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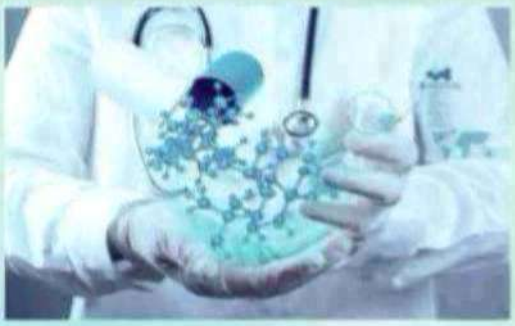

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# ТИББИЁТДА ЯНГИ КУН
# НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
# NEW DAY IN MEDICINE

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# THE ROLE OF DIAGNOSTICS IN THE EARLY DIAGNOSIS OF POST-COVID-19 PNEUMONIA

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✓ ***Resume***

***Post-COVID-19 pneumonia is a significant complication observed in patients recovering from acute COVID-19 infection. Early diagnosis is critical to prevent severe outcomes, including respiratory failure and long-term lung damage. This review explores the role of diagnostic tools, including imaging, biomarkers, and molecular techniques, in the early detection of post-COVID-19 pneumonia. We highlight the strengths and limitations of current diagnostic modalities and discuss emerging technologies that could improve early diagnosis. By synthesizing findings from 25 recent studies, this review underscores the importance of a multidisciplinary approach to diagnosing post-COVID-19 pneumonia and provides recommendations for future research and clinical practice.***

***Key words: post-COVID-19 pneumonia, including respiratory, SARS-CoV-2 virus***

# РОЛЬ ДИАГНОСТИКИ В РАННЕЙ ДИАГНОСТИКЕ ПНЕВМОНИИ ПОСЛЕ COVID-19

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✓ ***Резюме***

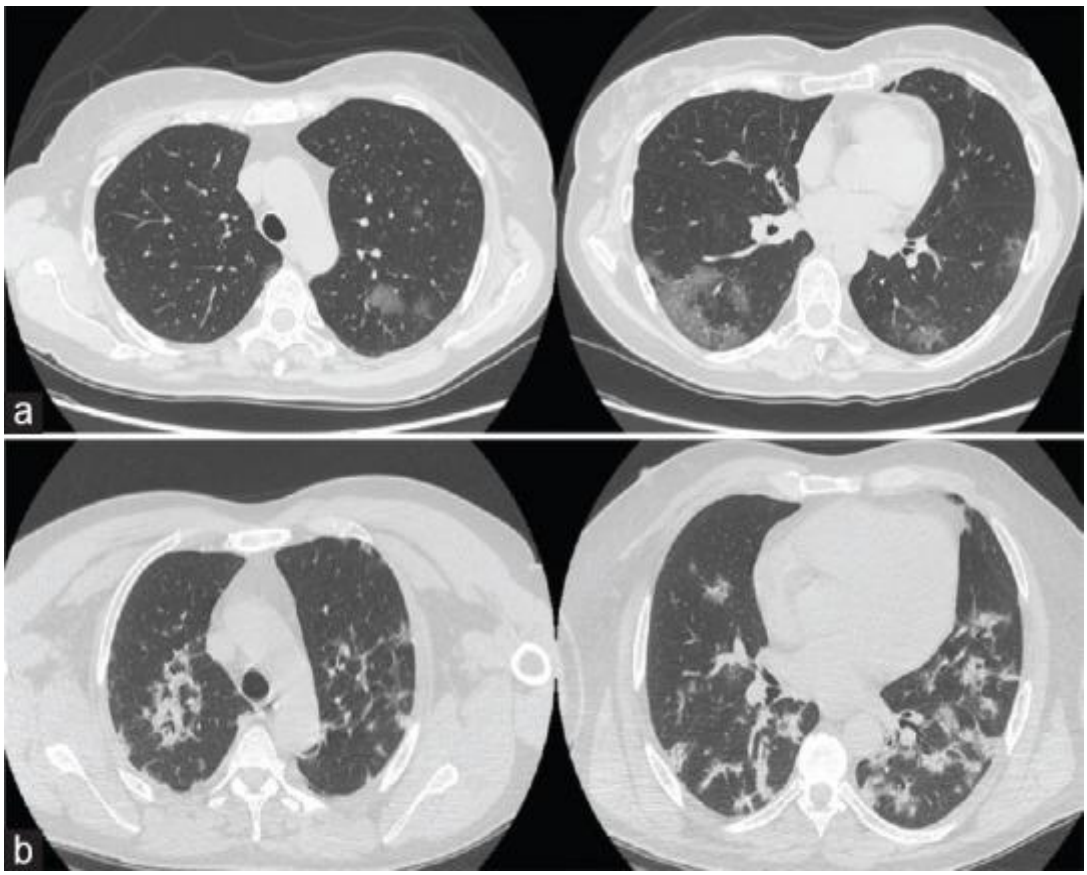
***Пневмония после COVID-19 является серьезным осложнением, наблюдаемым у пациентов, выздоравливающих после острой инфекции COVID-19. Ранняя диагностика имеет решающее значение для предотвращения тяжелых исходов, включая дыхательную недостаточность и долгосрочное повреждение легких. В этом обзоре изучается роль диагностических инструментов, включая визуализацию, биомаркеры и молекулярные методы, в раннем выявлении пневмонии после COVID-19. Мы подчеркиваем сильные и слабые стороны современных диагностических методов и обсуждаем новые технологии, которые могут улучшить раннюю диагностику. Синтезируя результаты 25 недавних исследований, в этом обзоре подчеркивается важность междисциплинарного подхода к диагностике пневмонии после COVID-19 и даются рекомендации для будущих исследований и клинической практики.***

***Ключевые слова: пневмония после COVID-19, включая респираторную, вирус SARS-CoV-2***

## Relevance

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has resulted in over 700 million confirmed cases worldwide as of 2023 [1]. While most patients recover fully, a significant proportion develop post-COVID-19 complications, including pneumonia. Post-COVID-19 pneumonia is characterized by persistent inflammation, fibrosis, and impaired lung function, often occurring weeks to months after the acute infection [2]. Early diagnosis is crucial to initiate timely interventions and prevent long-term morbidity.Diagnostic challenges arise due to the overlap of symptoms with other post-COVID-19 conditions, such as pulmonary fibrosis and secondary bacterial infections [3]. This review examines the role of diagnostic tools in identifying post-COVID-19 pneumonia at an early

stage, focusing on imaging, biomarkers, and molecular diagnostics. We also discuss the integration of these tools into clinical practice and their potential to improve patient outcomes.Biomarkers for Early Detection.Elevated levels of inflammatory markers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and ferritin, have been associated with post-COVID-19 pneumonia [10]. These biomarkers can help identify patients at risk of developing pneumonia during the recovery phase. For example, a 2020 study found that persistently high CRP levels were predictive of post-COVID-19 pneumonia in 70% of cases [11]. SP-D is a lung-specific biomarker that has shown promise in diagnosing post-COVID-19 pneumonia. Elevated SP-D levels correlate with alveolar damage and fibrosis, making it a useful tool for early detection [12]. A 2021 study reported that SP-D levels were significantly higher in patients with post-COVID-19 pneumonia compared to those without [13]. miRNAs are small non-coding RNAs that regulate gene expression and have been implicated in lung inflammation and fibrosis. Recent studies have identified specific miRNA signatures associated with post-COVID-19 pneumonia, offering a potential non-invasive diagnostic tool [14]. For instance, miR-21 and miR-155 have been shown to be upregulated in patients with post-COVID-19 pneumonia [15] PCR remains a cornerstone of COVID-19 diagnosis, but its role in post-COVID-19 pneumonia is limited. However, PCR can detect co-infections, such as bacterial or fungal pneumonia, which are common in post-COVID-19 patients [16]. A 2022 study highlighted the importance of PCR in identifying secondary infections in patients with persistent respiratory symptoms [17]. NGS allows for comprehensive analysis of the respiratory microbiome and can identify pathogens that may contribute to post-COVID-19 pneumonia.




A 2021 study used NGS to detect bacterial and fungal co-infections in 30% of post-COVID-19 pneumonia cases, underscoring its diagnostic value [18]. Despite advances in diagnostic tools, several challenges remain. The lack of standardized diagnostic criteria for post-COVID-19 pneumonia complicates early diagnosis [19]. Additionally, the high cost and limited availability of advanced imaging and molecular techniques hinder their widespread use [20]. Future research should focus on developing cost-effective, non-invasive diagnostic tools and integrating artificial intelligence (AI) to improve diagnostic accuracy [21]. Following these criteria, only patients belonging to scenario 1 with

negative COVID-19 test (or low test probability) or positive COVID-19 test but with low risk of disease progression should avoid imaging. Risks factors for disease progression are considered age >65 years, cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and immune-compromised patients. However, in case of worsening of respiratory status, an imaging examination becomes mandatory. If a different diagnosis is established, patients may follow the proper guidelines. In case of a negative COVID-19 test but with imaging features consistent with COVID-19 pneumonia (or in absence of an alternative diagnosis), it is suggested to repeat the test or pursue with other investigations (in case of scenario 2) or consider a presumptive diagnosis of COVID-19. The most common CT finding is GGO. Usual features are also GGO mixed to consolidations, mostly with air bronchogram. Consolidations, consolidations surrounded by GGO (”halo sign”), pleural thickening adjacent to parenchymal alterations, interlobular septal thickening and bronchovascular bundles thickening may be observed. Crazy paving is less common, while unusual alterations are nodules, cavitation, lymphadenopathies, pericardial effusion, pleural effusion, and pneumothorax. Although unilateral pneumonia may be observed in early involvement, COVID-19 pneumonia is usually multifocal and bilateral, commonly affecting peripheral and dorsal parts of the lungs. Alterations often have lower lobes predominance, even if all lobes may be affected. GGO and patchy consolidations are common findings in children[21].

- Typical appearance: peripheral and bilateral GGO or multifocal rounded GGO (both regardless of the coexistence of consolidation or crazy paving), findings of organizing pneumonia (OP) [Figure 3]
- Indeterminate appearance: nonrounded and nonperipheral GGO with either multifocal, diffuse, perihilar, or unilateral distribution (with or without consolidation), few very small nonrounded GGO with a nonperipheral distribution; absence of typical features [Figure 4]
- Atypical appearance: isolated lobar or segmental consolidation without GGO, discrete small nodules (centrilobular or with a tree-in-bud appearance), lung cavitation, or smooth interlobular septal thickening with pleural effusion; absence of typical or indeterminate features.

## Conclusion

Early diagnosis of post-COVID-19 pneumonia is essential to prevent severe outcomes and improve patient quality of life. Imaging techniques, biomarkers, and molecular diagnostics each play a critical role in identifying this condition at an early stage. A multidisciplinary approach, combining clinical evaluation with advanced diagnostic tools, is recommended for optimal patient care. Future research should aim to address current limitations and explore emerging technologies to enhance early diagnosis and treatment. Furthermore, both typical and indeterminate appearances cannot avoid DD. Regarding the typical appearance, suggested DD includes viral pneumonia, especially influenza, acute lung injury patterns, drug toxicity, and idiopathic or secondary diffuse lung diseases, especially those related to connective tissue diseases (CTD). CT and possibly, CXR, may also give prognostic information, evaluating the extent of lung involvement. However, CXR may fail in detecting early alteration, even if it allows to avoid patients transporting, reducing the risk of cross infection. Possibly, CXR and LUS might be utilized in combination for COVID-19 pneumonia screening, reducing the use of CT in selected cases.

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