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Original Article

Pulmonary Function Test Abnormalities in Subacute Cough: A Neglected Tool

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ABSTRACT

OBJECTIVE: Subacute cough is often considered a benign and self-limiting condition, and pulmonary function tests (PFTs) are not routinely performed during this period. This study aimed to evaluate PFT findings in patients with subacute cough compared with those in healthy controls.

MATERIAL AND METHODS: This retrospective, cross-sectional study included adults with subacute cough who underwent standardized spirometry, along with age- and sex-frequency matched healthy controls. Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and forced expiratory flow at 25–75% of the pulmonary volume ($FEF_{25–75}$) were recorded as absolute values and z-scores. Between-group comparisons were performed using analysis of covariance to adjust for age, sex, and height.

RESULTS: A total of 156 patients with subacute cough and 156 controls were analyzed. Patients with subacute cough demonstrated significantly lower FEV_1 and FVC z-scores, and lower $FEF_{25–75}$ values and z-scores (all $P < 0.001$). After adjustment, group differences remained significant for FVC, FEV_1 z-score, and $FEF_{25–75}$ (both absolute and z-score). Post-infectious cough was the most common diagnosis (37.8%), followed by asthma (25%); interstitial lung diseases (ILD) were also detected. FVC z-scores, absolute $FEF_{25–75}$, and $FEF_{25–75}$ z-scores were lower in the obstructive airway disease and ILD subgroups than in the post-infectious cough group. $FEF_{25–75}$ z-scores showed the greatest discriminatory ability across diagnostic categories.

CONCLUSION: Subacute cough encompasses a heterogeneous group of underlying diseases and should not be considered solely post-infectious. Patients with subacute cough may exhibit impaired PFTs, especially $FEF_{25–75}$ z-scores. PFTs may provide additional information for the evaluation of subacute cough.

KEYWORDS: Asthma, COPD, interstitial lung disease, pulmonary function tests

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INTRODUCTION

Cough is one of the most common symptoms prompting outpatient visits to pulmonary medicine services and represents a significant clinical and socioeconomic burden. Based on symptom duration, cough is classified as acute (<3 weeks), subacute (3–8 weeks), or chronic (>8 weeks).[1,2] While subacute cough is frequently considered a benign and self-limiting condition, most often following an upper respiratory tract infection (URTI), accumulating evidence suggests that it may also represent an early manifestation of underlying airway disease in a subset of patients.[3] The etiological spectrum of subacute cough includes post-infectious cough, upper airway cough syndrome, cough variant asthma (CVA), non-asthmatic eosinophilic bronchitis, atopic cough, and gastroesophageal reflux–related cough. Several of these conditions may present without overt airflow limitation on conventional spirometry, resulting in under-recognition during the subacute phase. These conditions may present with normal pulmonary function tests (PFTs), making early identification difficult without more sensitive functional assessments. The forced expiratory flow at 25–75% of the pulmonary volume ($FEF_{25–75}$ or maximal mid-

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expiratory flow) is a marker of small airway function. Previous studies have demonstrated significantly lower $FEF_{25–75}$ values in CVA patients compared to healthy controls or those with post-infectious cough.[4] Although conventional spirometry may be within normal limits, early small airway dysfunction can still be present and measurable through these indices. Identifying subtle physiological changes during the subacute phase may enable earlier diagnosis and treatment, especially with inhaled corticosteroids (ICS), and potentially prevent progression to chronic cough and improve patient outcomes.[5]

In clinical practice, patients presenting with subacute cough are frequently managed conservatively, and PFT is not routinely performed unless symptoms persist beyond eight weeks. This "wait-and-see" approach may delay the recognition of airway hyperresponsiveness or an obstructive defect in a subset of patients. Therefore, further data are needed to evaluate the role of PFT in this clinical context.

In this context, evaluating PFT findings in patients presenting with subacute cough may provide valuable insights into subclinical airway dysfunction. Therefore, we hypothesized that patients with subacute cough would have abnormal z-score–based spirometric parameters compared with healthy controls.

MATERIAL AND METHODS

Study Design and Population

This retrospective, cross-sectional, observational study was conducted at an academic hospital. Medical records of adult patients (≥18 years) who presented between January and June 2025 with a subacute cough lasting 3–8 weeks and who underwent standardized spirometry were reviewed. A control group consisting of age- and sex-frequency matched individuals without known pulmonary disease was selected from subjects who underwent spirometry during the same period for pre-employment, periodic health assessment, or routine check-up. Active or ex-smokers, patients with known chronic respiratory diseases [including asthma, chronic obstructive pulmonary disease, bronchiectasis, or interstitial lung disease (ILD)], acute upper or lower respiratory tract infection, pulmonary infection (such as pneumonia or tuberculosis), abnormal chest radiography or computed tomography (CT) findings, pregnancy, or inability to perform acceptable spirometry maneuvers were excluded. Patients with a previously established diagnosis of asthma, COPD, bronchiectasis, or ILD before the study evaluation were excluded. However, patients who were newly diagnosed with these conditions during the diagnostic work-up were not excluded and were reported in the results. The current study protocol was approved by the Local Ethics Committee of TOBB University of Economics and Technology (date: 22.10.2025; number: 34), and the study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki. All data were anonymized prior to analysis.

Main Points

- Subacute cough is commonly managed conservatively, yet a substantial proportion of patients have clinically relevant airway or parenchymal lung disease.
- Small airway dysfunction is a key physiological abnormality in subacute cough and is best captured by forced expiratory flow at 25–75% of the pulmonary volume ($FEF_{25–75}$) particularly the z-score.
- $FEF_{25–75}$ z-scores outperform forced expiratory volume in one second in differentiating between obstructive airway diseases during the subacute cough phase.
- Routine spirometry in patients with subacute cough may challenge the "wait-and-see" approach and enable earlier, etiology-driven diagnostic and therapeutic decisions.

Data Collection and Pulmonary Function Testing

Demographic data, including age, sex, and body mass index (BMI), were obtained from the hospital electronic information system. PFT parameters extracted from the laboratory database included forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow between 25% and 75% of FVC ($FEF_{25–75}$). All spirometric measurements were performed using the same calibrated spirometer in accordance with the American Thoracic Society and the European Respiratory Society (ERS) standards.[6] Absolute values and corresponding z-scores were recorded for analysis. Spirometric z-scores were calculated using the Global Lung Function Initiative reference equations.

Definition of Etiologic Diagnoses

Etiologic diagnoses were determined based on clinical evaluation, spirometric findings, radiologic evaluation, or multidisciplinary evaluation. Asthma was defined as the presence of compatible respiratory symptoms with either documented bronchodilator reversibility (increase in FEV_1 ≥12% and ≥200 mL after bronchodilator administration) or a prior physician diagnosis supported by treatment response to the ICS with or without long-acting beta-agonists. Chronic obstructive pulmonary disease (COPD) was defined by spirometric criteria demonstrating persistent airflow limitation (post-bronchodilator FEV_1/FVC <0.70) and/or radiological findings in the context of a compatible clinical history. ILDs were identified based on radiologic findings on chest CT and/or pathological findings, as determined by multidisciplinary evaluation. Gastroesophageal reflux disease (GERD)–related cough was defined based on compatible symptoms and multidisciplinary evaluation with or without ongoing anti-reflux therapy. Post-infectious cough was defined as cough persisting for 3–8 weeks following an URTI in the absence of alternative identifiable etiologies.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 22 (IBM, Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Normally distributed continuous variables are presented as mean ± standard deviation (SD), while categorical variables are expressed as number and percentage (%). Between-group comparisons were performed using the Student's t-test for normally distributed continuous variables and the chi-square test for categorical variables. In

addition, analysis of covariance (ANCOVA) was conducted to evaluate group differences in pulmonary function parameters after adjustment for age, sex, height, and BMI. Group-effect *P* values and partial eta-squared (η^2) were reported for adjusted analyses. A two-sided *P* value of <0.05 was considered statistically significant for all analyses.

RESULTS

Baseline Characteristics

A total of 312 individuals were included in the analysis, consisting of 156 patients with subacute cough and 156 healthy controls. Baseline demographic characteristics are presented in Table 1. Age and BMI were not statistically different between subacute cough group and healthy controls (50.4±1.2 vs. 53.4±1.6 years, *P* = 0.099; 27.4±0.35 vs. 27.2±0.44 kg/m^2, *P* = 0.292; respectively). Sex distribution differed significantly between groups, with a higher proportion of males in the subacute cough group (*P* = 0.041). Among the 156 patients with subacute cough, post-infectious cough (37.8%, n = 59) was the most frequent etiology; asthma was the second most common definitive diagnosis (25%, n = 39). GERD (7.1%, n = 11) and COPD (7.1%, n = 11) were tied for the third most prevalent causes of subacute cough (Figure 1). All definite diagnoses and their prevalence are presented in Supplementary Table 1.

Pulmonary Function Test Results

PFT results are summarized in Table 2. Absolute FEV_1 and FVC values were comparable between the subacute cough and control groups (FEV_1: 2.83±0.07 L vs. 2.69±0.08 L, *P* = 0.225; FVC: 3.40±0.09 L vs. 3.59±0.10 L, *P* = 0.149). In contrast, z-score–based spirometric indices demonstrated significant differences. The subacute cough group had significantly lower FEV_1 z-scores (−1.05±0.09 vs. −0.37±0.10, *P* < 0.001) and FVC z-scores (−1.30±0.09 vs. 0.24±0.10, *P* < 0.001). The FEV_1/FVC z-score was significantly higher in the subacute cough group compared with controls (*P* < 0.001). Small airways function was significantly impaired in patients with subacute cough. Both absolute $FEF_{25–75}$ values (2.36±0.14 L/s vs. 3.06±0.10 L/s, *P* < 0.001) and $FEF_{25–75}$ z-scores (−1.12±0.76 vs. −0.18±0.09, *P* < 0.001) were significantly lower than those observed in the control group.

Among the 136 patients with subacute cough who underwent bronchodilator reversibility testing, 31 (22.8%) showed a positive bronchodilator response. In the subacute cough group, the mean ± SD serum eosinophil count was 210±17 cells/µL. Serum eosinophil levels were significantly higher in the reversible group compared with the irreversible group (327±56 vs. 188±15 cells/µL, respectively; *P* = 0.009). No significant correlation was observed between serum eosinophil counts and FEF_{25-75} values.

Adjusted Analysis

Results of ANCOVA adjusted for age, sex, height, and BMI are shown in Table 3. After adjustment, statistically significant group effects persisted for FVC, FVC z-score, FEV_1 z-score, FEV_1/FVC z-score, and $FEF_{25–75}$ (absolute and z-score values; all *P* < 0.001). No significant group effect was observed for absolute FEV_1 values (*P* = 0.319). The largest effect sizes were observed for FVC z-score (partial η^2 = 0.283) and FEV_1/FVC

Table 1. Demographic characteristics

	Subacute cough group (n = 156)	Control group (n = 156)	*P*
Age (mean ± SD)	50.4±1.2	53.4±1.6	0.099
Gender, n (%)			
Female	73 (46.8%)	91 (58.3%)	0.041*
Male	83 (53.2%)	65 (41.7%)	
Body mass index (mean ± SD)	27.4±0.35	27.2±0.44	0.292

*$P < 0.05$
SD: standard deviation

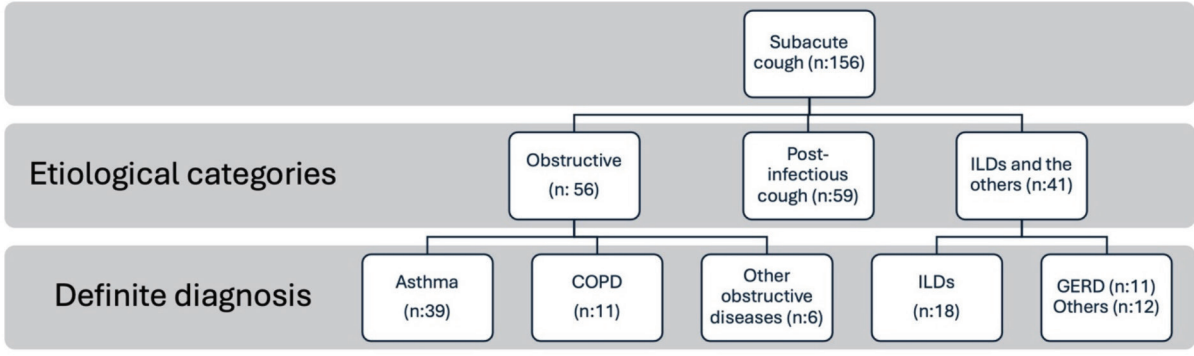

Figure 1. Diagnostic categories and most common final diagnoses of patients with subacute cough

COPD: chronic obstructive pulmonary disease, GERD: gastroesophageal reflux disease, ILDs: interstitial lung diseases

z-score (partial η^2 = 0.200), followed by FEF_{25-75} z-score (partial η^2 = 0.168).

PFT results were evaluated according to three main diagnostic categories comprising post-infectious cough, obstructive lung diseases (asthma, COPD, bronchiectasis), and ILDs and the others (GERD, etc.) (Figure 1); significant differences were observed in FEV_1 z-scores, $FEF_{25–75}$ absolute values, and $FEF_{25–75}$ z-scores across groups (Figure 2 and Supplementary Table 2). Overall comparisons demonstrated a statistically significant effect of diagnosis on FEV_1 z-scores ($P < 0.05$), with post-hoc analyses revealing significantly lower (more negative) FEV_1 z-scores in the obstructive disease groups compared with the post-infectious cough group (Figure 2B). Similarly, $FEF_{25–75}$ absolute values differed significantly among diagnostic groups ($P < 0.05$), showing a wider dispersion and lower central tendency in diagnoses characterized by small airway involvement (Figure 2C). $FEF_{25–75}$ z-scores showed the most significant intergroup differences (overall $P < 0.001$). Post-hoc analyses indicated that obstructive ventilatory pattern diagnoses such as asthma had significantly lower $FEF_{25–75}$ z-scores compared with other diagnostic categories (Figure 2D), even in cases where FEV_1 z-scores remained within normal limits.

DISCUSSION

This study demonstrates that subacute cough should not be presumed to be post-infectious by default, as our cohort exhibited a broad range of underlying conditions. Post-infectious cough was the most frequent etiology, while asthma (25%) represented the second most common etiology; GERD and COPD each accounted for 7.1% of etiologies. Importantly, a subset of patients was also diagnosed with ILDs, underscoring that clinically meaningful parenchymal pathology may be encountered even within a 3–8-week symptom window.

Although post-infectious cough was the most common etiology in our cohort, accounting for only 37.8% of cases, a substantial proportion of patients were diagnosed with asthma, other obstructive lung diseases, and ILDs. This finding is consistent with the study by Kwon et al.[5], who demonstrated that while post-infectious cough is common in the subacute phase, asthma-related phenotypes constitute a significant proportion of cases and are frequently under-recognized early in the disease course. Importantly, both the CHEST and ERS cough guidelines emphasize that symptom duration alone is insufficient to define etiology and that structural or inflammatory lung diseases may manifest before the chronic cough threshold is reached.[1,7]

A key physiological finding of this study is that z-score–based spirometric indices identified abnormalities that were not apparent on absolute spirometric volumes alone. Absolute FEV_1 and FVC values were comparable between the subacute cough and control groups, whereas FEV_1 and FVC z-scores were significantly lower in the subacute cough group. In addition, small airway function was consistently impaired, as reflected by lower $FEF_{25–75}$ values (both absolute and z-scores) in the subacute cough group. Collectively, these results indicate that deviation from predicted normative values (z-scores) may be more informative than absolute volumes in this clinical

Table 2. Pulmonary function tests results

	Subacute cough group (n = 156)	Control group (n = 156)	*P*
FEV_1 (L) [95% CI]	2.826±0.072 [2.683 – 2.969]	2.693±0.081 [2.531 – 2.855]	0.225
FEV_1 z-score [95% CI]	-1.054±0.087 [-1.227 – -0.882]	-0.367±0.096 [-0.556 – -0.177]	<0.001*
FVC (L) [95% CI]	3.399±0.086 [3.227 – 3.570]	3.587±0.096 [3.396 – 3.777]	0.149
FVC z-score [95% CI]	-1.300±0.931 [-1.485 – -1.116]	0.240±0.096 [0.045 – 0.435]	<0.001*
FEV_1/FVC z-score [95% CI]	0.615±0.110 [0.398 – 0.833]	-0.503±0.570 [-0.617 – 0.190]	<0.001*
FEF_{25-75} (L/s) [95% CI]	2.360±0.139 [2.145 – 2.576]	3.062±0.103 [2.856 – 3.266]	<0.001*
FEF_{25-75} z-score [95% CI]	-1.116±0.760 [-1.267 – -0.964]	-0.177±0.086 [-0.349 – -0.006]	<0.001*

*$P < 0.05$. Results are given as mean ± standard deviation with corresponding 95% confidence intervals (CI)
FEF_{25-75}: forced expiratory flow between 25% and 75% of FVC, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, CI: confidence interval

Table 3. Adjusted group effects on spirometric parameters in subacute cough compared with healthy controls

	Group effect (F)	*P* value	Partial η^2
FVC (L)	24.038	<0.001*	0.073
FVC z-score	121.247	<0.001*	0.283
FEV_1 (L)	0.995	0.319	0.003
FEV_1 z-score	25.784	<0.001*	0.077
FEV_1/FVC z-score	76.628	<0.001*	0.200
FEF_{25-75} (L/s)	18.082	<0.001*	0.056
FEF_{25-75} z-score	61.910	<0.001*	0.168

*$P < 0.05$. ANCOVA adjusted for age, sex, height and BMI
ANCOVA: analysis of covariance, BMI: body mass index, FEF_{25-75}: forced expiratory flow between 25% and 75% of FVC, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity

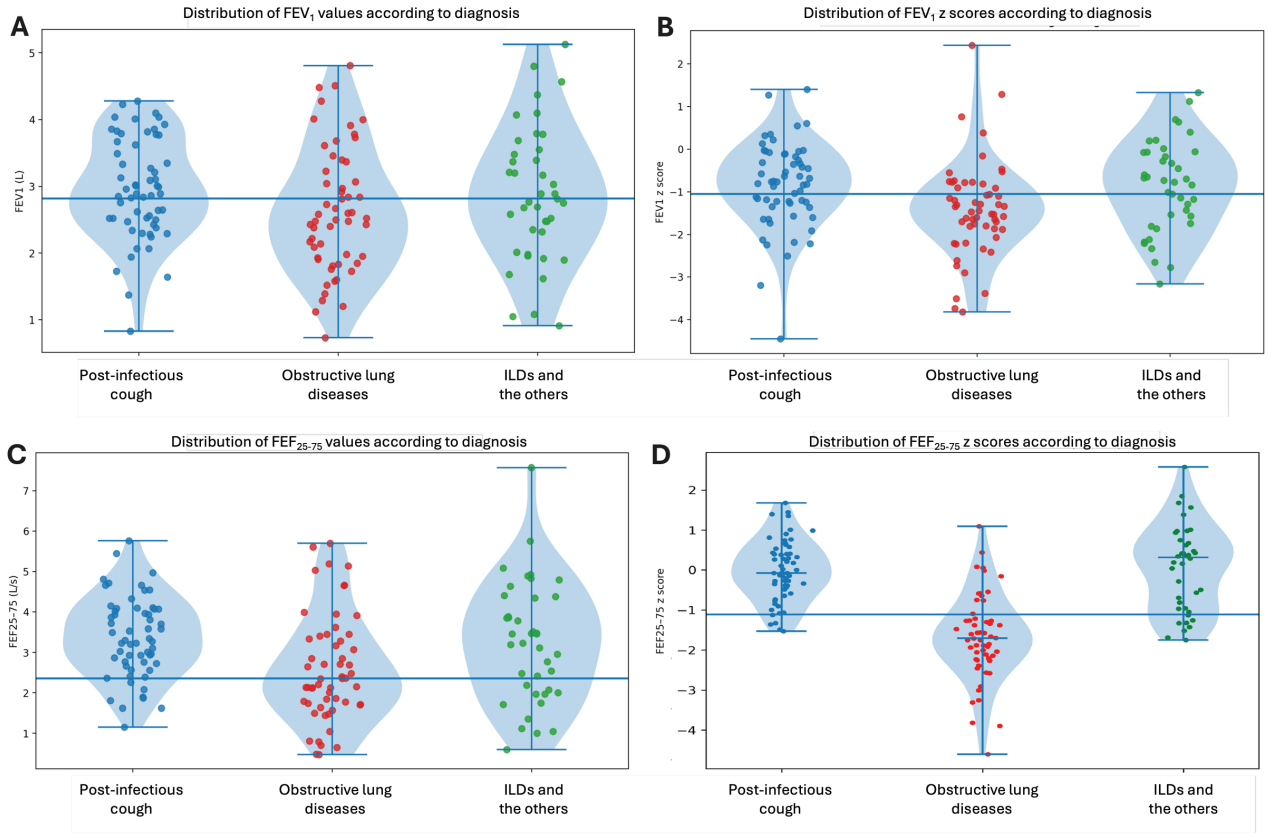

Figure 2. Distribution of spirometric parameters according to diagnosis. Violin plots illustrate the distribution of spirometric parameters across diagnostic groups, with overlaid dots representing individual patient measurements. (A) Distribution of FEV_1 values (L), (B) distribution of FEV_1 z-scores, (C) distribution of $FEF_{25–75}$ values (L/s), and (D) distribution of $FEF_{25–75}$ z-scores according to diagnosis. Horizontal reference lines indicate the mean value for each parameter across the patient population. Diagnostic categories include post-infectious cough, obstructive lung diseases, interstitial lung diseases and the others. Violin width reflects the kernel density of the distribution. Each dot represents an individual patient. Reference lines correspond to the cohort mean values

$FEF_{25–75}$: forced expiratory flow between 25% and 75% of forced vital capacity, FEV_1: forced expiratory volume in 1 second, ILDs: interstitial lung diseases, L: liter, L/s: liters per second

context. The discriminatory value of small-airway indices was further supported by adjusted analyses. After controlling for age, sex, height, and BMI, significant group effects persisted for FVC, FVC z-score, FEV_1 z-score, FEV_1/FVC z-score, and $FEF_{25–75}$ (absolute and z-score), whereas no significant group effects were observed for absolute FEV_1. The largest effect sizes were observed for the FVC z-score and the FEV_1/FVC z-score, followed by the $FEF_{25–75}$ z-score; this indicates that the most robust between-group separation was captured by standardized indices rather than raw volumes.

Beyond case–control comparisons, we observed that spirometric profiles differed across major diagnostic categories (post-infectious cough, obstructive lung diseases, and ILDs and the others (including GERD). Specifically, FEV_1 z-scores, $FEF_{25–75}$ absolute values, and $FEF_{25–75}$ z-scores varied significantly across these categories. Post-hoc testing indicated that obstructive disease categories had lower (more negative) FEV_1 z-scores than the post-infectious cough category, and that $FEF_{25–75}$ z-scores showed the most prominent intergroup differences, with obstructive-pattern diagnoses exhibiting significantly lower values than other diagnostic categories. These findings suggest that small airway indices, particularly $FEF_{25–75}$ z-scores, may provide incremental discriminatory value beyond FEV_1 for identifying subtle obstructive physiology during the subacute cough stage. These results are consistent with prior evidence indicating that mid-expiratory flow parameters are sensitive markers of early airway dysfunction.[4,5,8,9] In one study, patients with normal FEV_1 but positive bronchial hyperresponsiveness demonstrated significantly reduced $FEF_{25–75}$ values compared with patients without airway hyperresponsiveness, suggesting that small airway involvement precedes overt airflow limitation.[8] Similarly, a study reported that $FEF_{25–75}$ was superior to FEV_1 in differentiating CVA from other causes of chronic cough,[10] supporting the concept that small airway dysfunction plays a central role in cough-predominant obstructive phenotypes.[8-11] The recent study by Li et al.[4], evaluating PFTs in CVA with or without GERD, similarly demonstrated that combined assessment of spirometric indices improves diagnostic sensitivity. Together with our data, these findings suggest that reliance on FEV_1 alone may lead to underdiagnosis of obstructive disease in patients presenting with subacute cough. Our findings extend these observations to the subacute cough phase, indicating that $FEF_{25–75}$ abnormalities are detectable earlier than previously appreciated.

A noteworthy finding of this study is the identification of ILDs among patients presenting with a subacute cough. Although

ILDs are traditionally associated with chronic respiratory symptoms, cough is increasingly recognized as a common and sometimes early manifestation of these disorders. Cough may precede dyspnea in several ILD subtypes and can be a dominant presenting symptom, even in the absence of advanced radiologic disease.[12] Our findings support this observation and suggest that subtle reductions in FEF_{25-75} and FVC z-scores during the subacute phase may warrant further evaluation for underlying parenchymal lung disease. Current clinical practice often adopts a conservative approach to subacute cough, deferring extensive evaluation until symptoms persist beyond eight weeks. However, early diagnosis is associated with a better prognosis in ILDs. Our results provide objective evidence that spirometry performed during the subacute phase can uncover both obstructive and restrictive physiological abnormalities, facilitating earlier diagnosis and targeted management. Early identification of asthma may allow timely initiation of inhaled anti-inflammatory therapy, while recognition of a potential ILD can prompt appropriate imaging and specialist referral.

Study Limitations

Several limitations should be acknowledged. The retrospective, single-center design introduces the potential for selection bias, as only patients who underwent spirometry were included in the analysis. In routine clinical practice, spirometry is not systematically performed in all patients presenting with subacute cough and is often reserved for those with persistent symptoms or clinical suspicion of underlying airway disease. Consequently, the study population may represent a subgroup of patients in whom clinicians had already suspected physiological abnormalities, potentially resulting in an overrepresentation of pulmonary function abnormalities. Therefore, the results should be interpreted with caution and may not fully reflect the broader population of patients with subacute cough presenting in general clinical settings. The cross-sectional nature of the analysis precludes inference regarding prognosis, including whether early abnormalities in z-scores or FEF_{25-75} predict persistence of cough or progression to chronic airway disease. While FEF_{25-75} provided discriminatory information in our cohort, mid-expiratory flows can demonstrate greater variability than primary spirometric indices and should be interpreted in conjunction with the overall clinical context. Additionally, the study did not systematically incorporate tests of airway inflammation or hyperresponsiveness (fractional exhaled nitric oxide, induced sputum eosinophils, bronchial provocation) for all patients. Although ILDs were detected among the identified etiologies, the present dataset does not permit granular inferences about specific ILD subtypes.

CONCLUSION

These findings challenge a purely conservative "wait-and-see" approach for subacute cough. Our data indicate that performing spirometry during the subacute phase can uncover subtle obstructive physiology (captured particularly by FEV_1 z-score and FEF_{25-75}) and also raise suspicion for restrictive or parenchymal processes when patterns, such as lower FVC z-scores, are present. Consequently, spirometry may serve as an early, accessible tool to guide targeted diagnostic evaluation and earlier disease-specific management for patients who might otherwise be reassured that they have an uncomplicated post-infectious cough.

Ethics

Ethics Committee Approval: The current study protocol was approved by the Local Ethics Committee of TOBB Economics and Technology University (date: 22.10.2025; number: 34), and the study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

Informed Consent: This retrospective study was conducted using previously collected clinical data and pulmonary function test results. All data were anonymized prior to analysis, and no additional interventions were performed. The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study.

Footnotes

Authorship Contributions

Concept: A.Y., Design: A.Y., C.İ.A., Data Collection or Processing: A.Y., Analysis or Interpretation: A.Y., C.İ.A., Literature Search: A.Y., C.İ.A., Writing: A.Y., C.İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Tables 1, 2 Link: https://d2v96fxpocvxx.cloudfront.net/f6118de3-f656-440d-95f2-50c620149951/content-images/2ef38bb2-a0a7-4584-918d-5b6fd5b3e8a2.pdf

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