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ORIGINAL RESEARCH

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Impulse oscillometry in patients with persistent post-COVID-19 symptoms: A retrospective study

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Abstract

Introduction: Impaired lung function has been observed in patients following COVID-19 infection, with studies reporting persistent lung volume and diffusing capacity impairments. Some studies have demonstrated significantly higher small airway resistance in COVID-19 positive cases. This retrospective study aims to examine impulse oscillometry (IOS) data of patients with persistent symptoms after COVID-19 infection, focusing on the relationship between time and symptoms.

Material and Method: The study analyzed data from adult patients with persistent symptoms who underwent IOS testing within and after 84 days from the diagnosis date.

Result: The results showed that patients within 84 days and those between 31 and 84 days had higher small airway resistance values, indicating peripheral airway disease. Patients with dyspnea exhibited higher IOS values compared to those with cough symptoms, suggesting more significant impairment in the peripheral airways.

Conclusion: The study highlights the importance of using comprehensive diagnostic tools like IOS to assess respiratory impairments in post-COVID-19 patients, particularly in the small airways. Understanding the relationship between time and symptoms can provide valuable insights for the treatment of peripheral airway dysfunction in post-COVID-19 patients.

KEYWORDS

COVID-19, impulse oscillometry, lung function, post-COVID-19 symptoms, small airways

1 | INTRODUCTION

Numerous articles have reported impaired lung function in patients following Coronavirus Disease 2019 (COVID-19) infection. Studies have shown lung volume and diffusing capacity impairment persisting up to 6 months after the acute infection.[1,2] Impulse oscillometry (IOS) is a noninvasive method used to measure airway resistance without generating potentially infective aerosols. Certain investigations have yielded compelling evidence of significantly elevated small airway resistance in COVID-19 positive individuals both during the acute infection phase and after a 2-month follow-up,[3] as well as a 40-day follow-up.[4] Meanwhile, alternative research has directed its focus towards chest imaging and lung ultrasound in post-COVID-19 patients.[5,6] However, other studies did not find a significant increase in small airway resistance among COVID-19 inpatients.[7] In this retrospective study, we examine the IOS data of patients with persistent symptoms after COVID-19 infection in our hospital, focusing on the relationship between time and symptoms.

2 | MATERIALS AND METHODS

2.1 | Subject characteristics and design of study

This retrospective study reviewed the records of adult patients (≥20 years) with persistent symptoms following COVID-19 infection who underwent IOS testing at the Changhua Christian Hospital Pulmonary Function Laboratory between October 1, 2019, and December 31, 2022. Patients who underwent IOS examination more than 1 year after contracting COVID-19 were excluded. Basic demographic information was collected through chart review (Table 1). By world health organization (WHO) statement, post COVID-19 condition is usually diagnosed by a healthcare provider at least 3 months after a patient falls ill with COVID-19. This 3-month period allows healthcare providers to rule out the usual recovery period from an acute illness. The British Thoracic Society (BTS) guide recommends the evaluation of pulmonary function tests at 3 months post-discharge, especially at follow-up with patients suspected of having an interstitial disease.[8] Hence, the data were divided into two groups: one within 84 days from the diagnosis date to the examination date, and the other group after 84 days (Table 2). Based on numerous articles that discuss post-COVID-19 changes in lung function, the observed timeline typically spans around 1 month.[9–12] Within the group observed over an 84-day period, further categorization was undertaken, dividing the data into two subsets: the first encompassing up to 30 days, and the second covering the 31–84 day interval, for subsequent analysis (Table 3). Additionally, we categorized patients based on their subjective symptoms reported during consultation, including cough, dyspnea, and chest tightness. We aggregated the count of patients exhibiting these symptoms and conducted group-wise comparisons (Table 3). Symptom severity was not quantified.

TABLE 1 Basic characteristics of the patients with persistent post-COVID-19 symptoms.

	N	%
Age, mean ± SD (year)	87	47.63 ± 14.29
High, mean ± SD (cm)	80	162.06 ± 8.18
Weight, mean ± SD (kg)	74	65.46 ± 11.35
BMI, mean ± SD (kg/m^2)	74	24.88 ± 4.19
gender		
female	59	67.8
male	28	32.2
cough		
no	19	21.8
yes	68	78.2
Dyspnea		
no	31	35.6
yes	56	64.4
Chest tightness		
no	55	63.2
yes	32	36.8
IOS data		
R5Hz, mean ± SD (kPa/(L/s))	87	0.40 ± 0.11
R20Hz, mean ± SDSD (kPa/(L/s))	87	0.31 ± 0.08
X5Hz, mean ± SDSD (kPa/(L/s))	87	−0.10 ± 0.14
R5-R20, mean ± SD (kPa/(L/s))	87	0.09 ± 0.06
F_{res}, mean ± SD (1/s)	87	15.38 ± 4.06
AX, mean ± SD (kPa/L)	87	0.65 ± 0.50
FVC, mean ± SD (L)	87	3.19 ± 0.89
FEV1, mean ± SD (L)	87	2.70 ± 0.79
FEV1/FVC(%), mean ± SD (%)	87	106.20 ± 8.18
MMEF25-75% (%), mean ± SD (%)	87	86.82 ± 28.67

Abbreviations: IOS, impulse oscillometry; SD, Std. Deviation.

2.2 | Impulse oscillometry

Impulse oscillometry measurements were performed using the Jaeger Master Screen-IOS system, following the recommendations of the European Respiratory Society (ERS). Parameters such as the difference between resistance at 5 Hz and resistance at 20 Hz (R5–R20), respiratory system reactance (X5), resonance frequency (F_{res}), and the area of reactance (AX) were recorded. Small airway disease was defined as R5-R20 > 0.07 kPa/(L/s), X5 < −0.12 kPa/(L/s), F_{res} > 14.14 1/s, and AX > 0.44 kPa/L based on data from a central medical center in Taiwan.[13]

2.3 | Spirometry

Spirometry (Jaeger Masterscreen Body/Diff) was performed immediately after IOS. Recorded parameters include: forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), maximum expiratory flow rate (MMEF25-75%), FEV1/FVC ratio.

2.4 | Statistical analysis

Descriptive analyses were conducted on the demographic data to provide a comprehensive characterization of the sample. Post-COVID-19 data were categorized into two groups based on clinical diagnosis: one group comprising patients examined within 84 days from the diagnosis date, and the other group consisting of patients examined after 84 days. Moreover, within the group examined within 84 days, further subgroups were created based on a time frame of approximately 30 days before and after the diagnosis date. To assess the differences in clinical numerical records (R5Hz, R20Hz, X5Hz, R5-R20, F_{res}, and AX) as measured by the Jaeger Master Screen-IOS system,

TABLE 2 IOS data of two groups within and after 84 days.

	within 84 days (*N* = 64)				after 84 days (*N* = 23)				
	Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		*p* value
Days	36.52	18.33	0.00	1.00	133.00	34.10	0.00	1.00	<0.001*
R5Hz	0.41	0.12	0.09	1.06	0.37	0.09	−0.26	0.78	0.28
R20Hz	0.32	0.08	0.07	1.02	0.30	0.07	−0.20	0.93	0.39
R5-R20	0.09[a]	0.07	0.06	1.07	0.08[a]	0.05	−0.17	0.78	0.41
X5Hz	−0.11	0.05	−0.10	0.39	−0.06	0.26	0.27	1.84	0.86
Fres	15.83[a]	4.23	0.11	1.04	14.10	3.31	−0.31	0.81	0.11
AX	0.69[a]	0.54	0.09	1.09	0.53[a]	0.33	−0.25	0.66	0.39
FVC	3.14	0.86	−0.05	0.97	3.32	0.98	0.15	1.10	0.58
FEV1	2.67	0.74	−0.05	0.93	2.81	0.94	0.13	1.19	0.88
FEV1/F (%)	106.71	8.27	0.00	1.00	104.77	7.90	0.00	1.00	0.35
FEV1/FVC (L)	0.85	0.07	0.05	1.00	0.84	0.07	−0.14	1.02	0.46
MMEF (%)	87.39	28.76	0.00	1.00	85.23	29.02	0.00	1.00	0.85

Abbreviations: IOS, impulse oscillometry; SD, Std. Deviation.
[a]Meet the definition of small airway disease.
*$p < 0.05$.

TABLE 3 IOS data of two groups within and after 30 days

	within 30 days (*n* = 29)				between 31 and 84 days (*n* = 35)				
	Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		*p* value
Days	20.52	7.34	−0.87	0.40	49.77	13.37	0.72	0.73	<0.001[b]
X5Hz	−0.11	0.05	−0.13	0.89	−0.12	0.05	0.11	1.08	0.437
R5-R20	0.09[a]	0.06	−0.09	0.83	0.10[a]	0.08	0.07	1.13	0.898
Fres	15.56[a]	4.07	−0.06	0.96	16.05[a]	4.41	0.05	1.04	0.756
AX	0.62[a]	0.46	−0.13	0.85	0.75[a]	0.60	0.10	1.11	0.571
FVC	3.32	0.89	0.21	1.03	3.00	0.82	−0.17	0.95	0.249
FEV1	2.90	0.79	0.32	1.07	2.47	0.64	−0.26	0.87	0.046[b]
FEV1/F (%)	109.33	8.15	0.32	0.98	104.54	7.84	−0.26	0.95	0.013[b]
FEV1/FVC (L)	0.88	0.07	0.36	1.03	0.83	0.06	−0.30	0.89	0.012[b]
MMEF (%)	97.65	30.31	0.36	1.05	78.89	24.73	−0.30	0.86	0.009[b]

Note. (*N* = 64).
Abbreviations: IOS, impulse oscillometry; SD, Std. Deviation.
[a]Meet the definition of small airway disease.
[b]$p < 0.05$.

between the two patient groups, the Mann-Whitney U test was employed. This statistical method is specifically designed for assessing non-normally distributed continuous variables. The effectiveness of IOS testing in detecting small airway diseases was evaluated by analyzing IOS data based on various combinations of post-COVID-19 symptoms (Patient's subjective feeling: cough, dyspnea, chest tightness). Statistical significance was defined as a two-sided *p*-value < 0.05.

3 | RESULT

Data from 87 patients with COVID-19 infection and postinfection IOS measurements were collected. Among them, 64 patients were enrolled in the group within 84 days, and 23 patients were enrolled in the group after 84 days. The mean values of R5–R20, F_{res}, and Ax in all 87 patients met the definition of small airway disease (Table 1).

Within the group within 84 days, the mean values of R5–R20, F_{res}, and Ax also met the definition of small airway disease. In the group after 84 days, the mean values of R5–R20 and Ax met the definition of small airway disease (Table 2). There is no statistical significance found between two groups. Before 84 days, the group displayed relatively low average values for lung function (FVC, FEV1, FEV1/FVC, FEV1/FVC(%)), accompanied by high airway resistance (R5, R20, R5–R20, X5, Fres, and Ax).

The mean values of R5–R20, F_{res}, and Ax met the definition of small airway disease both in the group within 30 days and the group within 31–84 days (Table 3).

The values of FEV1, FEV1/FVC, FEV1/FVC(%) and MMEF were observed to be significantly lower between 31 and 84 days as compared to the measurements taken within 30 days (Table 3).

4 | DISCUSSION

In our study, all 87 post COVID-19 infection patients demonstrated mean values of three out of four parameters that met the definition of small airway disease. However, spirometry did not indicate any signs of obstruction or restrictive lung disease, including MMEF25-75% (is used to evaluate airflow in peripheral airways).[14,15] These findings highlight the significance of assessing peripheral airway function using IOS in post COVID-19 patients with preserved spirometry. By utilizing IOS, we can gain valuable insights into the state of the small airways, which may be affected even in the absence of detectable abnormalities in traditional spirometry measurements. This emphasizes the importance of employing comprehensive diagnostic tools to capture the full spectrum of respiratory impairments in post COVID-19 patients.

We are aware that more values of R5-R20, F_{res}, and AX, indicate increased nonuniformity in airflow distribution in peripheral airway. More absolute value of X5, which reflects the more possibility small airway collapse.[16] Our findings indicate a tendency towards greater nonuniformity in the peripheral airway within the <84 days group, accompanied by relatively low average lung function, although statistical significance was not observed. The observed result might be due to differences in group sizes or the overall population not being adequately large.

Further analysis within the <84 days group revealed that the flow in the distal airway was more nonuniform in the 31–84 days subgroup compared to the group within 30 days, although statistical significance was not observed in this case either (Table 3). In addition, it was observed that FEV1, FEV1/FVC, and MMEF exhibited significantly lower values between 31 and 84 days in contrast to the measurements captured within 30 days. Similar findings were also evident in the meta-analysis article,[17] which disclosed a higher prevalence of obstructive patterns in the study by You J et al, in comparison to the studies that gathered lung function data at an earlier timeframe (30 days after symptom onset and 38 ± 13.4 days after hospital discharge). This observation suggests that patients with persistent post COVID-19 symptoms between 31 and 84 days may have more nonuniform peripheral airway function and lower lung function. The underlying reason for this observed phenomenon remains unidentified. It could stem from the complex pathophysiology of COVID-19 infection or the intricate interplay within the course of the disease. Conversely, after 84 days, patients generally exhibit improvements in their peripheral airway function (Table 2).

Furthermore, our analysis of the IOS parameters in relation to symptoms (Table 4) revealed interesting findings. Patients presenting with three symptoms exhibited more IOS values compared to those with single or two symptoms. It is understandable that patients with multiple symptoms may have more severe uniformity in small airways and impaired lung function than those with only a single symptom. Additionally, among the single symptom assessed, patients experiencing dyspnea had more IOS values and lower lung volume compared to those with cough symptoms. This suggests that dyspnea may be associated with more significant impairment in the peripheral airways than cough symptoms in post COVID-19 patients. However, the relationship between the two symptom groups (Dyspnea & Chest tightness; Cough & Dyspnea) was less clear. Chest tightness is a nonspecific symptom that can be attributed to the respiratory system, cardiac system, or even emotions. Consequently, the outcome of this classification may not necessarily provide an accurate representation of the small respiratory tract and lung function. Lung diffusing capacity impairment and ventilatory impairment can contribute to subjective dyspnea. Unfortunately, we did not conduct DlCO inspections concurrently; otherwise, the data would have been presented more comprehensively.

5 | LIMITATION

According to our country's national health insurance system, only one-time inspection or examination can be used. Besides, we do not have IOS data for the patients before this illness. Therefore, we cannot distinguish whether the changes in oscillometry results were caused by COVID-19 or were already present before. We are also unable to collect complete medical history of patients, such as cardiopulmonary morbidities, because almost all patients are consulted through video calls. The composition of patient demographics matches real-world practical scenarios rather than clinical trial settings. Despite these limitations, our study is representative of real-world experience. Finally, the small sample size of this retrospective research reinforces the need for future studies that incorporate a larger number of patients.

6 | CONCLUSION

In conclusion, our study demonstrates that IOS can effectively detect small airway disease in post COVID-19 patients experiencing persistent symptoms, even in the absence of spirometric obstruction or restrictive lung disease. Furthermore, among patients with

TABLE 4 Analysis of IOS data based on different post-COVID-19 symptoms.

	Cough only (n = 26)				Dyspnea only (n = 6)				Dyspnea & Chest tightness (n = 11)				Cough & Dyspnea (n = 22)				Cough & Dyspnea& Chest tightness (n = 17)				
	Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		Abs Mean ± SD		Z Mean ± SD		p value
R5-R20	0.08[a]	0.05	−0.06	0.87	0.10[a]	0.04	0.21	0.62	0.10[a]	0.07	0.21	1.06	0.06	0.04	−0.50	0.60	0.12[a]	0.09	0.53	1.38	0.026[b]
X5Hz	−0.11	0.05	−0.06	1.11	−0.14[a]	0.06	0.22	0.51	−0.02	0.37	0.22	0.88	−0.10	0.03	−0.44	0.59	−0.09	0.06	0.45	1.26	0.283
Fres	15.52[a]	3.66	0.09	0.92	16.75[a]	3.94	0.40	0.99	15.55[a]	2.47	0.10	0.62	13.43[a]	3.08	−0.43	0.77	16.03[a]	5.65	0.22	1.42	0.239
AX	0.61[a]	0.43	−0.02	0.91	0.78[a]	0.36	0.33	0.75	0.69[a]	0.46	0.16	0.98	0.39	0.22	−0.48	0.47	0.85[a]	0.71	0.50	1.50	0.064
FVC	3.27	0.92	0.04	1.04	2.94	1.21	−0.33	1.37	3.02	0.55	−0.23	0.62	3.38	0.88	0.16	0.99	3.22	0.96	−0.01	1.08	0.68
FEV1	2.69	0.72	−0.05	0.91	2.49	1.31	−0.31	1.65	2.61	0.46	−0.15	0.58	2.84	0.80	0.14	1.01	2.81	0.91	0.10	1.14	0.678
FEV1/F (%)	103.91	6.96	−0.25	0.84	104.10	13.88	−0.23	1.69	108.22	8.64	0.27	1.05	105.63	6.71	−0.04	0.81	108.84	9.02	0.35	1.09	0.289
FEV1/ FVC (L)	0.83	0.06	0.00	1.00	0.82	0.11	0.00	1.00	0.87	0.08	0.00	1.00	0.84	0.06	0.00	1.00	0.87	0.08	0.00	1.00	0.333
MMEF (%)	80.93	22.97	−0.21	0.78	83.78	57.53	−0.12	1.96	88.31	19.86	0.04	0.68	86.51	24.01	−0.02	0.82	98.27	35.80	0.38	1.22	0.529

Abbreviations: IOS, impulse oscillometry; SD, Std. Deviation.

[a]Meet the definition of small airway disease.

[b]$p < 0.05$.

persistent symptoms between 31 and 84 days, there appears to be a higher degree of nonuniformity in the peripheral airway, and lower lung function compared to the group within 30 days. This could potentially be attributed to the progression of the disease course following a post-COVID-19 infection. All these findings highlight the importance of focusing on the treatment of peripheral airway abnormalities in post COVID-19 patients. Future follow-up studies should explore the efficacy of interventions such as fine particle bronchodilators and inhaled corticosteroids specifically targeting the peripheral airways.[18–21] By addressing these peripheral airway issues, we can potentially improve the respiratory outcomes and quality of life for individuals experiencing persistent symptoms following COVID-19 infection.

AUTHOR CONTRIBUTIONS

Chun-Yu Lu: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Resources. **Sheng-Hao Lin**: Resources; Supervision; Validation; Visualization. **Chun-Min Chen**: Methodology; Project administration; Resources; Software.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Please contact author for data requests.

ETHICS STATEMENT

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed in accordance with the amended Declaration of Helsinki. Written informed consent for impulse oscillometry was obtained from each patient. Data anonymization and privacy issues were strictly addressed. The study protocol was approved by the Human Ethics Committee of Changhua Christian Hospital (IRB No.:221127) and individual consent for this retrospective analysis was waived.

TRANSPARENCY STATEMENT

The lead author Sheng-Hao Lin affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. RESEARCH AND METHODOLOGY: This article is based on thorough research conducted from various reliable sources, including academic journals, industry reports, expert interviews, and publicly available data. All sources of information have been meticulously cross-checked to ensure accuracy and reliability. SOURCES OF INFORMATION: All information presented in this article has been sourced from reputable and verifiable references. Citations and references to these sources have been provided where appropriate to maintain the credibility and traceability of the data and statements made. CORRECTIONS AND FEEDBACK: We are committed to accuracy and integrity in our reporting. If any errors are identified or if there are suggestions for improvements, we welcome feedback from our readers. Please contact us at [contact information] with any concerns or comments. UPDATES AND REVISIONS: The information in this article reflects the state of knowledge at the time of publication. We acknowledge that new information may emerge over time, and we are committed to updating the content as necessary to reflect the most current and accurate data.

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