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The influence of obesity on IOS parameters in asthma, COPD, and other lung diseases: analyzed by random forest

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Abstract

Background This study investigates the impact of obesity on impulse oscillometry (IOS) parameters in individuals with asthma, chronic obstructive pulmonary disease (COPD), other lung diseases, and non-respiratory conditions. With rising obesity rates, understanding its effects on respiratory health is increasingly essential. We aimed to evaluate IOS parameters as predictors of respiratory dysfunction across different BMI categories, offering insights into managing complex cases involving obesity and lung disease.

Methods We retrospectively analyzed IOS data from 1,947 patients referred to a secondary care allergy and lung clinic. IOS parameters assessed included total and peripheral airway resistance (R_5 and R_{5-20}), resonant frequency (Fres), and reactance area (A_X), examined relative to BMI. The cohort included patients with asthma, COPD, other lung diseases, and controls. A weighted random forest model was used to assess the impact of IOS parameters on BMI prediction accuracy, adjusting for imbalances in BMI and disease groups.

Results Obesity significantly affected IOS parameters, with R_{5-20}, A_X, and Fres emerging as key markers across all diagnostic groups. Elevated R_{5-20}, A_X and Fres values in obese patients, regardless of lung disease status, indicated increased small airway resistance and dysfunction. These IOS features demonstrated high predictive value in BMI-related outcomes, suggesting they capture airway impairments tied to obesity beyond conventional respiratory diagnoses.

Conclusions IOS parameters, particularly R_{5-20}, A_X, and Fres are sensitive to obesity-associated airway changes and may serve as valuable markers for identifying respiratory impairment in obese individuals with or without lung disease.

Keywords Impulse oscillometry, Body mass index, Obesity, Respiratory dysfunction, Predictive modeling, Random forest analysis

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Background

The global increase in overweight and obesity rates has become a major public health challenge, with the World Health Organization (WHO) reporting that 43% of adults were classified as overweight and 16% as obese in 2022 [1]. This growing epidemic not only contributes to numerous metabolic disorders but also significantly affects respiratory health, particularly in individuals with chronic lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). A growing body of evidence highlights a strong, independent association between elevated body mass index (BMI) and alterations in respiratory mechanics, as measured by impulse oscillometry (IOS), across various pulmonary conditions [2–5].

Obesity negatively impacts lung function by reducing both static and dynamic lung volumes, particularly the expiratory reserve volume (ERV) and functional residual capacity (FRC). This decrease in lung volumes is linked to impaired airflow, which can exacerbate respiratory symptoms in patients with asthma and COPD [6].

Although previous studies have established a connection between BMI and IOS parameters, such as increased airway resistance and altered reactance, these investigations have primarily focused on simple associations without exploring the predictive potential of these metrics [7, 8]. As a result, there is a growing need to identify which IOS parameters are most predictive of respiratory impairment in obese individuals with lung diseases. To address this gap, our study employs advanced statistical learning methods, particularly a robust random forest model, to predict and analyze the key IOS parameters associated with BMI in patients with asthma, COPD, and other lung diseases. Unlike previous research, which mainly focused on correlations, our approach enables us to identify and rank the predictors that most significantly influence BMI groups across various lung diseases.

Materials and methods

Patients

This study was a retrospective, observational cohort involving 1,947 adult patients referred to our secondary care allergy and lung clinic between 2022 and 2023. All participants had lung-related symptoms or were suspected of reduced lung function. Patient records provided data from each visit.

Data collection

Lung function tests adhered to established protocols. Spirometry was performed using equipment from Medical Electronic Construction (M.E.C.) in line with ATS/ERS standards (found at "mecrd.eu") [9]. Fractional exhaled nitric oxide (Fe-NO) levels were measured with the NObreath device from Bedfont™.

For patients presenting with dyspnea or suspected lung disease, total lung capacity (TLC) and lung diffusion capacity for carbon monoxide (D_{LCO}) were assessed using the M.E.C. PFT Body system, applying reference values from the Global Lung Function Initiative (GLI) [7]. For plethysmography conducted before March 2023, ECSC reference values were used [9]. Patients eligible for a methacholine challenge test (defined by $FEV_1 \geq 1.5$ L and ≥ 60%, non-pregnant, and not breastfeeding) underwent bronchial provocation testing using a five-step dosimeter protocol with the aerosol provocation system (APS) from Viasys®, which automatically calculated administered doses (PD_{20}) based on a single concentration of 25 mg/mL methacholine (APS-SC) in SentrySuite version 3.20 [10]. A $PD_{20} \leq 0.4$ mg was classified as positive for bronchial hyperreactivity. Typically, Fe-NO and Impulse Oscillometry System (IOS) assessments were completed prior to spirometry and plethysmography.

Unlike traditional spirometry, IOS allows lung function assessment during relaxed tidal breathing, offering additional insights [11–13]. This study used the Vyntus™ IOS system, SentrySuite version 3.20 (Vyaire Medical, Hoechberg, Germany), which measures respiratory system resistance (Rrs) and respiratory system reactance (Xrs) across various airway regions through small pressure waves at different frequencies [13]. Reference values for Rrs and Xrs were estimated using equations that accounted for body position variability and potential ethnicity differences [14, 15].

We analyzed several IOS parameters, including R_5 (the respiratory resistance at 5 Hz, representing the total airway resistance), R_{20} (the respiratory resistance at 20 Hz, representing resistance in the central airways), the difference between R_5 and R_{20} ($R_{5\text{-}20}$, reflecting peripheral airway resistance), the absolute difference between measured and predicted value for reactance at 5 Hz (Diff-X_5), resonant frequency (Fres), and reactance area (A_X). These measurements collectively provide a detailed view of both central and peripheral airway functionality [13]. Small airway dysfunction (SAD) was defined as the presence of increased peripheral airway resistance and can be measured by R5-R20. R5-R20 has been validated in previous studies as a sensitive and specific marker of small airway mechanics [4]. SAD was assessed for its association with BMI and respiratory disease groups to provide insights into the interplay between obesity and airway dysfunction.

BMI and diagnostic groups

BMI was categorized into the following groups:

1. *Normal or Underweight*, where BMI < 25 kg/m².
2. *Overweight*, where BMI 25–29.9 kg/m².
3. *Obese*, where BMI 30–39.9 kg/m².

4. *Morbidly Obese*, where BMI ≥ 40 kg/m^2.

Patients were classified into diagnostic groups based on clinical diagnoses:

1. *Asthma Only*, i.e. Patients diagnosed exclusively with asthma.
2. *COPD (± Asthma)*, i.e. Patients diagnosed with chronic obstructive pulmonary disease (COPD), with or without concurrent asthma.
3. *Other Lung Conditions*, i.e. Patients diagnosed with conditions such as interstitial lung disease, bronchiectasis, post-COVID syndrome, and lung infections.
4. *Non-Lung Disease Conditions*, i.e. Patients diagnosed with conditions unrelated to lung disease, including rhinitis, sinusitis, dysfunctional breathing, or reflux.

Obstructive sleep apnea (OSA)

In the subgroup of patients with BMI ≥ 30 kg/m^2, it was documented whether they had been diagnosed with OSA (DG473).

Statistics

Statistical analysis

Analyses were performed using SPSS version 28 (IBM Corp., Armonk, NY) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) for random forest modeling [16]. To compare groups, a two-sample t-test or Wilcoxon rank-sum test was used, depending on the distribution of the continuous variables. Categorical data were analyzed using Fisher's exact test. Statistical significance was defined as $p < 0.05$.

Random forest modeling

Random forest models were used to identify key factors predictive of BMI groups, with the technique chosen for its ability to balance bias and variance. By combining multiple decision trees, random forests reduce the risk of overfitting and provide stable variable importance measures across diagnostic groups. The analysis was based on two key metrics: *Mean Decrease Accuracy (MDA)*, reflecting the percentage reduction in accuracy when a variable is permuted. Higher MDA scores indicate significant predictors of BMI. The other metric is *Mean Decrease Gini (MDG)*, measures a variable's influence on reducing Gini impurity, providing insight into classification accuracy [17].

The MDA and MDG values were classified into three impact levels: high (above the third quartile), moderate (between the second and third quartiles), and low (below the second quartile). Given the variation in BMI group representation across diagnostic categories, a weighted random forest model was applied to account for this imbalance. By assigning greater weight to underrepresented BMI groups, this approach enhanced accuracy and reduced bias in feature importance assessments. Consequently, the model provides a more reliable evaluation of the influence of IOS and clinical features on BMI, offering a refined understanding of BMI's significance across different respiratory patient groups and strengthening diagnostic and management insights.

Results

IOS metrics and diagnostic classification

The dataset comprised 860 patients diagnosed with asthma alone (44.2%) and 179 with COPD co-occurring with asthma (11.6%) (Table 1). Notably, there were no significant differences in IOS values between patients with COPD alone and those with co-occurring asthma, leading to their combination for subsequent analyses under "COPD".

Patients diagnosed with COPD exhibited notably higher IOS values compared to individuals in other diagnostic groups (Table 2). In contrast, asthma patients were generally younger, exhibited higher Fe-NO, FEV_1%, FEV_1/FVC ratios, and D_{LCO} levels, and had a lower total lung capacity (TLC). Asthma patients, compared to those with other lung diseases or no lung disease, demonstrated elevated Fe-NO levels, higher rates of positive bronchial methacholine provocation (BMP) tests, lower smoking prevalence, and generally higher IOS values.

Association between BMI and IOS

A significant positive association was observed between increasing BMI and elevated IOS values, alongside a decrease in FEV_1% (Table 1). Among diagnostic groups, COPD patients exhibited the highest IOS values, followed by those with asthma, other lung diseases, and those without lung disease (Fig. 1). Within each diagnostic category, obese patients had significantly higher IOS values compared to those with a BMI below 24.9 kg/m^2 (Fig. 1; Table 3).

Weighted random forest analysis

Tables 4–7 present the Mean Decrease Accuracy (MDA) and Mean Decrease Gini (MDG) values, categorized by impact levels, illustrating how features such as age, sex, FEV_1%, smoking status, and IOS parameters influence model performance and classification accuracy across diagnostic groups.

Key IOS variables by diagnostic group

Asthma patients

In patients with *asthma only*, variables with high-impact Mean Decrease Accuracy (MDA > 20), specifically R_{5-20}, A_X, and Fres, demonstrated substantial contributions to model accuracy and classification precision (see Table 4).

Table 1 Demographic and clinical characteristics of the study population (*N* = 1,947) stratified by BMI groups. The table includes data on asthma, chronic obstructive pulmonary disease (COPD), other lung diseases, and non-lung disease cases. Presented variables include age, gender, smoking status, and IOS parameters

BMI-groups (kg/m²)		**<24,9, *n*=713, gr.1**	**25-29,9, *n*=710, gr. 2**	**30-39,9, *n*=460, gr. 3**	**≥40, *n*=64, gr.4**	***P*-level for difference between groups**				
						4 vs. 3	**4 vs. 2**	**4 vs. 1**	**3 vs. 2**	**3 vs. 1**	**2 vs. 1**
Females,%, *n*=1947		71.5	51.3	59.1	73.4	0.028	0.001	0.75	0.008	0.001	0.001
FEV_1%, *n*=1943		89.1 (13-136)	88.2 (21-137)	84.8 (19-124)	78.0 (36-117)	0.001	0.001	0.001	0.001	0.001	0.29
Age, years, *n*=1947		49.6 (18-93)	56.9 818-91)	58.4 (20-88)	52.8 (18-87)	0.015	0.07	0.21	0.19	0.001	0.001
Smoking status	Current smoker,%	7.4	7.5	9.3	17.2	0.053	0.007	0.007	0.26	0.24	0.98
	Ex-smoker,%	33.4	46.8	44.8	34.4	0.11	0.056	0.87	0.49	0.001	0.001
	Never smoker,%	59.2	45.7	45.9	48.4	0.70	0.67	0.10	0.95	0.001	0.001
Asthma Only, **n (%)**		301 (42.2)	318 (44.8)	212 (46.1)	29 (45.3)	NA	NA	NA	NA	NA	NA
COPD (±Asthma), **n (%)**		118 (16.5)	146 (20.6)	81 (17.6)	16 (25)	NA	NA	NA	NA	NA	NA
Other Lung Conditions, **n (%)**		79 (11.1)	69 (9.7)	62 (13.5)	6 (9.4)	NA	NA	NA	NA	NA	NA
Non-Lung Disease Conditions, **n (%)**		215 (30.2)	177 (24.9)	105 (22.8)	13 (20.3)	NA	NA	NA	NA	NA	NA
R_5, (kPa/L/s), *n*=1947		0.35 (0.14-1.03)	0.39 (0.16-0.98)	0.47 (0.16-1.14)	0.56 (0.21-1.27)	0.001	0.001	0.001	0.001	0.001	0.001
R_5%, *n*=1947		100.2 (36-270)	113.1 (40-302)	132.7 (37-301)	157.2 (69-306)	0.001	0.001	0.001	0.001	0.001	0.001
$R_{5\text{-}20}$, (kPa/L/s), *n*=1946		0.036 (0-0.63)	0.074 (0-0.61)	0.119 (0-0.61)	0.184 (0-0.63)	0.001	0.001	0.001	0.001	0.001	0.001
A_X (kPa/L), *n*=1925		0.45 (0-7.8)	0.74 (0-7.9)	1.17 (0-7.2)	1.82 (0.2-6.9)	0.001	0.001	0.001	0.001	0.001	0.001

Continuous variables are presented as mean (minimum-maximum), with "NA" indicating not applicable

Notably, while all these variables showed high Mean Decrease Gini (MDG) values, A_X had a slightly lower MDG due to its interaction with other variables, such as Fres, which affects its classification purity as an independent predictor. This emphasizes the complementary role of these IOS metrics in accurately distinguishing asthma phenotypes.

Gender and R_5% emerged as variables with moderate predictive value, exhibiting balanced MDA and MDG scores. This indicates that gender and R_5% contribute reliably to classification accuracy, without significant trade-offs in model precision. By contrast, variables with lower MDA scores (MDA < 10), including Smoking, Diff-X5, Age, FEV1%, and R20, were associated with reduced impact on classification accuracy. Although these variables contributed less to the primary model's predictive strength, they still played a supporting role in reducing classification error.

COPD (± Asthma) patients

Among patients with *COPD (± Asthma)*, including those with co-existing asthma, high-impact variables (MDA > 7.0) were identified as Gender, $R_{5\text{-}20}$, A_X, and Fres (Table 5). However, their lower Mean Decrease Gini (MDG) values suggest these variables primarily enhance predictive accuracy through interaction effects rather than strong standalone contributions. R_5% and Gender demonstrated moderate influence in MDA, underscoring their relevance in assessing both central and peripheral airways. Conversely, variables such as Smoking, Diff-X_5, Age, FEV_1%, and R_{20} showed limited impact on prediction accuracy across BMI categories. In addition, we found an association between IOS values and FEV_1 / Global Initiatives for Chronic Obstructive Lung Disease (GOLD) stages; GOLD 1: $FEV_1 \geq 80\%$, GOLD 2: FEV_1 between 50 and 79.9%, GOLD 3: FEV_1 between 30 and 49.9%, GOLD 4: $FEV_1 < 30\%$ (Table 8).

Other lung conditions

Among patients with non-lung disease conditions, high-impact variables (MDA > 10) included $R_{5\text{-}20}$, A_X, and Fres, which were essential for both model accuracy and minimizing classification errors (Table 6). R_5% and Gender had moderate influence, with R_5% being more influential in error reduction. Lower-impact variables included Smoking, Diff-X_5, Age, FEV_1%, and R_{20}, which contributed to error minimization but had a lesser impact on overall model accuracy.

Non-Lung disease conditions

In individuals without lung disease, high-impact variables (MDA > 13) included $R_{5\text{-}20}$, A_X, and Fres, of which strongly influenced model accuracy, error reduction and classification. R_5% and Gender played moderate roles,

Table 2 Pairwise comparison of lung function, smoking status, Fe-NO, PD_{20}, and impulse oscillometry (IOS) parameters among patients diagnosed with asthma only, COPD (± asthma), other lung conditions, and Non-Lung disease conditions. The IOS parameters include total airway resistance (R_5), peripheral airway resistance (R_{5-20}), resonant frequency (Fres), and reactance area (A_X). Data are presented as means (minimum-maximum)

		Asthma Only,*n*=860; group 1	**COPD + COPD with co-existing asthma, *n*=361; subgroup 2**	**COPD, *n*=182; subgroup 2**	**COPD with co-existing asthma, *n*=179; subgroup 2**	**Other Lung Conditions, *n*=216; group 3**	**Non-Lung Disease Conditions, *n*=510; group 4**	**Difference between groups *p*-values**		
								3 vs. 4	**1 vs. 3**	**1 vs. 2**
Females,%, *n*=1947		63.0	60.1	61.5	58.7	63.4	58.2	Ns	Ns	Ns
Age, years, *n*=1947		51.1 (18-93)	64.3 (19-89)	65.9 (19-89)	62.7 (22-88)	59.5 (18-86)	52.8 (18-87)	<0.001	<0.001	<0.001
BMI, kg/m^2, *n*=1947		27.7 (15.9-59.1)	27.7 (16.2-52.7)	27.4 (16.2-47.1)	28.1 (17.7-52.7)	27.7 (16.9-45.9)	26.8 (17.8-54.6)	0.04	Ns	Ns
FEV_1, %predicted, *n*=1943		87.8 (25-136)	71.5 (13-118)	71.5 (13-118)	71.5 (21-110)	88.1 (37-137)	97.6 (50-129)	<0.001	Ns	<0.001
FEV_1/FVC-ratio, *n*=1938		0.74 (0.32-0.99)	0.60 (0.29-0.84)	0.61 (0.29-0.84)	0.60 (0.33-0.80)	0.76 (0.53-0.99)	0.78 (0.58-1.0)	0.005	0.004	<0.001
TLC, %predicted, *n*=1717		100.3 (65-165)	105.5 (61-177)	104.2 (61-177)	105.8 (76-154)	95.3 (60-144)	100.9 (54-142)	<0.001	<0.001	<0.001
D_{LCO}, %predicted, *n*=1598		104.8 (48-199)	89.0 (27-164)	83.4 (27-161)	94.5 (42-164)	94.0 (34-142)	104.2 (37-157)	<0.001	<0.001	<0.001
Smoking status, *n*=1946	Current smoker,%	4.1	17.7	20.3	15.1	7.9	8.6	Ns	0.02	<0.001
	Ex-smoker,%	31.4	78.9	74.2	83.8	34.3	33.1	Ns	Ns	<0.001
	Never smoker,%	64.5	3.3	5.5	1.1	57.9	58.2	Ns	Ns	<0.001
FeNO, ppb, *n*=1919		26.3 (0-226)	17.5 (0-174)	11.9 (0-99)	23.2 (0-174)	14.2 (2-56)	15.2 (0-101)	Ns	<0.001	<0.001
PD_{20} ≤400 µg, *n*=1535		36.2% (269/704)	34.0% (66/194)	14.7% (15/102)	53.3% (56/105)	11.0% (19/172)	5.8% (27/465))	0.023	<0.001	Ns
R_5, (kPa/L/s), *n*=1947		0.41 (0.16-1.27)	0.47 (0.17-1.12)	0.47 (0.17-1.12)	0.47 (0.20-1.08)	0.38 (0.15-1.14)	0.34 (0.14-1.02)	<0.001	0.002	<0.001
R_5%predicted, *n*=1947		118.5 (45-306)	130.2 (41-302)	128.1 (41-299)	132.3 (64-302)	106.1 (36-301)	100.1 (37-270)	0.04	0.001	<0.001
R_{5-20}, (kPa/L/s), *n*=1946		0.075 (0-0.56)	0.134 (0-0.63)	0.138 (0-0.63)	0.129 (0-0.58)	0.070 (0-0.59)	0.041 (0-0.46)	<0.001	Ns	<0.001
Fres, Hz, *n*=1919		15.5 (5.0-43.8)	19.2 (4.2-47.3)	19.2 (6.7-47.3)	19.2 (4.2-34.8)	14.2 (6.4-29.7)	12.2 (4.8-41.3)	<0.001	0.02	<0.001
A_X, (kPa/L), *n*=1916		0.75 (0-7.3)	1.47 (0-7.9)	1.53 (0-7.9)	1.42 (0-7.6)	0.64 (0-5.0)	0.36 (0-7.8)	<0.001	0.02	<0.001

Continuous variables are presented as mean (minimum-maximum. p-values > 0.05 are reported as "Ns" (non-significant)

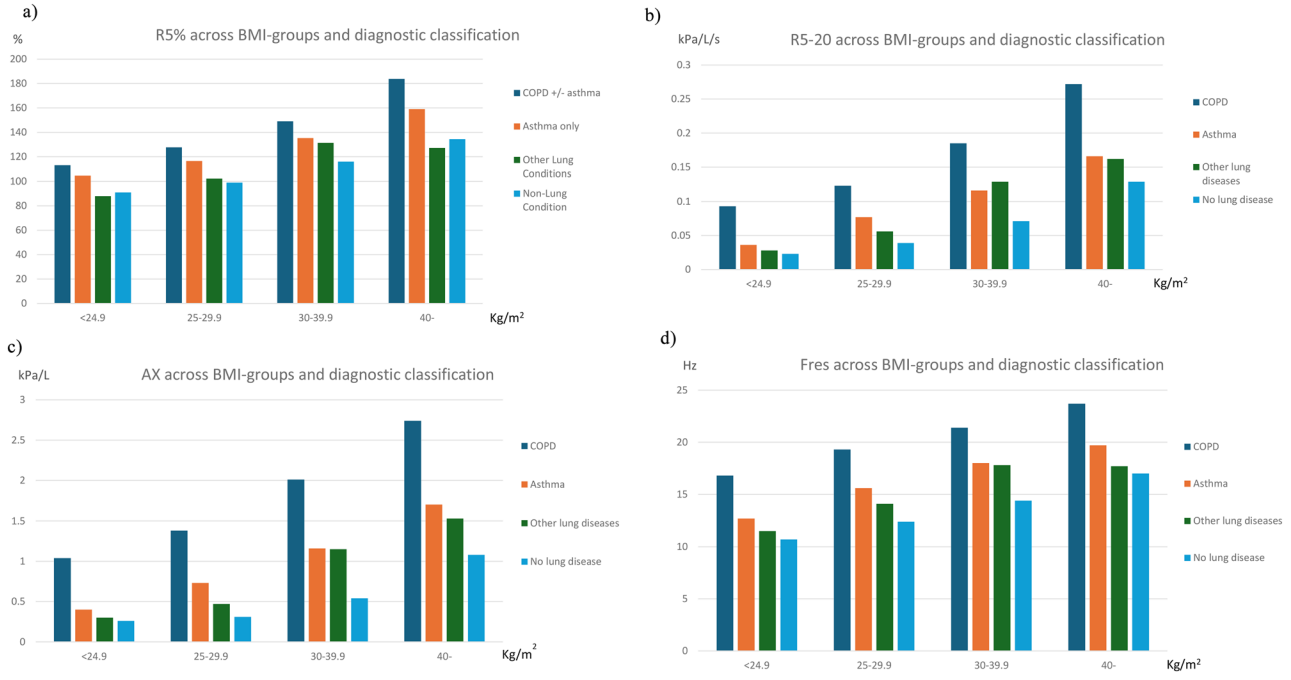

Fig. 1 IOS measures across four BMI-groups (1: Underweight or normal weight, 2: Overweight, 3: Obese and 4: Morbidly obese) and four disease groups (1: asthma only, 2: COPD (± asthma), 3: lung disease conditions, and 4: non-lung disease conditions). Each subfigure presents a bar chart showing the level of (**a**) R_5%, (**b**) $R_{5\text{-}20}$, (**c**) A_X, and (**d**) Fres

Table 3 Pairwise comparison of R_5%, $R_{5\text{-}20}$, and A_X in relation to the impact of obesity (body mass index) across disease classifications and its effect on IOS parameters (R_5%, $R_{5\text{-}20}$, A_X, Fres, and Diff-X_5). This table includes a comparison of our study's findings with those from other available studies

Study group and comparison	Study (ref.)	Number of patients	Difference between groups		
			R_5%	$R_{5\text{-}20}$	A_X
BMI ≥40 kg/^{2} Asthma versus Non-Lung Disease Conditions	Dixon (4)	31 vs. 22	+20%	0.06	+150%
	Our	29 vs. 13	+20%*	0.04*	+60%*
Asthma BMI ≥40 kg/^{2} vs. <25 kg/^{2}	Can (2)	24 vs. 31	+50%	0.10	+400%
	Our	29 vs. 301	+50%*	0.13*	+325%*
COPD (±Asthma) BMI ≥40 kg/^{2} vs. <25 kg/^{2}	Our	16 vs. 118	+60%*	0.18*	+160%*
Other Lung Conditions BMI ≥40 kg/^{2} vs. <25 kg/^{2}	Our	6 vs. 79	+45%*	0.13*	+400%*
Non-Lung Disease Conditions BMI ≥40 kg/^{2} vs. <30 kg/^{2}	de Albuquerque (3)	28 vs. 31	+40%	0.10	Fres: +50%
	Our	13 vs. 392	+40%*	0.11*	+56%*

* p-level <0.001

Table 4 Performance metrics for IOS parameters in patients with asthma only. Results include random forest analysis for IOS parameters (R_5%, R_{20}, $R_{5\text{-}20}$, A_X, Fres, and Diff-X_5), FEV_1%, and clinical features (gender, smoking, age). Metrics include MDA, MDG, and their respective categories

Feature	MDA	MDG	MDA_Category	MDG_Category
$R_{5\text{-}20}$	29.63	86.82	High	High
A_X	22.88	60.68	High	Low
Fres	22.08	68.68	High	High
R_5%	15.51	52.15	Moderate	Low
Gender	14.16	77.86	Moderate	High
Smoking	7.90	63.38	Low	Moderate
Diff-X_5	6.91	56.15	Low	Low
Age	4.19	7.66	Low	Low
FEV_1%	2.70	13.10	Low	Low
R_{20}	0.39	61.05	Low	Moderate

while Smoking, Diff-X_5, Age, FEV_1%, and R_{20}, contributed minimally to accuracy and error reduction (Table 7).

Common features across diagnostic groups

In all diagnostic groups, $R_{5\text{-}20}$, A_X, and Fres consistently stood out as the most influential variables for predicting BMI-related outcomes. These features significantly enhanced model accuracy and reduced classification errors, either through individual effects or interactions, underscoring their critical role across a range of patient profiles.

Table 5 Performance metrics for IOS parameters in patients with COPD with and without concurrent asthma. Results include random forest analysis for IOS parameters (R_5%, R_{20}, $R_{5\text{-}20}$, A_X, Fres, and Diff-X_5), FEV_1%, and clinical features (gender, smoking, age). Metrics include MDA, MDG, and their respective categories

Feature	MDA	MDG	MDA_Category	MDG_Category
$R_{5\text{-}20}$	12.50	8.20	High	Low
A_X	8.57	23.11	High	Low
Fres	7.76	22.45	High	Low
R_5%	7.56	25.91	Moderate	Moderate
Gender	7.34	27.76	Moderate	High
Smoking	4.91	25.03	Low	Moderate
Diff-X_5	2.49	29.49	Low	High
Age	0.22	22.80	Low	Low
FEV_1%	-0.07	6.10	Low	Low
R_{20}	-0.36	28.48	Low	High

Table 6 Performance metrics for IOS parameters in patients with other lung conditions. Results include random forest analysis for IOS parameters (R_5%, R_{20}, $R_{5\text{-}20}$, A_X, Fres, and Diff-X_5), FEV_1%, and clinical features (gender, smoking, age). Metrics include MDA, MDG, and their respective categories

Feature	MDA	MDG	MDA_Category	MDG_Category
$R_{5\text{-}20}$	17.72	19.27	High	Moderate
A_X	12.13	19.68	High	High
Fres	10.84	19.85	High	High
R_5%	9.49	18.64	Moderate	Moderate
Gender	7.00	4.01	Moderate	High
Smoking	1.47	3.60	Low	Low
Diff-X_5	1.34	13.14	Low	Low
Age	0.53	15.46	Low	Low
FEV_1%	-2.37	14.13	Low	Low
R_{20}	-3.73	13.06	Low	Low

Table 7 Performance metrics for IOS parameters in patients with non-lung disease conditions. Results include random forest analysis for IOS parameters (R_5%, R_{20}, $R_{5\text{-}20}$, A_X, Fres, and Diff-X_5), FEV_1%, and clinical features (gender, smoking, age). Metrics include MDA, MDG, and their respective categories

Feature	MDA	MDG	MDA_Category	MDG_Category
$R_{5\text{-}20}$	20.29	33.56	High	High
A_X	17.34	46.86	High	High
Fres	13.50	42.25	High	High
R_5%	12.66	35.00	Moderate	Moderate
Gender	11.94	36.98	Moderate	Low
Smoking	3.90	9.46	Low	Low
Diff-X_5	2.91	26.51	Low	Low
Age	2.50	7.16	Low	Moderate
FEV_1%	1.78	28.18	Low	Low
R_{20}	-0.53	33.40	Low	Low

In the subgroup of patients with obesity or morbid obesity, 54 out of 524 (9.1%) were diagnosed with obstructive sleep apnea as a comorbidity. Patients with obstructive sleep apnea exhibited higher IOS values in the peripheral airways (Table 9).

Table 8 Association between IOS values and FEV_1 according to GOLD stages

GOLD stage	1 FEV_1 ≥80%; *N*=126	2 FEV1: 50-79.9%; *N*=187	3 FEV_1: 30-49.9%; *N*=41	4 FEV_1 <30%; *N*=7
R5%	104.9 (30.6)	134.4 (41.0)	176.0 (48.7)	204.4 (70.2)
R20, kPa/L/s	0.31 (0.06)	0.35 (0.08)	0.36 (0.08)	0.33 (0.10)
R5-20, kPa/L/s	0.06 (0.07)	0.14 (0.10)	0.28 (0.16)	0.33 (0.16)
AX, kPa/L	0.60 (0.73)	1.52 (1.26)	3.40 (1.97)	4.63 (2.20)
Fres, Hz	14.4 (5.5)	20.4 (6.6)	26.4 (5.3)	30.7 (3.7)
BMI, kg/m^2	26.9 (4.9)	28.1 (6.1)	28.7 (7.0)	26.7 (5.9)

Continuous variables are presented as mean (SD)

Table 9 Comparison of patient characteristics, FEV_1, diagnostic classification, and IOS results of OSA and non-OSA patients

	BMI ≥30 kg/m^2		
IOS parameter	OSA, *N*=48 (9.2%)	Non-OSA, *N*=476 (90.8%)	*P*-level
R5%	155.2 (43.1)	133.8 (41.3)	<0.001
R20, kPa/L/s	0.36 (0.07)	0.35 (0.09)	0.40
R5-20, kPa/L/s	0.18 (0.13)	0.12 (0.10)	0.003
AX, kPa/L	1.78 (1.57)	1.22 (0.10)	0.017
Fres, Hz	20.6 (6.3)	18.2 (6.0)	0.013
BMI, kg/m^2	37.4 (6.2)	34.4 (4.3)	<0.001
Age, years	62.1 (12.7)	57.3 (15.4)	0.06
Females, %	43.8	62.6	0.04
FEV_1, %	79.3 (19.1)	84.5 (16.1)	0.09
Asthma, N	20 (41.7%)	219 (46.0%)	0.36
COPD ±Asthma, N	12 (25.0%)	84 (17.6%)	0.45
Orther disease, N	16 (33.3%)	173 (36.3%)	0.36

Continuous variables are presented as mean (SD)

Discussions

This study explored the influence of IOS parameters across varying BMI levels in patients with asthma, COPD (with or without asthma), other lung diseases, and healthy controls. Our findings reveal that both obesity and obstructive lung diseases, such as asthma and COPD, independently correlate with small airway dysfunction (SAD), with obesity exerting a more profound effect on IOS parameters than respiratory disease alone. These results align with previous studies and provide critical insights into the compounded impact of BMI and lung disease on small airways and respiratory health.

Across all diagnostic groups, $R_{5\text{-}20}$, A_X, and Fres emerged as the most impactful variables in predicting BMI-related outcomes, as reflected by high Mean Decrease Accuracy (MDA > 7.0) values. This consistency highlights their critical roles in enhancing model accuracy and minimizing classification errors, either individually or through interaction effects, underscoring their broad relevance across diverse patient profiles. $R_{5\text{-}20}$, which measures respiratory resistance, and A_X, reflecting

airway reactance, proved especially valuable in assessing small airway function, while Fres contributed to the evaluation of overall airway mechanics. However, the relatively low Mean Decrease Gini (MDG) values for these variables suggest that their predictive power likely stems from interaction effects rather than strong independent influence. This aligns with our broader conclusion that both obesity and lung disease significantly influence small airway function, but their combined effects, mediated by complex interactions among IOS parameters; yield the most accurate predictions.

This observation is consistent with findings by Dixon et al. [4], who reported a pronounced impact of obesity on IOS parameters among asthmatic patients with high BMI. The distinctive characteristics of their control group (notably low IOS values) compared to ours and other studies [18, 19], might amplify obesity's effects on IOS measures in their sample, underscoring the importance of careful control group selection. Similarly, Oppenheimer et al. [20] noted a substantial increase in $R_{5\text{-}20}$ among obese individuals with self-reported asthma compared to controls, reinforcing the role of obesity in narrowing airways, even in the absence of a formal respiratory disease diagnosis.

In studies focused on severe asthma, such as that by Chan et al. [2], obesity's impact on IOS parameters parallels our findings across all asthma severities, while Albuquerque et al. [3] observed that obesity in patients without lung disease elevates IOS parameters like R_5%, $R_{5\text{-}20}$, and Fres. This effect is likely due to reduced functional residual capacity (FRC), promoting airway narrowing and closure, with metabolic inflammation in "obese asthma" possibly exacerbating airway hyperresponsiveness [21].

Our findings suggest that integrating IOS measurements into routine spirometry may enhance detection of SAD, particularly in patients with high BMI, as IOS can reveal respiratory dysfunction where spirometry alone might not [22, 23]. Notably, the improvements in IOS following weight loss post-bariatric surgery [20], further support its potential as a sensitive marker of respiratory function, especially in patients with higher BMI. Additionally, IOS has shown sensitivity in identifying uncontrolled asthma [24–26], underscoring its clinical relevance for detecting subtle airway abnormalities.

Obstructive sleep apnea (OSA) is a condition marked by recurrent upper airway obstruction and is commonly associated with obesity [27]. OSA is linked to increased R_5 and decreased X_5 - even when patients are awake and in seated position [28, 29]. Güngördü et al. examined IOS indices between obese and non-obese patients with OSA and found significantly higher R_5, $R_{5\text{-}20}$, A_X, and Fres values in the obese group compared to the non-obese counterparts [29]. However, no statistically significant differences were observed in R_{20}. Their findings suggest that both OSA and obesity may contribute to small airway dysfunction. Our results further support a link between OSA and SAD; however, the limited number of patients prevented us from determining whether this association is independent.

Future studies should explore the interplay between OSA, COPD, asthma and obesity - considering body composition – to better understand their combined impact on small airways function.

Nevertheless, further research is needed to establish IOS parameters as independent predictors of respiratory disease. While $R_{5\text{-}20}$, A_X, and Fres consistently contributed to predictive models, other variables like Gender and R_5% had variable impacts across patient groups, suggesting potential for more tailored models. Future studies examining interaction effects could clarify IOS parameters' role in personalized respiratory assessment and treatment.

Strengths and limitations

This study's real-life design, featuring a broad and representative sample, enhances generalizability. However, the absence of specific data on central vs. peripheral obesity or body composition (fat vs. fat-free mass) represents a limitation, as central obesity has been linked more closely to FRC and expiratory reserve volume (ERV) reductions [22, 30]. Another potential limitation of our study is the lack of data on OSA in those patients with BMI less than 30 kg/m^2, which may influence IOS parameters. Additionally, while asthma diagnoses were confirmed by pulmonary specialists, some patients may not align with clinical trial eligibility criteria, potentially limiting comparability with rigorously controlled samples [31, 32]. Furthermore, the absence of disease severity scores for asthma is a limitation of our study, as disease severity may influence IOS parameters [33]. Intrabreath oscillometry is a highly sensitive tool for evaluating disease control in adults with severe asthma [33]. However, we have incorporated Fe-NO and FEV_1, which are associated with asthma activity [34].

Conclusions

This study underscores the significant influence of obesity on respiratory mechanics, particularly in relation to small airway dysfunction (SAD), with the effects most pronounced in individuals with asthma, COPD, or both. Our findings support previous research [18–20], by indicating that obesity not only compounds the airway limitations caused by respiratory diseases but also introduces additional restrictions independently. IOS parameters; especially $R_{5\text{-}20}$, A_X, and Fres; emerged as high-impact variables in predicting BMI-related outcomes across all diagnostic groups, demonstrating strong utility in

enhancing model accuracy and capturing subtle airway alterations that may otherwise be undetectable with spirometry alone.

The consistently high Mean Decrease Accuracy (MDA) values for R_{5-20}, A_X, and Fres highlight their importance in predictive accuracy across diverse patient profiles, although their lower Mean Decrease Gini (MDG) values suggest that interaction effects likely drive their predictive contributions. These findings suggest that integrating IOS into routine clinical practice, in conjunction with spirometry, could be particularly beneficial for patients with obesity or respiratory symptoms, even when spirometry results appear normal. Further research examining the relationship between IOS parameters and specific body composition factors, particularly central fat distribution, could clarify the role of central obesity in amplifying small airway limitations. Additionally, future studies exploring the predictive potential of IOS parameters for clinical outcomes in obese patients with respiratory diseases may inform more targeted interventions, such as weight management strategies, that could improve respiratory health and overall quality of life.

Abbreviations

IOS	Impulse Oscillometry System
BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
OSA	Obstructive Sleep Apnea
SAD	Small Airway Dysfunction
R_5	Resistance at 5 Hz
R_{20}	Resistance at 20 Hz
R_{5-20}	Difference between Resistance at 5 Hz and 20 Hz (Peripheral Airway Resistance)
A_X	Reactance Area
FRC	Functional Residual Capacity
ERV	Expiratory Reserve Volume
FEV_1	Forced Expiratory Volume in 1 s
DXA	Dual-energy X-ray Absorptiometry
MDA	Mean Decrease Accuracy
MDG	Mean Decrease Gini
Fe-NO	Fractional Exhaled Nitric Oxide
FVC	Forced Vital Capacity
TLC	Total Lung Capacity
D_{LCO}	Diffusion Capacity for Carbon Monoxide
PD_{20}	Dose of Methacholine Resulting in 20% Decrease in FEV1

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
Author 1 was responsible for data collection, contributed to the study design, performed part of the data analysis, and participated in manuscript preparation and writing. Authors 2 and 3 contributed to the interpretation of the results and provided critical insights. Author 4 performed the data analysis and wrote the most part of the manuscript. All authors read, reviewed and approved the final manuscript.

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Data availability
The dataset supporting the conclusions of this article is avalable on Figshare and can be accessed at: https://figshare.com/articles/dataset/This_dataset_contains_information_related_to_physiological_measurements_and_Body_Mass_Index_BMI_among_individuals_It_has_been_used_for_statistical_analyses_to_generate_insights_into_various_health_and_physiological_factors_/28297205?file=51984299.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki. The Regional Health Research Ethics Committees in the Capital Region in Denmark waived the need for formal ethical approval of the project (no. F-24081729). Informed consent from participants in this retrospective study was not obtained.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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