Editorial paper

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The role of pulmonary function tests in the management of patients with connective tissue diseases and lung involvement

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A variety of connective tissue diseases (CTDs), such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), rheumatoid arthritis (RA), polymyositis/dermatomyositis (PM/DM), and mixed connective tissue disease (MCTD), can involve the lungs as part of their systemic manifestations. Pulmonary lesions may even precede the onset of fully symptomatic CTD. Pulmonary complications are frequent and represent a significant cause of morbidity and mortality in these patients [1].

The patterns of functional impairment in CTDs vary significantly, depending on the underlying pathophysiological process. A broad range of pathologies can affect lung function, including interstitial lung diseases (e.g., pulmonary fibrosis and organizing pneumonia), pulmonary vascular diseases (e.g., obliterative vasculopathy, pulmonary thromboembolism, vasculitis), extrapulmonary restrictions (such as pleural disease and respiratory muscle weakness), and airway involvement (including bronchiectasis, constrictive bronchiolitis, exudative bronchiolitis, and follicular bronchiolitis), with centrilobular emphysema particularly common in smokers [2]. These abnormalities can be identified by characteristic morphological changes on high-resolution computed tomography or through histopathological analysis of biopsy specimens, both of which can lead to lung function impairment (see Table I for potential functional disturbances related to underlying pathophysiological processes) [3].

Pulmonary function tests (PFTs) are essential tools for evaluating, diagnosing, and monitoring lung involvement in patients with CTDs. Commonly used tests include spirometry, lung volume measurements, gas transfer tests, blood gas analysis at rest, and the 6-minute walk test (6MWT). From a practical standpoint, spirometry and gas transfer measurements are particularly important in the diagnostic and therapeutic process and should be mandatory for patients with CTD.

Spirometry measures air volume and flow during inhalation and exhalation, with key parameters including forced vital capacity (FVC). A decrease in FVC suggests restrictive lung disease, often associated with interstitial lung disease (ILD). Forced expiratory volume in 1 second (FEV_1), when decreased with a preserved FVC, indicates obstructive lung disease (reduced FEV_1/FVC ratio). Conversely, a normal or increased FEV_1/FVC ratio with a reduced FVC points to restrictive disease, commonly seen in CTD-related ILD. For patients with potential airway involvement (e.g., in RA), a bronchodilator response (improvement in FEV_1 and/or FVC after bronchodilator administration) can help distinguish reversible from irreversible airway obstruction, aiding in the evaluation of coexisting asthma or chronic obstructive pulmonary disease (COPD). Spirometry tests should be performed and interpreted according to current recommendations [4, 5].

The lung transfer factor for carbon monoxide (TL_{CO}) measures the lung's ability to transfer gas from the alveoli into the bloodstream. It is a sensitive test for detecting early lung involvement, particularly in ILD and pulmonary vascular disease (e.g., pulmonary hypertension). A reduced TL_{CO} can indicate early lung disease even when spirometry and lung volume measurements are normal. The gas transfer is often impaired in diseases such as SSc and MCTD due to pulmonary vascular or interstitial abnormalities. The transfer coefficient of the lung for carbon monoxide (K_{CO}), also known as the "Krogh coefficient", integrates factors such as gas permeability, solubility, and tissue properties to provide a measure of how effectively gases diffuse through biological barriers. A higher K_{CO} indicates more efficient diffusion, while a lower K_{CO} suggests greater resistance to gas transfer. Guidelines for measurement techniques, predicted values, and interpretation have been published in recent years [5–7].

The prevalence of lung involvement among patients with CTDs varies depending on the specific disease. It is estimated that 70–90% of patients with SSc develop some form of lung involvement, most commonly ILD or

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Table I. Patterns of pulmonary function impairment associated with the more frequent pulmonary complications of connective tissue disease

	Pattern of ventilatory impairment	Lung transfer factor for carbon monoxide (TL_{CO})	Arterial gases at rest
Interstitial lung disease (e.g. pulmonary fibrosis)	Restrictive defect (reduced FVC, TLC, FEV_1/FVC may be supranormal)	Reduced, but K_{CO} levels low normal or mildly reduced	Hypoxia at rest a feature of advanced disease
Pulmonary vascular disease	Normal	Reduced; TL_{CO}, K_{CO} severely reduced in pulmonary hypertension	Hypoxia at rest often present in moderate pulmonary hypertension
Airway involvement	Mixed or obstructive defect (reduced FEV_1/FVC, normal or reduced FVC and TLC)	Highly variable	Hypoxia at rest a feature of end-stage disease
Extrapulmonary restriction	Restrictive defect; reduction in peak flow may indicate muscle weakness	TL_{CO} levels low normal or mildly reduced; K_{CO} levels supranormal	In very severe disease, hypercapnic respiratory failure, alveolar–arterial oxygen gradient normal
Diffuse alveolar hemorrhage	Variable, often mildly restrictive	TL_{CO} and K_{CO} levels may be strikingly increased if hemorrhage is recent (< 72 h)	Variable; hypoxia and widening of alveolar–arterial oxygen gradient frequent

FEV_1 – forced expiratory volume in 1 second, FVC – forced vital capacity, K_{CO} – transfer coefficient of the lung for carbon monoxide, TLC – total lung capacity, TL_{CO} – lung transfer factor for carbon monoxide.

pulmonary hypertension. In SLE, approximately 20–50% of patients exhibit lung involvement, including pleural disease, ILD, and pulmonary hypertension. In RA, 10–30% of patients develop lung disease, such as ILD, pleural disease, or airway obstruction. Additionally, up to 40% of patients with PM/DM may experience lung involvement, primarily in the form of ILD [8]. These statistics highlight the significant risk of pulmonary complications in CTD patients, underscoring the importance of regular monitoring with PFTs for early detection and management, even in asymptomatic individuals, as was clearly stated in recent American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) recommendations [9].

Serial PFTs are critical for tracking lung disease progression over time. A decline in FVC by 10% or TL_{CO} by 15% annually may indicate the progression of ILD or the onset of pulmonary hypertension, prompting more aggressive treatment [10, 11]. Pulmonary function test results can guide treatment decisions, such as the initiation of immunosuppressive therapy for ILD, vasodilator therapy for pulmonary hypertension, or antifibrotic therapy for progressively fibrotic diseases. In some cases, worsening PFT results may lead to consideration of lung transplantation.

The quality of the PFTs performed is crucial, as the differences in results can be small and may approach the acceptable variability within a single measurement session. Therefore, tests should be conducted in centers with extensive experience [4, 6]. Unfortunately, in many centers, the quality of spirometry testing still falls short of optimal standards [12]. Regular training is essential to improve and maintain proficiency [13].

It is also important to consider the potential pneumotoxic effects of certain drugs used to treat CTDs. Baseline PFTs should be performed before starting therapy, and lung function should be monitored regularly throughout treatment.

In conclusion, pulmonary function tests are indispensable in managing patients with CTDs and lung involvement. They provide valuable diagnostic and prognostic information, guide therapeutic decisions, and monitor treatment response. Early detection of lung disease through PFTs can lead to timely interventions, improving outcomes and the quality of life for patients with CTDs.

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