



**FUNCTIONAL STATE OF THE CARDIORESPIRATORY SYSTEM IN PATIENTS  
WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH DIFFERENT  
PHENOTYPES DURING REHABILITATION STAGES**

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**Abstract Background:** Chronic obstructive pulmonary disease (COPD) represents a heterogeneous condition characterized by persistent respiratory symptoms and airflow limitation. The disease manifests different phenotypes including emphysematous and bronchitic variants, each presenting unique cardiorespiratory challenges.

**Objective:** This study aimed to investigate the functional state of the cardiorespiratory system in COPD patients with different phenotypes during rehabilitation stages and develop individualized rehabilitation programs.

**Methods:** One hundred patients with stage II-III COPD were divided into four groups based on phenotype and exacerbation frequency. Comprehensive pulmonary rehabilitation including breathing exercises, physical training, acupuncture, massage, and transcutaneous nerve-muscle stimulation was conducted alongside standard pharmacotherapy.

## **1. Introduction**

Chronic obstructive pulmonary disease (COPD) has emerged as a leading cause of morbidity and mortality worldwide, affecting 7.8 to 19.7% of populations across different countries. The World Health Organization projects that by 2030, COPD will rank third in global mortality among all diseases, with its significance continuing to escalate due to risk factor exposure and population aging.

COPD represents a heterogeneous lung condition characterized by chronic respiratory symptoms including dyspnea, cough, and sputum production, accompanied by exacerbations resulting from airway damage and alveolar involvement. The disease typically progresses to disability approximately ten years post-diagnosis, underscoring the critical need for early intervention and comprehensive management strategies.

Recent advances in COPD classification have led to the identification of distinct phenotypes, primarily emphysematous and bronchitic variants. The emphysematous phenotype predominantly features parenchymal destruction with alveolar loss and elastic property deterioration, while the bronchitic phenotype exhibits airway remodeling and obstruction. This phenotypic heterogeneity significantly influences disease progression, treatment response, and rehabilitation outcomes.



The cardiorespiratory system in COPD patients experiences profound alterations due to persistent inflammation, hypoxemia, endothelial dysfunction, oxidative stress, and cytokine imbalance. Studies demonstrate that each 10% reduction in FEV1 increases cardiovascular mortality risk by 28% and non-fatal coronary events by 20%. These findings emphasize the systemic nature of COPD and the critical importance of integrated cardiorespiratory assessment during rehabilitation.

## **2. Literature Review**

### **2.1 COPD Phenotypes and Pathophysiology**

The classification of COPD into distinct phenotypes has revolutionized disease understanding and management. The emphysematous phenotype, characterized by progressive alveolar destruction and loss of elastic recoil, typically presents with severe dyspnea, reduced body mass index, and lower diffusing capacity. Conversely, the bronchitic phenotype demonstrates airway inflammation, mucus hypersecretion, and more frequent exacerbations with relatively preserved lung parenchyma.

Recent literature has identified additional phenotypes including the overlap syndrome combining features of COPD and asthma, and the frequent exacerbator phenotype defined by two or more exacerbations annually. Each phenotype exhibits unique inflammatory profiles, progression patterns, and responses to therapeutic interventions, necessitating tailored rehabilitation approaches.

### **2.2 Cardiovascular Manifestations in COPD**

COPD demonstrates significant cardiovascular comorbidity, with systemic inflammation serving as a unifying mechanism. Chronic low-grade inflammation promotes atherosclerosis development, arterial stiffness, and endothelial dysfunction. Hypoxemia and hypercapnia further contribute to pulmonary hypertension and right ventricular dysfunction, culminating in cor pulmonale in advanced cases.

Studies indicate that cardiovascular disease represents the leading cause of death in mild-to-moderate COPD, accounting for approximately 30% of mortality. The inflammatory cascade involving elevated C-reactive protein, interleukin-6, and tumor necrosis factor-alpha levels establishes a bidirectional relationship between COPD and cardiovascular pathology, creating a syndrome of mutual aggravation.

### **2.3 Pulmonary Rehabilitation in COPD**

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines emphasize pulmonary rehabilitation as a cornerstone of comprehensive COPD management. Evidence demonstrates that rehabilitation programs incorporating exercise training, education, and behavioral modification significantly improve exercise capacity, reduce dyspnea, enhance quality of life, and decrease healthcare utilization. However, optimal program design must account for phenotypic variations, comorbidities, and individual patient characteristics to maximize efficacy and ensure sustainable benefits.



### **3. Materials and Methods**

#### **3.1 Study Design and Participants**

This prospective observational study enrolled 100 patients diagnosed with COPD stages II-III according to GOLD criteria. Participants were stratified into four groups of 20 patients each based on phenotype classification and exacerbation frequency:

- Group 1: Emphysematous phenotype without frequent exacerbations
- Group 2: Bronchitic phenotype without frequent exacerbations
- Group 3: Emphysematous phenotype with frequent exacerbations
- Group 4: Bronchitic phenotype with frequent exacerbations

Within each group, 10 patients received adjuvant herbal therapy with immunostimulatory, anti-inflammatory, and adaptogenic properties alongside standard rehabilitation protocols.

#### **3.2 Rehabilitation Protocol**

All participants underwent comprehensive pulmonary rehabilitation on top of standard pharmacotherapy. The rehabilitation program included:

- Breathing exercises targeting respiratory muscles
- Progressive resistance training for upper and lower extremities
- Aerobic conditioning using stationary cycling
- Traditional acupuncture at standardized points
- Therapeutic massage
- Transcutaneous neuromuscular electrical stimulation
- Terrenkur (graduated terrain walking)

#### **3.3 Assessment Methods**

**Laboratory Investigations:** Complete blood count, urinalysis, lipid profile, coagulation studies (fibrinogen, fibrinolytic activity, prothrombin time, thrombin time, activated partial thromboplastin time), C-reactive protein, blood glucose, creatinine, T-helper cells (CD3+CD4+), neutrophil counts, cytokine analysis, and sputum examination.

**Instrumental and Functional Studies:** Chest radiography/computed tomography, electrocardiography, spirometry, peak flow metry, echocardiography, and six-minute walk test.

**Statistical Analysis:** Data were analyzed using Statistica software with Student-Fisher t-test for significance determination. P-values <0.05 were considered statistically significant.

### **4. Results and Discussion**

#### **4.1 Baseline Characteristics**

Baseline demographic and clinical characteristics demonstrated significant phenotypic variations. The emphysematous groups exhibited lower body mass index, more severe dyspnea scores, and reduced exercise capacity compared to bronchitic phenotypes. Conversely, bronchitic patients presented with higher exacerbation rates, increased sputum production, and more pronounced airway inflammation markers.

#### **Table 1. Baseline Pulmonary Function Parameters by Phenotype**



Parameter	Emphysema (n=40)	Bronchitis (n=40)	P-value
FEV1 (% predicted)	48.3 ± 6.2	52.1 ± 5.8	<0.05
FVC (% predicted)	62.4 ± 7.1	69.3 ± 6.5	<0.01
FEV1/FVC ratio	0.58 ± 0.07	0.62 ± 0.06	<0.05
6MWT distance (m)	312 ± 45	348 ± 38	<0.01

These findings align with established literature demonstrating distinct pathophysiological profiles between COPD phenotypes. The more pronounced airflow limitation in emphysematous patients reflects progressive parenchymal destruction, while bronchitic patients exhibited relatively preserved lung volumes with predominant airway obstruction.

#### 4.2 Cardiovascular Assessment

Echocardiographic evaluation revealed significant differences in cardiac structure and function across phenotypes. The emphysematous groups demonstrated more pronounced right ventricular enlargement and elevated pulmonary artery pressures, consistent with the hypoxemic burden and progressive pulmonary vascular remodeling. Bronchitic phenotypes exhibited higher prevalence of left ventricular diastolic dysfunction, potentially related to systemic inflammation and atherosclerotic burden.

**Table 2. Cardiovascular Parameters by Phenotype and Exacerbation Frequency**

Parameter	Group 1	Group 2	Group 3	Group 4
LVEF (%)	58.3±4.2	56.7±3.8	55.2±4.5	54.8±4.1
sPAP (mmHg)	34.2±5.6	31.8±4.9	38.7±6.2	35.3±5.4
RV diameter (mm)	28.4±3.2	26.7±2.8	31.2±3.8	29.5±3.4
CRP (mg/L)	8.2±2.1	9.6±2.4	12.3±3.2	14.7±3.8

Note: LVEF = Left ventricular ejection fraction; sPAP = Systolic pulmonary artery pressure; RV = Right ventricle; CRP = C-reactive protein. Group 1: Emphysematous without frequent exacerbations; Group 2: Bronchitic without frequent exacerbations; Group 3: Emphysematous with frequent exacerbations; Group 4: Bronchitic with frequent exacerbations.

#### 4.3 Rehabilitation Outcomes

Following 12 weeks of comprehensive rehabilitation, all groups demonstrated significant improvements in pulmonary function, exercise capacity, and quality of life metrics. The



magnitude of improvement varied by phenotype, with bronchitic patients achieving greater gains in FEV1 (mean increase 8.4% vs. 5.2% in emphysematous groups,  $p < 0.05$ ) but smaller improvements in exercise tolerance.

Notably, patients receiving adjuvant herbal therapy exhibited enhanced outcomes across multiple parameters. This subgroup demonstrated superior improvements in inflammatory markers, with CRP levels decreasing by an average of 42% compared to 28% in the standard rehabilitation group ( $p < 0.05$ ). These findings suggest potential synergistic benefits of combining traditional and modern rehabilitation approaches.

The six-minute walk test revealed differential responses to rehabilitation across phenotypes. Emphysematous patients demonstrated mean distance improvements of 68 meters (21.8% increase from baseline), while bronchitic patients achieved 52-meter gains (14.9% increase). These improvements correlated significantly with reductions in dyspnea scores and enhanced quality of life assessments.

#### **4.4 Immunological and Coagulation Parameters**

Immunological assessment revealed significant phenotype-related variations in T-helper cell populations and cytokine profiles. Frequent exacerbators (Groups 3 and 4) demonstrated elevated levels of pro-inflammatory cytokines including IL-6 and TNF-alpha, consistent with persistent systemic inflammation. Rehabilitation protocols, particularly when supplemented with herbal therapy, produced measurable improvements in these inflammatory markers.

Coagulation studies identified a hypercoagulable state in COPD patients, especially pronounced in the frequent exacerbator phenotypes. Elevated fibrinogen levels and shortened activated partial thromboplastin time correlated with exacerbation frequency and cardiovascular comorbidity. Rehabilitation interventions produced modest but significant improvements in these parameters, potentially contributing to reduced cardiovascular risk.

#### **4.5 Quality of Life and Exacerbation Rates**

Quality of life assessments using standardized instruments revealed substantial benefits across all rehabilitation groups. The most pronounced improvements occurred in domains of physical functioning, symptom burden, and emotional well-being. Importantly, the 12-month follow-up period demonstrated sustained benefits with a 34% reduction in exacerbation frequency among rehabilitated patients compared to historical controls. This reduction translated to decreased healthcare utilization, fewer hospital admissions, and improved long-term outcomes.

### **5. Conclusion**

This comprehensive investigation of cardiorespiratory function in COPD patients with different phenotypes during rehabilitation stages has yielded several important findings. The study demonstrates that phenotypic classification provides valuable prognostic information and guides individualized rehabilitation strategies.

Key conclusions include:

- Emphysematous and bronchitic COPD phenotypes exhibit distinct cardiorespiratory profiles requiring tailored rehabilitation approaches



- Comprehensive pulmonary rehabilitation produces significant improvements in pulmonary function, exercise capacity, and cardiovascular parameters across all phenotypes
- Frequent exacerbator phenotypes demonstrate more pronounced systemic inflammation and cardiovascular involvement, necessitating intensified monitoring and intervention
- Adjuvant herbal therapy with immunostimulatory properties enhances rehabilitation outcomes, particularly in inflammatory marker reduction
- Individualized rehabilitation programs based on phenotype, exacerbation history, and comorbidity profile optimize therapeutic outcomes

The practical significance of this research lies in establishing evidence-based frameworks for phenotype-specific rehabilitation strategies. By recognizing the heterogeneity within COPD and tailoring interventions accordingly, clinicians can optimize resource utilization, improve patient outcomes, and reduce disease burden. The integration of traditional complementary therapies with modern rehabilitation protocols represents a promising avenue for enhanced COPD management.

Future research should focus on identifying biomarkers predicting rehabilitation response, optimizing program duration and intensity, and evaluating long-term outcomes across diverse populations. The development of precision rehabilitation approaches incorporating genetic, phenotypic, and comorbidity profiles holds significant promise for advancing COPD care and improving patient quality of life.

This study contributes to the growing body of evidence supporting comprehensive, individualized rehabilitation as a cornerstone of modern COPD management, complementing pharmacological interventions and addressing the multisystem nature of this chronic disease.

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