-severe asthma, in addition to having a negative impact on the quality of life and physical activity of affected patients [6,11]. Therefore, the objective of the present study was to evaluate the relationship between DH and symptom control in patients with moderate-severe asthma using the Asthma Control Test (ACT) questionnaire. The secondary objective was to evaluate the relationship between DH and respiratory symptoms, quality of life, anxiety and depression, small airway dysfunction, and daily physical activity.

Methods

Study Design

The present work was a cross-sectional, multicenter, nationwide, observational study performed by pulmonologists and including patients with moderate-severe asthma. The inclusion criteria were as follows: age between 18 and 70 years (both included); diagnosis of moderate-severe asthma according to the criteria of the Spanish Guidelines for the Management of Asthma (GEMA) or the Global Initiative for Asthma (GINA) guidelines; ability to perform all the necessary study procedures, including acceptable and reproducible spirometry, oscillometry, and the 6-minute walk test (6MWT); and informed consent to participate in the study. The exclusion criteria were as follows: being a smoker or former smoker with a cumulative smoking index of ≥10 pack-years; body mass index of ≥30 km/m^2; pregnancy; an asthma exacerbation within the 4 weeks prior to inclusion in the study; contraindications to the 6MWT; significant respiratory diseases other than asthma, such as COPD, bronchiectasis, diffuse interstitial lung disease, and tuberculosis; hyperventilation syndrome, defined as a score ≥23 on the Nijmegen questionnaire; diagnosis of anemia (hemoglobin, ≤11 g/dL); acute myocardial infarction and/or unstable angina 1 month prior to inclusion in the study; congestive heart failure; and any mental or other disability that prevents the patient from understanding and following the study procedures.

Study Variables and Data Collection

The main objective of the study was to compare the degree of asthma control between asthma patients with and without DH. The level of asthma control was assessed through the ACT, which has been validated for patients older than 12 years and consists of 5 questions with 5 possible answers scored from 1 (minimum score) to 5 (maximum score) [15,16]. An ACT score ≥20 is indicative of well-controlled asthma, whereas a score between 19 and 16 suggests partially controlled asthma, and a score ≤15 is indicative of poorly controlled asthma. The degree of asthma control was also classified according to the GEMA guidelines [3], which assess the frequency of symptoms, the need for rescue medication, lung function, and history of exacerbations (Supplementary Table 1).

The 6MWT was performed twice in a 30-m corridor in accordance with American Thoracic Society (ATS) guidelines [17]. Before and immediately after the second walk, patients were instructed on the performance of an inspiratory capacity maneuver using a calibrated pneumotachograph. From at least 3 acceptable trials, the better of 2 reproducible maneuvers (within 5% or 60 mL) was recorded for analysis. DH was defined as a reduction in inspiratory capacity after the 6MWT with respect to the prewalk value.

Secondary variables included the following: sociodemographic and anthropometric data; comorbidities related to asthma; history of asthma, including date of diagnosis, severity, degree of control, seasonality, and current maintenance treatment; history of sensitization to aeroallergens; quality of life measured using the Asthma Quality of Life Questionnaire (miniAQLQ) of Juniper et al [18,19]; score in the Hospital Anxiety and Depression Questionnaire (HADS) [20,21]; score in the YALE Physical Activity Survey (YPAS) [22,23]; the degree of dyspnea measured according to the modified Medical Research Council (mMRC) scale [24]; treatment adherence measured through the Test of Adherence to Inhalers (TAI) [25]; and the degree of fatigue measured by the modified Borg scale [26]. A brief description of each scale is provided in the Supplementary Material.

Lung function was assessed using exhaled nitric oxide according to ATS/European Respiratory Society (ERS) recommendations [27]. Oscillometry measurements were performed using a multifrequency signal (5, 11, and 19 Hz) provided by a device compliant with ERS technical standards (Resmon Pro FULL V3, Restech) [28]. Patients underwent a single oscillometry measurement in a seated position wearing a nose clip with cheeks supported to decrease upper airway shunt compliance. After excluding the first 3 breaths, at least 10 artifact-free breaths automatically selected by the oscillometry device were analyzed, ensuring a recording time >30 seconds for breathing frequencies up to 20 breaths/min and the inclusion of only complete breathing cycles. The following oscillometry parameters were recorded: respiratory system resistance (Rrs) and respiratory system reactance (Xrs) at 5 Hz (R5, X5), as well as their within-breath inspiratory components (R5insp, X5insp) and expiratory components (R5exp, X5exp). The equations of Oostveen et al [29] were used as reference values. Spirometry was performed after oscillometry according to the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) guidelines [30]. Finally, static lung volumes were measured by plethysmography, according to ATS/ERS recommendations [31].

Statistical Analysis

Qualitative variables were represented as absolute and relative frequency distributions; quantitative variables were expressed as mean (SD) or mean (IQR) according to their distribution. In comparisons between 2 groups of patients with continuous variables, parametric tests (*t*/Welch *t*) or a nonparametric test (Mann-Whitney) were used, depending on the characteristics of the study variables (normality and homoscedasticity). The relationship between continuous variables was evaluated using the Pearson or Spearman linear correlation coefficients, depending on the normality of the variables. The χ^2 test or Fisher exact test was used, as appropriate, in the analysis of the contingency tables. Statistical significance was established at $P \leq .05$. All statistical analyses were performed using SAS (version 9.4).

Table 1. Baseline Sociodemographic and Clinical Characteristics of the Sample.

Sex, No. (%)	
Male	41 (26.6)
Female	113 (73.4)
Median (IQR) age, y	49.5 (40.0-57.0)
Median body mass index, kg/m^2	25.3 (22.6-27.6)
Smoking history, No. (%)	
Current smoker	0 (0.0)
Former smoker	42 (27.3)
Never smoker	112 (72.7)
Median (IQR) pack-years[a]	3.2 (1.3-6.5)
Comorbidities, No. (%)	
Nasosinusal polyposis	55 (35.7)
Gastroesophageal reflux	32 (20.8)
Intolerance to NSAIDs	21 (13.6)
Chronic airflow limitation	12 (7.8)
Obstructive sleep apnea	2 (1.3)
Median (IQR) asthma duration[b], y	12.7 (6.0-23.1)
Asthma severity, No. (%)	
Persistent moderate	72 (46.8)
Persistent severe	82 (53.2)
Asthma control according to GEMA, No. (%)	
Well controlled	101 (65.6)
Partially and poorly controlled	53 (34.4)
Exacerbations within the prior 12 months, No. (%)	25 (16.2)
Median (IQR) number of exacerbation episodes per patient[c]	1.0 (1.0-2.0)
Type of exacerbation[d], No. (%)	
Severe	27 (84.4)
Moderate	5 (15.6)
Median duration of the exacerbation episode[d], days	5.0 (5.0-9.0)
Level of health care, No. (%)[d]	
Primary health care	18 (60.0)
Hospital health care	12 (40.0)
Hospital admissions, No. (%)[d]	7 (21.9)

Abbreviations: GEMA, Spanish Guidelines for the Management of Asthma; NSAID, nonsteroidal anti-inflammatory drug.
[a]Data from 42 patients categorized as former smokers.
[b]Time from diagnosis until inclusion in the study.
[c]Based on 25 patients with at least one exacerbation within the prior 12 months.
[d]Based on 32 exacerbations reported by 25 patients.

Ethics Approval and Consent to Participate

All participants provided their written informed consent to participate. The study was approved by the Ethics Committee of Getafe Hospital, Getafe (Madrid), Spain. The study was conducted in accordance with the Declaration of Helsinki.

Results

Data were gathered from 154 patients, whose baseline sociodemographic and clinical characteristics are shown in Table 1.

Primary Objective

DH was found in 97 patients (63% [95%CI, 54.9%-70.6%]). The median change in inspiratory capacity in this subgroup was –190 (–350 to –90) mL, while the remaining patients exhibited a median increase in inspiratory capacity of 150 (80-320) mL. No statistically significant differences were observed in the ACT scores between patients with and without DH (22.0 [18.0-24.0] vs 23.0 [20.0-24.0]; *P*=.411) (Figure 1A). Furthermore, no significant correlation was identified between the mean change in inspiratory capacity during the 6MWT and ACT scores (r=–0.083, *P*=.307). Within the DH group, the percentage of patients with controlled asthma was marginally lower than that of those without DH (70.1% vs 78.9%), although this difference was not statistically significant (Figure 1B).

Dynamic Hyperinflation and Clinical Characteristics of Asthma

In the DH group, the percentage of patients with partially and poorly controlled asthma, according to the asthma control level defined by GEMA, was higher than that of those without DH (40.2% vs 24.6%; *P*=.048), reaching statistical significance (Table 2).

No statistically significant differences were found between DH and asthma duration or severity at inclusion in the study. However, compared with patients without DH, those who exhibited DH had lower symptom seasonality (15.5% vs 28.9%; *P*=.034), as well as reduced cutaneous sensitivity to aeroallergens (45.4% vs 68.4%; *P*=.014) (Table 2). Moreover, no statistically significant differences were observed between DH and adherence (Table 2).

In terms of symptoms, dyspnea (mMRC ≥1) was more prevalent among patients with DH than among those who did not have DH (58.5% vs 42.1%; *P*=.024; Figure 2A). Furthermore, DH patients had more severe dyspnea, as evidenced by a higher dyspnea score (0.9 [0.9] vs 0.5 [0.6]; *P*=.009). Additionally, patients with DH had higher fatigue levels, as assessed by the modified Borg scale prior to the 6MWT (median, 0.0 [0.0-2.0] for DH patients vs median 0.0 [0.0-0.0] for non-DH patients; *P*=.004). However, no significant differences were observed in the miniAQLQ scores between DH and non-DH patients (median, 5.4 [4.5-6.6] vs 5.7 [4.9-6.5]; *P*=.422) (Table 2). Similarly, no significant differences were detected in the various dimensions of the miniAQLQ questionnaire (Figure 2B).

Table 2. Comparison of Anthropometric and Clinical Characteristics of Asthma Patients With and Without Dynamic Hyperinflation.[a]

	DH patients (n=97)	Non-DH patients (n=57)	*P* Value
Males, No. (%)	28 (28.9)	13 (22.8)	.411
Median (IQR) age, y	52.0 (42.0-59.0)	48.0 (39.0-55.0)	.058
Median (IQR) body mass index, kg/m^2	25.6 (22.6-28.0)	25.2 (22.5-26.6)	
Smoking history, No. (%)			.340
Current smoker	0 (0.0)	0 (0.0)	
Former smoker	29 (29.9)	13 (22.8)	
Never smoker	68 (70.1)	44 (77.2)	
Median (IQR) pack-years	5.0 (2.0-7.5)	1.8 (0.7-4.0)	.050
Mean (SD) comorbidities			
Nasosinusal polyposis	36 (37.1)	19 (33.3)	.636
Gastroesophageal reflux	22 (22.7)	10 (17.5)	.448
NSAIDs	13 (13.4)	8 (14.0)	.912
Chronic airflow limitation	10 (10.3)	2 (3.5)	.212
Median (IQR) asthma duration, y	12.1 (6.1-21.2)	12.9 (5.1-25.0)	.639
Asthma severity, No. (%)			.222
Moderate persistent	49 (50.5)	23 (40.4)	
Severe persistent	48 (49.5)	34 (59.6)	
Asthma control degree according to GEMA, No. (%)			.048
Well controlled	58 (59.8)	43 (75.4)	
Partially or poorly controlled	39 (40.2)	14 (24.6)	
Exacerbations in the last 12 mo, No. (%)	15 (15.5)	10 (17.5)	0.735
Hospital admissions in the last 12 mo, No. (%)	4 (4.2)	3 (5.3)	.710
Asthma symptoms seasonality, No. (%)	15 (15.5)	17 (28.9)	.034
Cutaneous sensitivity to aeroallergens, No. (%)	44 (45.4)	39 (68.4)	.014
Treatment adherence, median (IQR)			
TAI 10 score[b]	50.0 (47.0-50.0)	50.0 (47.0-50.0)	.704
Level of adherence[c]			.772
Good adherence	50 (51.5)	32 (56.1)	
Intermediate adherence	29 (29.9)	14 (24.6)	
Poor adherence	18 (18.6)	11 (19.3)	
Health-related quality of life, median (IQR) miniAQLQ score	5.4 (4.5-6.6)	5.7 (4.9-6.5)	.422
Anxiety and depression components, median (IQR)			
Anxiety HAD score	5.0 (3.0-7.0)	5.0 (3.0-7.5)	.913
Depression HAD score	4.0 (1.0-6.5)	2.0 (1.0-3.0)	.002
Daily physical activity, median (IQR)			
Energy expenditure	13839.0 (8101.8-19855.3)	13211.1 (8784.9-22896.6)	.572
Domestics tasks	4275.0 (2370.0-6440.0)	4020.0 (2240.0-7765.5)	.893
Outdoor tasks	0.0 (0.0-0.0)	0.0 (0.0-0.0)	.444
Other person care tasks	0.0 (0.0-1292.5)	0.0 (0.0-500.0)	.183
Free time tasks	2584.2 (1204.5-4137.3)	3369.6 (2249.6-4930.0)	.019
Sedentarism, No. (%)	54 (56.3)	28 (50.0)	.456

Abbreviations: DH, dynamic hyperinflation; GEMA, Spanish Guidelines for the Management of Asthma; HAD, Hospital Anxiety and Depression Scale; miniAQLQ, mini Asthma Quality of Life Questionnaire; NSAIDs, nonsteroidal anti-inflammatory drugs; TAI, Test of Adherence to Inhalers.
[a]Data are shown as mean (SD), median (IQR), or No. (%) according to their type and distribution. Comparisons between groups are by *t*, Mann-Whitney, or χ^2 test.
[b]TAI 10 score: mean (SD) of DH patients, 47.4 (5.0); mean (SD) of non-DH patients, 47.9 (3.5)
[c]Level of adherence: good adherence (TAI 10 score = 50), intermediate adherence (46 ≤ TAI 10 score ≤ 49), poor adherence (TAI 10 score ≤ 45)

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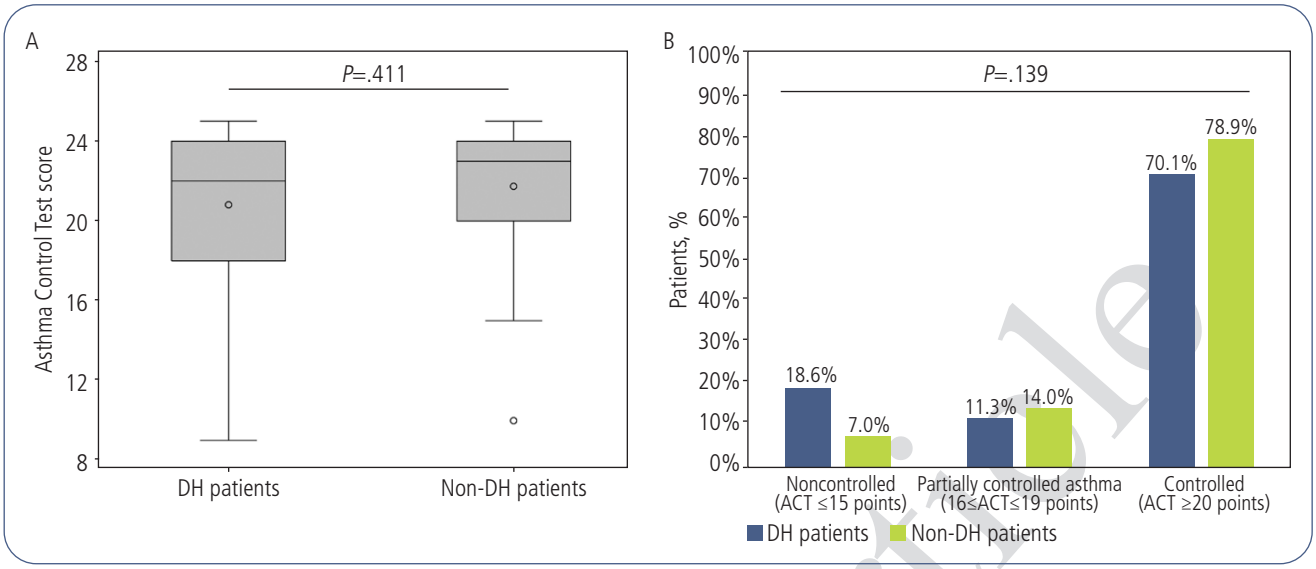

Figure 1. Control of asthma symptoms (ACT) based on dynamic hyperinflation (DH). A, Comparison of the ACT score between DH and non-DH patients (Mann-Whitney). B, Comparison of levels of symptomatic control between DH and non-DH patients (χ^2).

No differences were found for frequency of anxiety between patients with and without DH (77.1% vs 75.0%; *P*=.086) or for the reported level of anxiety (Table 2). In contrast, depression was more frequent in patients with DH than in those without DH (19.2% vs 1.8%; *P*=.007), with higher levels of depression indicated by the HAD score (4.0 [1.0-6.5] vs 2.0 [1.0-3.0]; *P*=.002) (Figure 2C and 2D).

Finally, no differences were detected in the frequency of sedentary behaviour or in the total activity time or summary physical activity index. However, individuals with DH spent less time engaging in leisure activities and devoted less energy to free-time tasks (Supplementary Figure 1 and Table 2).

Dynamic Hyperinflation and Lung Function

As shown in Table 3, no differences were identified between the presence or absence of DH in dynamic or static lung volumes, exercise tolerance assessed by the 6MWT, or exhaled nitric oxide fraction. However, with respect to the small airway, patients with DH had higher respiratory system reactance than patients without DH (median, 0.4 [–0.1 to 1.0] vs 0.1 [–0.2 to 0.5] $cmH_2O/L/s$; *P*=.032) (Table 3). In turn, the magnitude of dynamic hyperinflation (assessed as the change in inspiratory capacity) was related to expiratory 5 Hz resistance (R5, $cmH_2O/L/s$) (r=0.165, *P*=.041) and inspiratory 5 Hz reactance (Xr, predicted %) (r=–0.166; *P*=.041; Figure 3). No statistically significant relationship was found between DH and the remaining variables in oscillometry (Supplementary Figure 1).

Discussion

According to our results, the percentage of patients presenting DH (63%) was lower than those previously reported in the literature. In a study by van der Meer et al [6] including 77 nonsmoking patients with moderate-severe asthma, 80.5% (95%CI, 71.7%-89.4%) had DH. In the case of patients with mild asthma, the prevalence has been estimated at 11.1% (95%CI, 4.3%-18.0%) among those without exercise-induced bronchoconstriction, increasing to 75.6% (95%CI, 62.8%-88.8%) in individuals with this additional condition [32]. Regarding the relationship between DH and asthma control, represented as the ACT score, we found no statistically significant differences between DH and non-DH in patients with moderate-severe asthma. However, a higher proportion of patients with partially and poorly controlled asthma was observed in the DH group when the degree of asthma control was evaluated according to the GEMA guidelines. This difference was statistically significant. Similar discrepancies between the Asthma Control Questionnaire (ACQ) scores and the GINA guidelines classification have been reported [33]. Although the ACT is a validated questionnaire, the study by Olaguibel et al [33] clearly illustrates that the established cut-off points of asthma control questionnaires may not be adequate for daily clinical practice. Therefore, ACT cut-off points should be adjusted to the study population to ensure better discrimination of the level of control according to the GEMA guidelines [33,34].

In the study by van der Meer et al [6], when the results were analyzed linearly, the scores in all the questionnaires were significantly related to the metronome-paced tachypnea–based measurement of DH, since higher levels of DH correlated with poorer scores on questionnaires such as the ACQ, Clinical COPD Questionnaire, and the St. George Respiratory Questionnaire. However, in our case, it must be noted that these patients were from very specialized units in which they are closely followed up, with less than 20% reporting poor adherence to inhaled treatment. In addition, data were gathered during the COVID-19 pandemic, when patients were

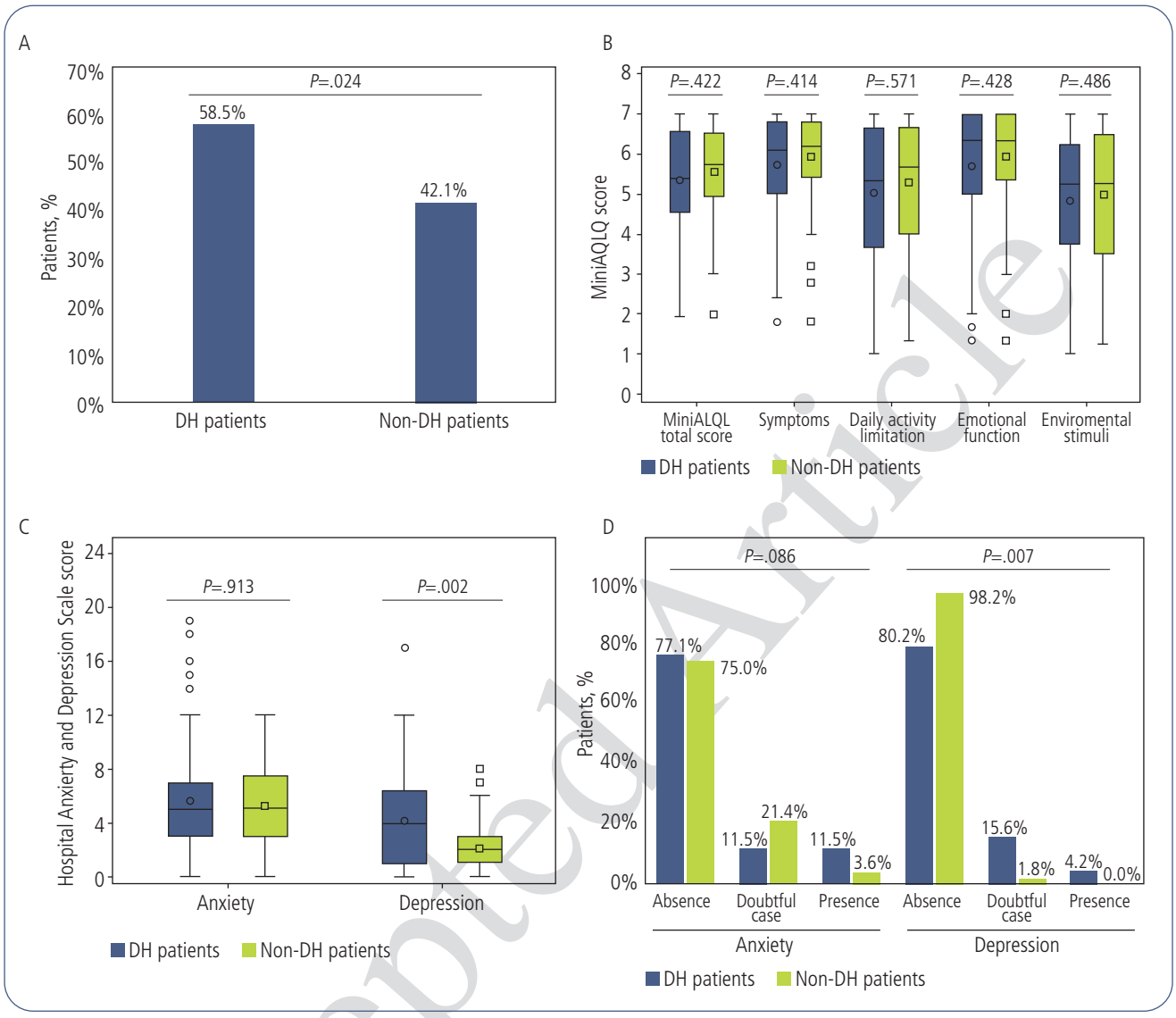

Figure 2. Differences between DH and non-DH patients for dyspnea (mMRC ≥1) (A), quality of life (MiniAQLQ score) (B), anxiety and depression (HADS score) (C), and the percentage of patients with anxiety or depression (D).
The statistical analysis of quality of life and comparison of HAD scores of anxiety and depression were performed using the Mann-Whitney test, while the comparisons of patient percentage with anxiety and depression and degree of dyspnea were performed using the χ^2 test. DH indicates dynamic hyperinflation; AQLQ, Asthma Quality of Life Questionnaire; HADS, Hospital Anxiety and Depression Score.

very careful with their respiratory diseases and lockdown was in force.

Our data did not evidence a relationship between DH and quality of life, although patients with DH tended to score more poorly than those without DH. However, as previously stated, the data in this study were from very well-controlled patients treated in a specialized unit, thus indicating that the baseline quality of life values were already very high, thus potentially explaining the absence of a statistically significant difference between the groups. In comparison, no significant differences were observed between patients with and without an end-expiratory lung volume/total lung capacity ratio ≥75%, indicating severe DH. However, patients with this ratio tended to have higher scores in the COPD assessment test, which indicated poorer quality of life [35]. As for patient well-being, while no meaningful differences were observed in the case of anxiety, a statistically significant relationship between DH and both HAD scores and the percentage of patients with depression was reported. These findings are important, since asthma patients with a higher disease burden usually experience reduced quality of life due to their condition, leaving them more prone to depression and anxiety [36,37].

The results presented here point to an association between DH and both dyspnea and reduced exercise capacity, a relationship already established in the scientific literature. Regarding dyspnea, patients with asthma undergoing high-dose methacholine challenge reported early during the course of the test the 4 dominant qualities of dyspnea in asthma, that is, inspiratory difficulty (a decrease in FEV_1 of 46.1% [1.1%] and a decrease in inspiratory capacity of 1.06 [0.06] L), chest

Table 3. Comparison of Exercise Tolerance and Lung Function Tests Between Asthma Patients With or Without Dynamic Hyperinflation.[a]

	DH patients (n=97)	Non-DH patients (n=57)	*P* Value
6MWT, median (IQR)			
Total walked distance, m	528.0 (480.0-600.0)	544.0 (504.0-594.0)	.353
Baseline lower limb fatigue in Borg scale	0.0 (0.0-2.0)	0.0 (0.0-0.0)	.004
Post-6MWT lower limb fatigue in Borg scale	3.0 (1.0-5.0)	3.0 (0.0-5.0)	.202
FeNO, ppb	28.0 (15.0-51.0)	26.0 (11.0-60.0)	.798
Lung volumes			
Mean (SD) FVC, % pred.	101 (18)	99 (17)	.491
Mean (SD) FEV_1, % pred.	86 (22)	86 (21)	.856
Mean (SD) FEV_1/FVC	71 (13)	73 (11)	.273
TLC, % pred.	109 (98-123)	105 (98-118)	.485
FRC, % pred.	126 (105-148)	120 (110-140)	.584
Oscillometry parameters			
R5insp, % pred.	116 (91-140)	108 (83-154)	.501
R5exp, % pred.	136 (103-173)	120 (93-174)	.261
Total resistance at 5 Hz, % pred.	129 (99-157)	115 (89-166)	.423
Total R5-R19, cmH2O/L/s	1 (0-1)	0 (0-1)	.086
X5insp, % pred.	82 (64-98)	87 (61-120)	.270
X5exp, % pred.	114 (78-157)	111 (61-157)	.353
ΔXrs, $cmH_2O/L/s$	0 (-0-1.0)	0 (-0-1)	.032
Total reactance at 5 Hz, % pred.	98 (77-138)	101 (67-147)	.832

Abbreviations: DH, dynamic hyperinflation; FeNO, fractional exhaled nitric oxide; FEV_1, forced vital volume at 1 second; FRC, functional residual capacity; FVC, forced vital capacity; TLC, total lung capacity; 6MWT, Six-Minute Walking Test; R5insp, inspiratory resistance at 5Hz; R5exp, expiratory resistance at 5 Hz; R5-R19, difference between total resistance at 5 Hz and total resistance at 19 Hz; X5insp, inspiratory reactance at 5 Hz; X5exp, expiratory reactance at 5 Hz; ΔXrs, difference in inspiratory and expiratory reactance.

[a]Data are shown as mean (SD), median (IQR), or No. (%) according to their type and distribution. Comparisons between groups are by the t, Mann-Whitney, or χ^2 tests.

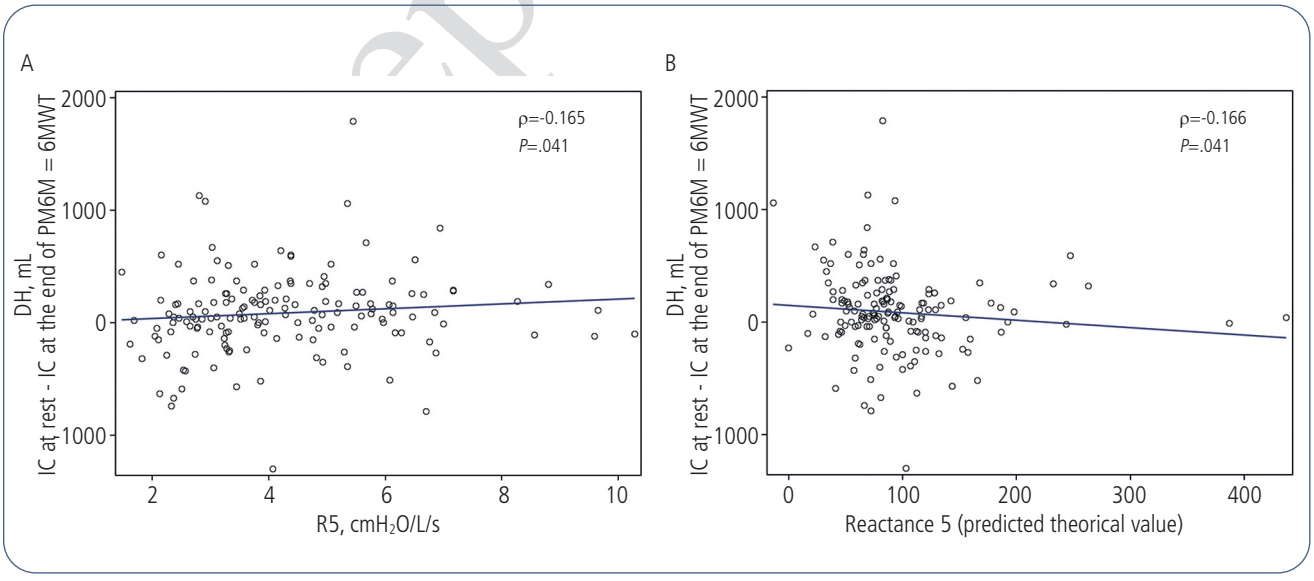

Figure 3. Relationship between magnitude of DH and oscillometric parameters.
A, Relationship between expiratory 5 Hz resistance (R5) and magnitude of hyperinflation (assessed as change in inspiratory capacity). B, Relationship between inspiratory 5 Hz reactance (Xr) and magnitude of hyperinflation. DH indicates dynamic hyperinflation; IC, inspiratory capacity; 6MWT, 6-minute walk test.

tightness, unsatisfied inspiration, and work at the highest methacholine dose [10]. More recently, in the performance of this test among 58 patients with mild-severe asthma, the increase in dyspnea, determined by the Borg score, was associated with a deterioration in FEV_1 (correlation coefficient, –0.434, $P<.01$) and both R5-R20 (correlation coefficient, 0.523; $P<.01$) and Xr5 (correlation coefficient, –0.382; $P<.01$). In addition, the multivariate regression analysis showed that the slope of X5 was significantly associated with the slope of the Borg score independently of the slope for FEV_1 (X5, β=0.431, $P<.01$; and FEV_1, β=0.569, $P<.01$; R^2, 0.997) [38]. In the case of exercise limitation, Kosmas et al [9] reported a significant correlation between maximal exercise work rate (WR_{max}) and oxygen uptake and changes in inspiratory capacity (a marker of DH) between rest and 90% of WR_{max} among patients with tidal expiratory flow limitation. In addition, all 13 patients with this condition exhibited a decrease in inspiratory capacity between rest and 90% of WR_{max}.

Our results point to a relationship between R5 values and DH in oscillometry, with a positive correlation in asthma patients. These results might highlight the importance of respiratory system resistance in prediction of DH in patients with asthma. In comparison, Tiller et al [39] studied patients with COPD, finding an association between HD and some impulse oscillometry variables in 15 patients (AX, resonant frequency [Fres], R5, X5, R5-R20, and Z5 at peak pre- and postbronchodilator exercise values). Likewise, we recorded a significant difference in ΔXrs, with higher values obtained among patients with DH, thus reflecting the dynamic compression of the airways and the limitation to expiratory flow. Dellacà et al [40] found a difference between mean inspiratory and expiratory reactance (ΔXrs), with a specificity and sensitivity of 100% in patients with COPD who underwent forced oscillation techniques.

Oscillometry is a valuable tool for the diagnosis and management of asthma, demonstrating greater sensitivity than spirometry in detecting bronchial reversibility and hyperresponsiveness. Asthma patients typically present with increased R5, AX, and Fres values, as well as a more negative X5, than healthy controls [41]. The utility of oscillometry has been established in pediatric and adult populations, with ERS-recommended cut-off points for evaluating the bronchodilator response [28]. Additionally, oscillometry aids in assessing small airway dysfunction, a critical determinant of disease severity and control. Moreover, it facilitates prediction of impaired asthma control, particularly in patients with diminished symptom perception. Its role in monitoring and predicting treatment response further underscores its clinical relevance in asthma management [42-45].

Our study was limited by its observational nature, which might include measurement error, collinearity, confounding variables, selection bias, and information bias. On the other hand, the inclusion of data from a real-world setting and the inclusion of participants from different centers can be highlighted as strengths of the study.

In conclusion, DH is frequent in patients with moderate-severe asthma controlled in specialized units. No relationship was found between DH and uncontrolled asthma according to the ACT score. However, the proportion of patients with uncontrolled asthma (according to GEMA) was statistically higher in the DH group. Moreover, patients who experienced DH had a more intense level of dyspnea, more marked sensitization to aeroallergens, and more frequent depression. Although the increase in operative lung volumes during exercise is not associated with changes in spirometry or exhaled nitric oxide values, affected patients show increased respiratory system reactance and a directly proportional relationship between the magnitude of hyperinflation and expiratory resistance and reactance at 5 Hz, suggesting that the presence of DH is associated with some degree of small airway dysfunction.

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Conflicts of Interest

In the last 3 years, VP has received honoraria for speaking at sponsored meetings from AstraZeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK, Luminova-Medwell, and Sanofi; assistance for travel to meetings from AstraZeneca and Chiesi; fees for consultancy from AstraZeneca, Chiesi, GSK, and Menarini. In the last 3 years, JS has received honoraria for speaking at sponsored meetings from Chiesi and GSK; assistance for travel to meetings from Chiesi and Sanofi; fees for consultancy from Chiesi and Sanofi. In the last 3 years, CC has received honoraria for speaking at sponsored meetings from Chiesi, Sanofi, Novartis, GSK, and AstraZeneca; assistance for travel to meetings from Chiesi, Sanofi, AstraZeneca, and Gebro; and fees for consultancy from GSK, AstraZeneca, Sanofi, and Novartis. In the last 3 years, FG-R has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Menarini, Rovi, Sanofi, and Novartis; consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, and Laboratorios Esteve; and research grants from GlaxoSmithKline, Menarini, ROCHE Pharma, and Chiesi. In the last 3 years, LS-P has received speaker fees from Sanofi and GlaxoSmithKline; and assistance with travel to meetings from Chiesi, AstraZeneca, Rovi, and ROCHE Pharma.

References

1. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: Executive Summary and Rationale for Key Changes. Am J Respir Crit Care Med. 2022;205:17-35.
2. Chowdhury NU, Guntur VP, Newcomb DC, Wechsler ME. Sex and gender in asthma. Eur Respir Rev. 2021;30:210067.
3. Plaza Moral V, Alobid I, Álvarez Rodríguez C, Blanco Aparicio M, Ferreira J, García G, et al. GEMA 5.3. Spanish Guideline on the Management of Asthma. Open Respir Arch. 2023;5:100277.

4. Zhang L, He L, Gong J, Liu C. Risk Factors Associated with Irreversible Airway Obstruction in Asthma: A Systematic Review and Meta-Analysis. Biomed Res Int. 2016;2016:9868704.
5. Calverley PMA. Dynamic hyperinflation: is it worth measuring? Proc Am Thorac Soc. 2006;3:239-44.
6. van der Meer AN, de Jong K, Hoekstra-Kuik A, Bel EH, Ten Brinke A. Dynamic hyperinflation impairs daily life activity in asthma. Eur Respir J. 2019;53:1801500.
7. O'Donnell DE, Revill SM, Webb KA. Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2001;164:770-7.
8. Benfante A, Di Marco F, Terraneo S, Centanni S, Scichilone N. Dynamic hyperinflation during the 6-min walk test in severely asthmatic subjects. ERJ Open Res. 2018;4:00143-2017.
9. Kosmas EN, Milic-Emili J, Polychronaki A, Dimitroulis I, Retsou S, Gaga M, et al. Exercise-induced flow limitation, dynamic hyperinflation and exercise capacity in patients with bronchial asthma. Eur Respir J. 2004;24:378-84.
10. Lougheed MD, Fisher T, O'Donnell DE. Dynamic hyperinflation during bronchoconstriction in asthma: implications for symptom perception. Chest. 2006;130:1072-81.
11. Sorkness RL, Kienert C, O'Brien MJ, Fain SB, Jarjour NN. Compressive air trapping in asthma: effects of age, sex, and severity. J Appl Physiol (1985). 2019;126:1265-71.
12. Tantucci C, Guerini M, Boni E, Corda L, Pini L. Tidal airway closure during bronchoconstriction in asthma: usefulness of lung volume measurements. J Asthma. 2011;48:33-40.
13. Grandi Silva A, Duarte Freitas P, Ferreira PG, Stelmach R, Carvalho-Pinto RM, Salge JM, et al. Effects of weight loss on dynamic hyperinflation in obese women asthmatics. J Appl Physiol (1985). 2019;126:413-21.
14. Takeda T, Oga T, Niimi A, Matsumoto H, Ito I, Yamaguchi M, et al. Relationship between small airway function and health status, dyspnea and disease control in asthma. Respir Int Rev Thorac Dis. 2010;80:120-6.
15. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol. 2004;113:59-65.
16. Vega JM, Badia X, Badiola C, López-Viña A, Olaguíbel JM, Picado C, et al. Validation of the Spanish version of the Asthma Control Test (ACT). J Asthma. 2007;44:867-72.
17. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111-7.
18. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. Eur Respir J. 1999;14:32-8.
19. Sanjuàs C, Alonso J, Sanchís J, Casan P, Broquetas JM, Ferrie PJ, et al. [The quality-of-life questionnaire with asthma patients: the Spanish version of the Asthma Quality of Life Questionnaire]. Arch Bronconeumol. 1995;31:219-26.
20. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361-70.
21. De las Cuevas C, García-Estrada A, de Rivera L. Hospital anxiety and depression scale" y psicopatología afectiva. An Psiquiatría (Madrid). 1995;11:126-30.
22. Donaire-Gonzalez D, Gimeno-Santos E, Serra I, Roca J, Balcells E, Rodríguez E, et al. [Validation of the Yale Physical Activity Survey in chronic obstructive pulmonary disease patients]. Arch Bronconeumol. 2011;47:552-60.
23. Dipietro L, Caspersen CJ, Ostfeld AM, Nadel ER. A survey for assessing physical activity among older adults. Med Sci Sports Exerc. 1993;25:628-42.
24. Fletcher C. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). Br Med J. 1960;2:1665.
25. Plaza V, Fernández-Rodríguez C, Melero C, Cosío BG, Entrenas LM, de Llano LP, et al. Validation of the "Test of the Adherence to Inhalers" (TAI) for Asthma and COPD Patients. J Aerosol Med Pulm Drug Deliv. 2016;29:142-52.
26. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14:377-81.
27. American Thoracic Society, European Respiratory Society. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am J Respir Crit Care Med. 2005;171:912-30.
28. King GG, Bates J, Berger KI, Calverley P, de Melo PL, Dellacà RL, et al. Technical standards for respiratory oscillometry. Eur Respir J. 2020;55:1900753.
29. Oostveen E, Boda K, van der Grinten CPM, James AL, Young S, Nieland H, et al. Respiratory impedance in healthy subjects: baseline values and bronchodilator response. Eur Respir J. 2013;42:1513-23.
30. García-Río F, Calle M, Burgos F, Casan P, Del Campo F, Galdiz JB, et al. Spirometry. Spanish Society of Pulmonology and Thoracic Surgery (SEPAR). Arch Bronconeumol. 2013;49:388-401.
31. Bhakta NR, McGowan A, Ramsey KA, Borg B, Kivastik J, Knight SL, et al. European Respiratory Society/American Thoracic Society technical statement: standardisation of the measurement of lung volumes, 2023 update. Eur Respir J. 2023;62:2201519.
32. Mediano O, Casitas R, Villasante C, Martínez-Cerón E, Galera R, Zamarrón E, et al. Dynamic hyperinflation in patients with asthma and exercise-induced bronchoconstriction. Ann Allergy Asthma Immunol. 2017;118:427-32.
33. Olaguibel JM, Quirce S, Juliá B, Fernández C, Fortuna AM, Molina J, et al. Measurement of asthma control according to Global Initiative for Asthma guidelines: a comparison with the Asthma Control Questionnaire. Respir Res. 2012;13:50.
34. Alvarez-Gutiérrez FJ, Medina-Gallardo JF, Pérez-Navarro P, Martín-Villasclaras JJ, Martin Etchegoren B, Romero-Romero B, et al. [Comparison of the Asthma Control Test (ACT) with lung function, levels of exhaled nitric oxide and control according to the Global Initiative for Asthma (GINA)]. Arch Bronconeumol. 2010;46:370-7.
35. Zhao L, Peng L, Wu B, Bu X, Wang C. Effects of dynamic hyperinflation on exercise capacity and quality of life in stable COPD patients. Clin Respir J. 2016;10:579-88.
36. Chen H, Gould MK, Blanc PD, Miller DP, Kamath TV, Lee JH, et al. Asthma control, severity, and quality of life: quantifying the effect of uncontrolled disease. J Allergy Clin Immunol. 2007;120:396-402.

37. Haselkorn T, Fish JE, Zeiger RS, Szefler SJ, Miller DP, Chipps BE, et al. Consistently very poorly controlled asthma, as defined by the impairment domain of the Expert Panel Report 3 guidelines, increases risk for future severe asthma exacerbations in The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study. J Allergy Clin Immunol. 2009;124:895-902.e1-4.
38. van der Wiel E, Postma DS, van der Molen T, Schiphof-Godart L, Ten Hacken NHT, van den Berge M. Effects of small airway dysfunction on the clinical expression of asthma: a focus on asthma symptoms and bronchial hyper-responsiveness. Allergy. 2014;69:1681-8.
39. Tiller NB, Cao M, Lin F, Yuan W, Wang CY, Abbasi A, et al. Dynamic airway function during exercise in COPD assessed via impulse oscillometry before and after inhaled bronchodilators. J Appl Physiol 1985. 2021;131:326-38.
40. Dellacà RL, Santus P, Aliverti A, Stevenson N, Centanni S, Macklem PT, et al. Detection of expiratory flow limitation in COPD using the forced oscillation technique. Eur Respir J. 2004;23:232-40.
41. Kim HY, Shin YH, Jung DW, Jee HM, Park HW, Han MY. Resistance and reactance in oscillation lung function reflect basal lung function and bronchial hyperresponsiveness respectively. Respirology. 2009;14(7):1035-41. doi: 10.1111/j.1440-1843.2009.01605.x. PMID: 19740263.
42. Cottee AM, Seccombe LM, Thamrin C, King GG, Peters MJ, Farah CS. Bronchodilator Response Assessed by the Forced Oscillation Technique Identifies Poor Asthma Control With Greater Sensitivity Than Spirometry. Chest. 2020;157(6):1435-41. doi: 10.1016/j.chest.2019.12.035
43. Tang FSM, Rutting S, Farrow CE, Tonga KO, Watts J, Dame-Carrol JR, et al. Ventilation heterogeneity and oscillometry predict asthma control improvement following step-up inhaled therapy in uncontrolled asthma. Respirology. 2020;25(8):827-35. doi: 10.1111/resp.13772
44. Antonicelli L, Tontini C, Marchionni A, Lucchetti B, Garritani MS, Bilò MB. Forced oscillation technique as method to document and monitor the efficacy of mepolizumab in treating severe eosinophilic asthma. Allergy. 2020;75(2):433-6. doi: 10.1111/all.13938.
45. Goorsenberg AWM, d'Hooghe JNS, Slats AM, van den Aardweg JG, Annema JT, Bonta PI. Resistance of the respiratory system measured with forced oscillation technique (FOT) correlates with bronchial thermoplasty response. Respir Res. 2020;21(1):52. doi: 10.1186/s12931-020-1313-6.

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