ORIGINAL ARTICLE PULMONOLOGY

NORTH CLIN ISTANB 2025;12(6):682–689
doi: 10.14744/nci.2025.95777

The relationship of impulse oscillometry results with respiratory muscle strength and exercise capacity in patients with emphysema

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ABSTRACT

OBJECTIVE: Assessment of small airway function, respiratory mechanics, respiratory muscle strength, and exercise capacity plays a crucial role in both pharmacological and non-pharmacological treatment planning, as well as in evaluating treatment efficacy in patients with emphysema. Impulse oscillometry (IOS) allows for the evaluation of the physiological properties of both large and small airways, along with lung parenchyma involvement. This study aimed to in*vestigate small airway function and respiratory mechanics related to lung parenchyma using IOS and to examine their relationship with respiratory muscle strength and exercise capacity in emphysema patients.

METHODS: Thirty patients diagnosed with emphysema by high-resolution computed tomography (HRCT) and airway obstruction based on GOLD (Global Initiative for Chronic Obstructive Lung Diseases) spirometric criteria were included in this study. Demographic characteristics, IOS parameters, respiratory muscle strength (MIP, MEP), and exercise capacity (Endurance Shuttle Walk Test [ESWT], VO_2 peak) were analyzed. The study was approved by the Ankara Kecioren Training and Research Hospital Ethics Committee (approval number: 2012-KAEK-15/2210) and conducted in accordance with the Declaration of Helsinki.

RESULTS: There was a statistically significant positive correlation between GOLD spirometric stages and IOS parameters, particularly the resistance difference at 5 and 20 Hz (R5-R20) and reactance area (AX). A significant negative correlation was observed between GOLD stages and reactance at 5 Hz (X5), maximal inspiratory pressure (MIP), ESWT, and VO_2 peak. Additionally, MIP was negatively correlated with R5, R5-R20, and AX, but positively correlated with X5. VO_2 peak was negatively correlated with R5, R20, R5-R20, and AX, while it was positively correlated with X5, MIP, and maximal expiratory pressure (MEP). ESWT was negatively correlated with R5, R5-R20, and AX, and positively correlated with X5.

CONCLUSION: This study demonstrated that emphysema involves impairment of small airways and lung parenchyma, which can be effectively assessed using IOS. The impaired respiratory mechanics significantly decrease exercise capacity. Prioritizing therapies that target small airways may enhance pharmacological outcomes, and the observed correlation between IOS parameters and respiratory muscle strength may provide guidance for inhaler selection in clinical practice.

Keywords: Emphysema; exercise capacity; muscle strength; oscillometry.

Cite this article as: *Kosak H, Satar S, Ergun P. The relationship of impulse oscillometry results with respiratory muscle strength and exercise capacity in patients with emphysema. North Clin Istanb 2025;12(6):682–689.*

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease characterized by persistent airflow limitation and respiratory symptoms, related to structural changes in the airways and alveoli resulting from long-term exposure to harmful gases and particles [1]. The primary patho-

Received: June 27, 2025 *Revised:* July 15, 2025 *Accepted:* August 31, 2025 *Online:* December 26, 2025

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physiological feature of COPD, namely airflow limitation, arises from small airway disease and lung parenchymal destruction (emphysema), both of which can vary between individuals [1].

Emphysema, a clinical and pathological phenotype of COPD, is characterized by the irreversible enlargement of airspaces distal to the terminal bronchioles and destruction of the surrounding lung parenchyma [2]. In such patients, pathophysiological changes including decreased elastic recoil, mechanical disadvantage of the diaphragm due to hyperinflation, reduced dynamic compliance, and peripheral muscle weakness due to chronic inflammation are commonly observed. These mechanisms contribute to the development of clinical manifestations such as dyspnea, reduced exercise capacity, and impaired quality of life [3, 4].

Impulse oscillometry (IOS) is a technique that evaluates respiratory function using sound waves, allowing measurement of the physiological properties of both large and small airways, as well as lung parenchyma. Although applicable to all age groups due to its independence from patient effort and cooperation, the literature regarding its use in adult pulmonary diseases remains limited [5, 6].

Studies have shown that, in addition to alveolar wall damage, there is a loss of elastic fibers in the small conducting airways. This suggests that structural damage is not limited to the alveoli but also affects the small airways [7]. In emphysema, evaluating small airway function, respiratory mechanics, respiratory muscle strength, and exercise capacity is crucial for determining both pharmacological and non-pharmacological treatment needs, as well as for monitoring treatment effectiveness.

This prospective observational study aims to assess small airway functions and lung parenchyma-related respiratory mechanics using IOS in individuals diagnosed with emphysema, and to investigate the relationship between these results and respiratory muscle strength and exercise capacity.

Highlight key points

- IOS effectively reflects peripheral airway dysfunction in emphysema.
- Key parameters (X5, AX, R5–R20) correlate with inspiratory muscle strength and exercise capacity.
- Reactance values (X5, AX) are superior to resistance values for assessing disease severity.

MATERIALS AND METHODS

Study Population

This study was conducted with 30 patients over the age of 18 who presented to the Pulmonary Rehabilitation Clinic of the University of Health Sciences, Ankara Ataturk Sanatorium Training and Research Hospital between January 28, 2021, and March 2021, and were diagnosed with emphysema by high-resolution computed tomography (HRCT).

Patients were excluded if they were undergoing treatment for malignancy, had contraindications for exercise testing or respiratory muscle strength measurement [8, 9], exhibited significant parenchymal pathology other than emphysema on HRCT, or were unable to provide informed consent.

For each participant, data were collected on age, sex, comorbidities, smoking history (pack-years), and the use of long-term oxygen therapy. Pulmonary function test (PFT) results were achieved from patient records, and values for forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio were recorded. Based on these results, each patient was staged according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and documented in the study form.

The activity level causing dyspnea was assessed for all patients, and the results were evaluated using the Modified Medical Research Council (mMRC) dyspnea scale. Each patient's score on the scale was recorded in the study form [10].

Throughout the study, infection control measures were rigorously implemented. A minimum interval of 15 minutes was maintained between each patient, and the testing room was regularly ventilated. Single-use mouthpieces and filters were used for each test and were disposed of in medical waste bins immediately afterward. Devices used during testing were disinfected in accordance with the manufacturer's instructions.

This study was approved by the Clinical Research Ethics Committee of Ankara Kecioren Training and Research Hospital on 26 January 2021 (approval number: 2012-KAEK-15/2210). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants in compliance with institutional and national ethical guidelines.

Impulse Oscillometry

IOS is a method used to assess respiratory function by measuring airway resistance (R) and reactance (X) parameters through sound waves. IOS measurements are performed during tidal breathing [5]. The test is conducted using a device system comprising a loudspeaker, adapter, pneumotachograph, transducer, and computer. Low-pressure sound waves of various frequencies, generated by the loudspeaker, are delivered to the airways via the mouth. These sound waves superimpose onto the patient's spontaneous breathing, and the signals reflected from the airways are analyzed using software linked to pressure and flow transducers. The frequency of sound waves used in IOS typically ranges from 5 to 35 Hz (Hertz).

Impedance (Z), which reflects the overall mechanical response of the respiratory system, represents the total force required to transmit a pressure wave and consists of R and X components [11].

Resistance is defined as the energy required to maintain airflow in the area through which the sound wave is transmitted. Total airway resistance is evaluated using the resistance at 5 Hz (R5), while proximal airway resistance is represented by resistance at 20 Hz (R20). Peripheral airway resistance is calculated as the difference between R5 and R20 Hz (R5–R20) [11].

The area of reactance (AX) represents the area under the reactance curve between 5 Hz and the resonant frequency (Fres), providing information about the elastic properties of the respiratory system.

In this study, respiratory function was assessed using the Carefusion Vyntus Jaeger IOS device (Germany). The IOS device was checked and calibrated daily. For each patient, values for R5, R20, R5–R20, reactance at 5 Hz (X5) and AX were obtained and recorded in the study form [5].

To avoid influencing patient performance, IOS measurements were conducted prior to exercise testing. All tests were performed in accordance with the guidelines of the European Respiratory Society (ERS) [12]. During the test, patients were seated in an upright and comfortable position with their head in a neutral position. The mouthpiece was fully sealed with the lips to prevent air leakage. To compensate for the compliance of the cheeks, the patients placed their hands firmly over them, and the nose was occluded using a nasal clip.

Respiratory Muscle Strength

Respiratory muscle strength was assessed using a portable electronic mouth pressure measurement device (Micro RPM, CareFusion, UK). For the measurement of maximal inspiratory pressure (MIP), patients were instructed to perform a maximal inspiratory effort lasting 1–3 seconds following a full expiration, while wearing a nose clip to occlude nasal airflow and sealing the mouthpiece tightly with their lips. For the measurement of maximal expiratory pressure (MEP), after a full inspiration, patients were similarly asked to perform a maximal expiratory effort lasting 1–3 seconds, using a nose clip and ensuring proper sealing of the mouthpiece.

Assessment Of Exercise Capacity

The Incremental Shuttle Walk Test (ISWT) and the Endurance Shuttle Walk Test (ESWT) were used to assess the patients' exercise capacity. Both tests were performed in accordance with the 2014 guidelines of the ERS [13]. The tests were conducted indoors on a flat, hard surface. Two cones were placed 9 meters apart.

Patients were instructed to start walking upon hearing an audio signal from a speaker, walk around the cone, wait for the next signal, and continue walking back and forth between the cones at progressively increasing speeds according to the audible signals.

Before the tests, patients were given a minimum of 15 minutes to rest. Baseline measurements were taken, including resting blood pressure, heart rate, oxygen saturation, dyspnea, and fatigue scores.

At the end of the test, the patient was seated and post-exercise measurements were recorded, including oxygen saturation, heart rate, blood pressure, and the severity of dyspnea and fatigue. The total distance walked and the estimated predicted peak oxygen uptake (VO2 peak) value calculated from this distance are recorded. Based on 85% of the estimated VO_2 peak, the target walking speed was determined. The patient was then instructed to walk between the cones at this fixed speed, guided by audio signals. The total walking duration was recorded in the study form.

Statistical Analysis

The demographic and clinical characteristics of patients who met the study criteria were evaluated using descriptive statistical values such as frequency (n), percentage (%), mean, and standard deviation. The relationship between IOS results and respiratory muscle strength and

TABLE 1. Results of patients

	Mean±SD	Median	Minimum	Maximum
Age (year)	59.17±8.26	58.50	46	75
Smoking history (p/y)	43.43±26.61	40	0	120
mMRC score	1.70±0.53	2	1	3
FEV_1 %	59.03±24.55	62.00	25	115
FVC %	77.90±20.34	80.50	30	125
FEV_1/FVC	58.43±15.65	61.10	26.9	87.76
GOLD stage	2.30±1.05	2	1	4
R5 (kPa/L/s)	0.45±0.17	0.44	0.20	1.00
R20 (kPa/L/s)	0.28±0.8	0.27	0.16	0.45
R5-R20 (kPa/L/s)	0.16±0.14	0.14	0.01	0.72
X5 (kPa/L/s)	-0.17±0.10	-0.17	-0.39	0.02
MIP (cmH_2O)	78.27±16.07	81	50	103
MEP (cmH_2O)	116.40±26.71	113	60	166
ISWT (meter)	371.33±119.42	365	180	600
ESWT (minute)	9.33±6.87	6	2.15	20
VO_2 peak (ml/kg/min)	13.47±2.99	13.31	8.69	19.19

p/y: Package/year; mMRC: Modified Medical Research Council; FEV_1: Forced expiratory volume in one second; FVC: Forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; IOS: Impulse oscillometry; R5; Resistance at 5 Hz; R20: Resistance at 20 Hz; R5-R20:Difference between R5 and R20; X5: Reactance at 5 Hz; AX: The area of reactance; MIP: Maximal inspiratory pressure; MEP: Maximal expiratory pressure; ISWT: Incremental Shuttle Walk Test; ESWT: Endurance Shuttle Walk Test; VO_2 peak: Predict peak oxygen uptake; SD: Standard deviation.

exercise capacity was analyzed using Pearson correlation analysis. In addition, the assumptions of normal distribution were verified using the Shapiro-Wilk test prior to performing Pearson correlation and regression analyses. To assess whether IOS parameters could predict respiratory muscle strength and exercise capacity scores, simple linear regression analysis was performed.

Given the limited number of studies directly focusing on the subject of this research, no reliable reference for the expected effect size could be identified. Consequently, it was not feasible to define a hypothetical effect size for conducting a formal power analysis. The study was therefore designed based on available resources and field conditions. Due to time and financial constraints, the analysis was planned to include data from a minimum of 30 participants. This sample size was determined by considering the minimum number of participants required to allow for the valid application of parametric statistical methods under the study conditions. This limitation confers a pilot character to the study and is intended to provide preliminary insights that may guide future research involving larger sample sizes.

A significance level of $p<0.05$ was considered statistically significant for all analyses. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 30 patients (29 males, 1 female) who presented to the pulmonary rehabilitation clinic and met the study criteria were included. The average smoking history was 43.43±26.61 pack-years, with a median value of 40 pack-years (Table 1).

According to GOLD spirometric staging based on FEV_1%, 8 patients (26.7%) were in stage 1, 10 (33.3%) in stage 2,7 (23.3%) in stage 3, and 5 (16.7%) in stage 4 (Table 1).

Among the identified comorbidities were congestive heart failure in 2 patients (6.7%), hyperlipidemia in 2 (6.7%), diabetes mellitus (DM) in 4 (13.3%), benign prostatic hyperplasia (BPH) in 3 (10%), hypertension in 9 (30%), and atherosclerotic heart disease (ASHD) in 6 (20%). Four patients were receiving long-term oxygen therapy.

Table 2. Correlation between impulse oscillometry parameterswith mMRC, GOLD spirometric stages, respiratory muscle strength and exercise capacity results of patients

	R5 (kPa/L/s)	R20 (kPa/L/s)	R5-R20 (kPa/L/s)	X5 (kPa/L/s)	AX
mMRC score					
r	0.130	0.027	0.149	-0.270	0.198
p	0.492	0.887	0.432	0.149	0.294
GOLD stage					
r	0.244	-0.100	0.401	-0.443	0.500
p	0.193	0.597	**0.028**	**0.014**	**0.005**
MIP (cmH_2O)					
r	-0.426	-0.277	-0.389	0.606	-0.526
p	**0.019**	0.138	**0.034**	**<0.001**	**0.003**
MEP (cmH_2O)					
r	-0.305	-0.335	-0.255	0.342	-0.305
p	0.101	0.070	0.174	0.064	0.101
ISWT (meter)					
r	-0.584	-0.372	-0.406	0.454	-0.502
p	**<0.001**	**0.043**	**0.026**	**0.012**	**0.005**
ESWT (minute)					
r	-0.502	-0.162	-0.391	0.379	-0.472
p	**0.005**	0.391	**0.032**	**0.039**	**0.008**
VO_2 peak (ml/kg/min)					
r	-0.584	-0.372	-0.406	0.454	-0.502
p	**<0.001**	**0.043**	**0.026**	**0.012**	**0.005**

mMRC: Modified Medical Research Council; GOLD: Global Initiative for Chronic Obstructive Lung Disease; MIP: Maximal inspiratory pressure; MEP: Maximal expiratory pressure; ISWT: Incremental Shuttle Walk Test; ESWT: Endurance Shuttle Walk Test; VO_2 peak: Predict peak oxygen uptake; IOS: Impulse oscillometry; R5; Resistance at 5 Hz; R20: Resistance at 20 Hz; R5-R20: Difference between R5 and R20; X5: Reactance at 5 Hz; AX: The area of reactance; r: Pearson correlation. Statistically significant p-values were given as bold.

The mean R5–R20 value was 0.16±0.14 kPa/L/s, and in 80% of the patients this value was above 0.07. The mean AX value was 1.84±1.36, with 86.6% of patients having an AX value above 0.33 (Table 1).

The mean MIP was 78.27±16.07 cmH_2O; no patients had a value below 30 cmH_2O. The mean MEP was 116.40±26.71 cmH_2O, with no patients scoring below 40 cmH_2O (Table 1).

According to the statistical analysis results (Table 2).

A significant negative correlation was found only between smoking history and the X5 parameter (p=0.046, r=-0.367).

Although observational associations were noted between dyspnea severity and increased airway resistance, decreased elastic recoil, and compliance, no statistically significant relationship was found between mMRC dyspnea score and IOS parameters (p>0.05).

Significant positive correlations were identified between GOLD stage and both R5–R20 (p=0.028, r=0.401) and AX (p=0.005, r=0.500), while a significant negative correlation was found with X5 (p=0.014, r=-0.443).

A significant negative correlation was observed between GOLD stage and MIP (p=0.045, r=-0.369).

Significant negative correlations were found between GOLD stage and ISWT distance (p=0.025, r=-0.409), ESWT duration (p=0.015, r=-0.441), and VO_2 peak (p=0.025, r=-0.409).

MIP showed significant negative correlations with R5 (p=0.019, r=-0.426), R5–R20 (p=0.034, r=-0.389),

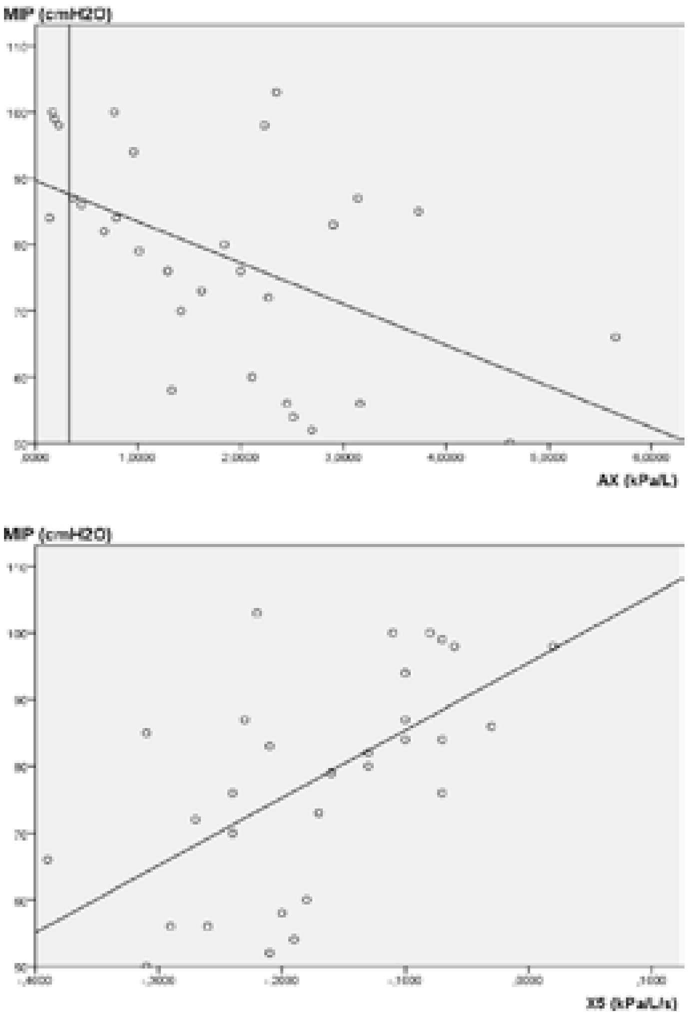

FIGURE 1. Correlation between X5 and AX with MIP. Scatter plot.

MIP: Maximal inspiratory pressure; X5: Reactance at 5 Hz; AX: Reactance area.

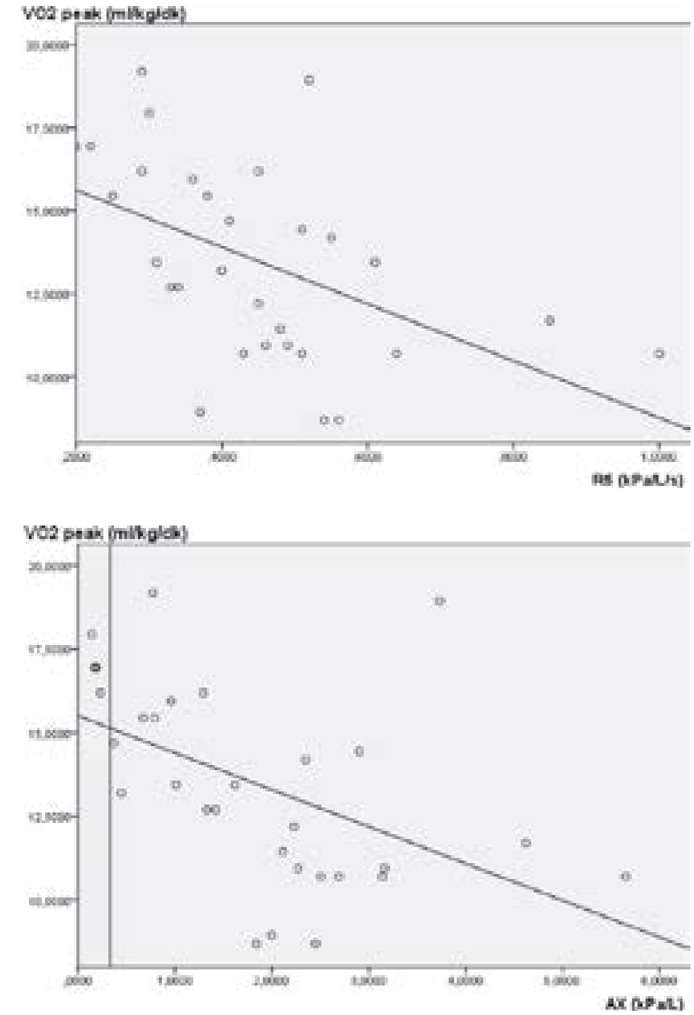

FIGURE 2. Correlation between R5 and AX with VO2 peak. Scatter plot.

R5: Resistance difference at 5; AX: Reactance area; VO2 peak: Predict peak oxygen uptake.

and AX ($p=0.003$, $r=-0.526$), and a significant positive correlation with X5 ($p<0.001$, $r=0.606$) (Fig. 1).

No statistically significant relationship was found between IOS parameters and MEP ($p>0.05$).

Significant positive correlations were observed between both MIP and MEP with VO_2 peak ($p<0.001$, $r=0.637$; $p=0.039$, $r=0.379$, respectively).

VO_2 peak showed significant negative correlations with R5 ($p<0.001$, $r=-0.584$), R20 ($p=0.043$, $r=-0.372$), R5–R20 ($p=0.026$, $r=-0.406$), and AX ($p=0.005$, $r=-0.502$); and a significant positive correlation with X5 ($p=0.012$, $r=0.454$) (Fig. 2).

ESWT duration was significantly negatively correlated with R5 ($p=0.005$, $r=-0.502$), R5–R20 ($p=0.032$, $r=-0.391$), and AX ($p=0.008$, $r=-0.472$); and positively correlated with X5 ($p=0.039$, $r=0.379$).

DISCUSSION

This study investigated the relationship between IOS parameters, respiratory muscle strength and exercise capacity in patients with emphysema. The greatest changes were observed in X5, AX, and R5–R20, respectively. These results suggest that small airways, elastic recoil, and compliance are more prominently affected than total airway resistance. It was also demonstrated that the increase in resistance is more pronounced in small airways compared to large airways.

The need for evaluating small airways and respiratory mechanics in patients with emphysema has brought attention to the use of the IOS, which allows measurement during tidal breathing with minimal patient cooperation. Although studies on the use of IOS in COPD have increased in recent years, the number of studies focusing specifically on IOS-based assessments of respiratory function and mechanics in emphysematous patients remains limited in the literature [11].

Li et al. [14] reported no significant correlation between mMRC dyspnea scores and pulmonary function test results; however, correlations were reported for IOS parameters R5, R5–R20, and AX. A significant relationship was also identified between CAT (COPD Assessment Test) scores and R5. In the present study, although increased airway resistance, reduced elastic recoil, and decreased compliance were associated with greater dyspnea perception, no statistically significant correlation was found between mMRC scores and IOS parameters. This may be explained by the unidimensional nature of the mMRC scale and the influence of extrapulmonary factors on dyspnea perception.

Gong et al. [15] have suggested that changes in X5 may be useful for monitoring COPD progression. Several studies have reported that reactance measurements are more strongly correlated with pulmonary function than resistance measurements [15]. Consistent with this, our study identified significant correlations between GOLD spirometric stages and X5, AX, and R5–R20, with higher correlation coefficients for reactance parameters compared to resistance parameters. These findings indicate that as disease severity increases, small airway resistance increases while elastic recoil decreases.

A negative association was observed between GOLD stage and exercise capacity. Notably, the correlation coefficient was higher for endurance test duration compared to VO_2 peak, supporting the hypothesis that dynamic hyperinflation is a major mechanism of dyspnea in emphysematous patients [7].

In the study by Kim et al. [16], reductions in MIP and MEP values were reported in COPD patients, with a significant negative correlation between MIP and GOLD stage, while no significant correlation was found for MEP. Similarly, in our study, MIP decreased with advancing GOLD stage, while MEP remained unchanged.

Frantz et al. [17] observed increased pulmonary resistance and reduced reactance in symptomatic COPD patients despite normal spirometric findings. In our study, respiratory muscle strength and exercise capacity were compared with both IOS and spirometry data, and IOS parameters showed higher correlation coefficients.

In the study by Khalil et al. [18], no significant correlation was found between spirometry and MIP; however, a significant correlation was identified between MIP and six-minute walking distance. In our study, MIP was correlated with all IOS parameters except R20, with the strongest correlation observed with X5. This suggests that respiratory muscle strength may be more closely associated with the elastic properties of the lungs and air trapping.

It is well-established that expiratory muscle weakness in COPD is associated with systemic inflammation and has limited correlation with pulmonary function, being more closely linked to cough effectiveness. Consistent with this, our study found no statistically significant correlation between MEP and IOS parameters.

As the disease progresses, functional impairment and exercise limitation are known to increase [19]. The associations found between VO_2 peak and IOS parameters in this study indicate that impaired respiratory mechanics play a key role in reduced exercise capacity in emphysema.

This study has several limitations that should be acknowledged. Being conducted at a single center may limit the generalizability of the findings. In addition, time and financial constraints restricted both the sample size and the overall scope of the study. The predominance of male participants, which reflects the demographic characteristics commonly seen in COPD populations, may have introduced a gender-based sampling bias. The lack of longitudinal follow-up data hinders the ability to evaluate changes in IOS parameters or clinical outcomes over time. Moreover, the study was conducted during the COVID-19 pandemic, which could have influenced patient access, routine clinical workflows, and overall participation.

Conclusion

These results indicate that, in patients with emphysema, not only parenchymal destruction but also small airways are affected, and impairments in respiratory mechanics involving peripheral airways can be assessed using IOS. Additionally, the findings support the notion that impaired respiratory mechanics significantly contribute to reduced exercise capacity in emphysema, highlighting the importance of targeting small airways in pharmacological treatment strategies. The correlation between IOS parameters and inspiratory muscle strength may serve as a guide in selecting inhaler therapies. IOS can be utilized to identify ventilatory limitations indicating pulmonary rehabilitation and to evaluate treatment efficacy in emphysema patients. Furthermore, IOS parameters such as X5 and AX may potentially be used in combination with plethysmographic methods for patient selection and assessing changes in respiratory mechanics following bronchoscopic lung volume reduction procedures.

Ethics Committee Approval: The Ankara Kecioren Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.01.2021, number: 22012-KAEK-15/2210).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Use of AI for Writing Assistance: The authors declared that artificial intelligence–assisted technologies (such as large language models, chatbots, or image generators) were not used in the preparation of this study.

Authorship Contributions: Concept – HK, SS, PE; Design – HK, SS, PE; Supervision – HK, SS, PE; Fundings – HK, SS, PE; Materials – HK, SS, PE; Data collection and/or processing – HK, SS, PE; Analysis and/or interpretation – HK, SS, PE; Literature search – HK, SS, PE; Writing – HK, SS, PE; Critical review – HK, SS, PE.

Peer-review: Externally peer-reviewed.

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