

Н. Худжейри, Т. Расакумар

**ПОСТКОВИДНЫЙ ФИБРОЗ ЛЕГКИХ; ФАКТОРЫ РИСКА РАЗВИТИЯ
ЗАБОЛЕВАНИЙ ЛЕГКИХ, СВЯЗАННЫХ С ПАНДЕМИЕЙ**

Научный руководитель: канд. мед. наук, доц. И.Л. Арсентьева

Кафедра пропедевтики внутренних болезней

Белорусский государственный медицинский университет, г. Минск

N. Houjeiry, T. Rasakumar

**POST-COVID LUNG FIBROSIS; RISK FACTORS
PANDEMIC-RELATED LUNG DISEASE**

Tutor: PhD in Medicine, assistant professor I.L. Arsentyeva

Department of Propaedeutics of internal diseases

Belarusian State Medical University, Minsk

Резюме. В данном исследовании изучается связь постковидного лёгочного фиброза (ПКЛФ) с функциональными нарушениями, лабораторными маркерами и факторами риска. Проведён систематический обзор и мета-анализ данных пациентов, перенёсших COVID-19. Обсуждается клиническая значимость снижения диффузионной способности лёгких (СДСЛ), роль воспалительных маркеров (СРБ, НЛИ (нейтрофильно-лимфоцитарный индекс)), а также индивидуализированный подход к раннему выявлению и мониторингу ПКЛФ в практике внутренних болезней.

Ключевые слова: постковидный лёгочный фиброз, снижение диффузионной способности лёгких, факторы риска, пропедевтика внутренних болезней, SARS-CoV-2.

Resume. This study examines the prevalence of post-COVID lung fibrosis (PCLF) and its association with functional impairment, laboratory markers, and risk factors. A systematic review and meta-analysis of data from patients who recovered from COVID-19 was conducted. The clinical significance of reduced diffusing capacity of the lungs for carbon monoxide (DLCO), the role of inflammatory markers (CRP), NLR (Neutrophil Lymphocyte Ratio), and an individualized approach to early detection and monitoring of PCLF in internal medicine practice are discussed.

Keywords: Post-COVID lung fibrosis, DLCO, risk factors, propaedeutics of internal diseases, SARS-CoV-2.

Relevance. The COVID-19 pandemic has affected over 700 million individuals globally, with a substantial proportion developing severe pneumonia and acute respiratory distress syndrome (ARDS). As survival rates improve, attention has shifted to long-term sequelae, particularly post-COVID pulmonary fibrosis (PCPF) – a condition that may affect hundreds of thousands of survivors. Within propaedeutics and internal medicine, understanding the natural history, functional defects, and risk factors of PCPF is essential for early identification, monitoring, and therapeutic intervention. Fibrotic lung changes lead to progressive dyspnea, reduced quality of life, and increased long-term mortality 1, 2.

Aim: to analyze the prevalence of post-COVID lung fibrosis across different clinical severity groups and evaluate the functional and laboratory predictors of fibrotic outcomes.

Objectives:

1. To analyze the prevalence of PCLF in relation to acute COVID-19 severity (moderate vs. severe/critical cases).

2. To evaluate the correlation between functional pulmonary defects (particularly DLCO reduction) and the development of persistent fibrosis.

3. To assess laboratory risk factors (CRP, LDH, D-dimers, NLR, albumin) and clinical predictors (age, ICU admission, mechanical ventilation) for early identification of patients at risk for PCLF.

Materials and methods. A systematic review and meta-analysis were conducted using global data on post-COVID lung fibrosis for post-COVID patients in hospitals in Sri Lanka. Studies examining survivors at 1–3 years post-infection were analyzed. Functional assessment included diffusing capacity of the lungs for carbon monoxide (DLCO), spirometry, and imaging correlates. Laboratory parameters during acute illness (CRP, LDH, D-dimers, NLR, albumin, hemoglobin) and clinical variables (age, disease severity, ICU admission, mechanical ventilation, comorbidities, and specific treatments such as baricitinib and remdesivir) were evaluated. All analyses were conducted in compliance with biomedical ethics and data confidentiality standards.

Results and their discussion. Functional assessment revealed that reduced DLCO is the most prevalent and persistent pulmonary function abnormality, affecting 38–49% of survivors at 1–3 years post-infection. This defect is more common than restrictive or obstructive patterns and serves as an early marker of fibrotic changes. Disease severity during acute infection showed a strong association with fibrotic sequelae: the incidence of PCLF rose from 2.08% in moderate cases to 8.22% in severe cases. Critical illness requiring ICU admission and mechanical ventilation conferred the highest risk. Advanced age consistently emerged as a significant predictor, reflecting reduced regenerative capacity and age-related immune dysregulation. Laboratory parameters provided valuable prognostic information: elevated LDH (OR 1.004, 95% CI 1.000–1.007), elevated CRP (aOR 1.005, 95% CI 1.001–1.009), elevated D-dimers, elevated fibrinogen, and elevated neutrophil-to-lymphocyte ratio (NLR) correlated strongly with fibrotic outcomes. Hypoalbuminemia (OR 0.871, 95% CI 0.778–0.974) indicated poor nutritional status and increased inflammatory burden. Interestingly, higher hemoglobin levels (OR 1.194, 95% CI 1.032–1.387) showed a paradoxical association with increased PCLF risk, possibly reflecting hemoconcentration in severe illness.

Regarding treatment-related risk factors, baricitinib (a Janus kinase inhibitor) showed an unexpected association with increased fibrosis risk (OR 5.633, 95% CI 1.642–19.548), although residual indication bias cannot be excluded. Remdesivir, the first approved antiviral for COVID-19, was not consistently associated with fibrotic outcomes. The clinical trajectory of PCLF was variable: some patients showed partial regression or complete recovery, while others demonstrated persistent stable fibrosis or progression, necessitating long-term follow-up.

Conclusions:

1. Post-COVID lung fibrosis is a clinically relevant sequela with highest incidence (8.22%) in patients who had severe acute COVID-19, compared to 2.08% in moderate cases.

2. Reduced DLCO, affecting 38–49% of survivors at 1–3 years, is the most persistent functional abnormality and an early marker of fibrotic involvement in propaedeutic assessment.

3. Key risk factors for PCLF include: disease severity, advanced age, elevated

inflammatory markers (LDH, CRP, D-dimers, NLR), hypoalbuminemia, and extensive acute radiological involvement.

4. Unexpected associations (baricitinib with increased fibrosis risk, higher hemoglobin with PCLF) require further investigation but highlight the importance of individualized risk assessment.

5. The variable clinical trajectory (regression, persistence, or progression) emphasizes the need for structured long-term follow-up of COVID-19 survivors within internal medicine practice.

Literature

1. Rathnapala, A., Wickramasinghe, S., Tilakaratne, D., et al, The utilization pattern of surgical lung biopsies (SLB) for the diagnosis of interstitial lung diseases (ILD) in Sri Lanka, *European Respiratory Journal*, 54 (suppl 63) PA4719(2019)

2. Undugodage, C., Perera, N., De Silva, H.D.K., et al, Respiratory manifestations of long COVID syndrome and pulmonary function abnormalities at 3-months after COVID-19 infection: A single center experience from Sri Lanka, *Journal of the Ceylon College of Physicians*, 47(1): p.11-16(2022)

3. Wickramasinghe, S., Gudur, S., Southworth, T., et al, Prevalence and Management of Post Covid fibrosis in tertiary care unit – A single centre experience
European Respiratory Journal, 62 (suppl 67) PA3918(2023)

4. Abdelrafie, N., Eltayeb, L. B., Yassin, H. M., New Insights on Post-COVID-19 Pulmonary Fibrosis: Risk Factors and Clinical Correlations, *International Journal of Biomedicine*, 14(4): 664-672(2024)

5. Ghatak, T., Thakur, S., State of the Globe: A Glimmer of Hope – Biomarkers for Diagnosing COVID-19 Pulmonary Fibrosis, *Journal of Global Infectious Diseases*, 16(2): 43-44(2024)

6. Mulu, G. B., Atinafu, B. T., Tarekegn, F. N., The Global Prevalence of Pulmonary Fibrosis Among Post-COVID-19 Follow-up Patients: Systematic Review and Meta-analysis: 2021, *Infectious Diseases in Clinical Practice*, 31(1): e1190(2023)

7. Shu, Y., He, L., Liu, C., Impact of anti-fibrotic medications on post-COVID-19 pulmonary fibrosis: A systematic review and meta-analysis, *International Journal of Infectious Diseases*, 147: 107193(2024)