*Innov Biosyst Bioeng*, 2025, vol. 9, no. 4, 16-27
doi: 10.20535/ibb.2025.9.4.325335

Review

# DIAGNOSIS OF COVID-19-ASSOCIATED CARDIOPULMONARY PATHOLOGY FROM CT DATA USING ARTIFICIAL INTELLIGENCE: A REVIEW OF METHODS AND FUTURE RESEARCH DIRECTIONS

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Received 30 December 2024; Accepted 23 September 2025

The COVID-19 pandemic highlighted the critical role of chest computed tomography (CT) in diagnosing and managing viral pneumonia, while also creating an unsustainable workload for radiologists. Machine learning (ML) has emerged as a powerful solution to this challenge. This article provides a comprehensive review of machine learning methods for the automated analysis of COVID-19-associated cardiopulmonary pathology on CT images.

We synthesize key findings from foundational and advanced studies. Recent advances demonstrate that machine learning models, particularly those integrating deep learning with quantitative texture analysis, can accurately classify hallmark lesions (e.g., ground-glass opacity, consolidation), differentiate between acute and Long COVID lung changes, and distinguish viral pneumonia from other conditions. These texture-based biomarkers provide objective measures of underlying biological processes such as alveolar inflammation and interstitial fibrosis.

In this review, we elucidate the relationship between CT radiologic patterns (ground-glass opacities, the crazy-paving pattern, consolidation, and fibrotic changes) and the corresponding biological processes – alveolar exudate, interstitial edema, and tissue remodeling. Their quantitative representation via texture and morphometric features in machine learning models yields noninvasive biomarkers that deepen understanding of COVID-19 pathophysiology and support clinical decision-making for risk stratification and disease monitoring. Future research should focus on developing more robust, computationally efficient models and integrating them into clinical workflows. There is also great potential in using these quantitative tools to create non-invasive biomarkers for tracking disease progression, aiding clinical trial stratification for novel therapeutics, and informing health-economic decisions on resource allocation.

**Keywords:** artificial intelligence; COVID-19; diagnosis, computer-assisted; diffuse alveolar damage; disease progression; machine learning; pneumonia, viral; pulmonary fibrosis; tomography, x-ray computed

## Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, precipitated an unprecedented global health crisis, placing immense strain on diagnostic resources. According to the World Health Organization (WHO), by the end of 2024, over 770 million confirmed cases and more than 7 million deaths had been reported [1]. COVID-19 remains a leading cause of mortality among respiratory diseases worldwide [2].

Chest computed tomography (CT) rapidly emerged as a front-line imaging modality, valued not only for its high sensitivity in detecting viral pneumonia [3] but also for its crucial role in assessing disease severity, guiding patient triage, and monitoring treatment response [4]. The characteristic radiological patterns observed in COVID-19 – such as ground-glass opacities (GGO), consolidation, and the "crazy-paving" pattern – are direct visual correlates of the underlying pathophysiology [5]. GGO corresponds to partial filling of the alveolar spaces with inflammatory exudate or fluid and thickening of the lung interstitium, representing a stage of diffuse alveolar damage where lung architecture is still discernible. In contrast, consolidation indicates a more advanced stage of lung injury, where alveolar air is completely replaced by pathological material, rendering the lung tissue dense and opaque. However, the sheer volume of CT examinations generated during pandemic peaks created a significant diagnostic bottleneck, overwhelming radiologists and risking delays in clinical decision-making. This clinical and logistical challenge underscored the urgent need for automated computational tools capable of rapidly and accurately interpreting these complex imaging findings, thereby setting the stage for the widespread application of machine learning in the fight against COVID-19.

The primary objective of this review is to provide a critical and comprehensive examination of the ma-

chine learning methods applied to the diagnosis and assessment of COVID-19-associated cardiopulmonary pathology from chest CT images. This review synthesizes the evolution of the field, from foundational techniques rooted in texture analysis and classical machine learning to the application of advanced deep learning architectures, such as convolutional neural networks, and the emerging frontier of multimodal artificial intelligence.

Specifically, this review aims to:

1. Synthesize the state-of-the-art by summarizing the key methodologies and performance of influential studies.

2. Bridge the technological and biological domains by emphasizing how computational biomarkers derived from CT images correspond to underlying pathophysiological processes like alveolar inflammation and fibrosis.

3. Critically evaluate the principal limitations and challenges of current models, including issues of generalizability, clinical integration, and computational cost.

4. Identify and delineate promising directions for future research aimed at developing more robust, clinically integrated, and impactful diagnostic tools for current and future epidemiological crises.

## 1. Diagnostic Approaches in COVID-19

The diagnosis of COVID-19 is a crucial element in managing the pandemic. There are several approaches to diagnosis, each with its own advantages and limitations depending on the clinical context.

The polymerase chain reaction (PCR) test is considered the gold standard for detecting the SARS-CoV-2 virus [6]. It is a nucleic acid amplification test (NAAT) that detects viral RNA through reverse transcription polymerase chain reaction (RT-PCR). For PCR testing, a nasopharyngeal swab is taken, and the viral RNA is amplified for detection. This method provides high sensitivity and specificity. According to studies, the sensitivity of PCR can reach up to 95% under optimal conditions [7], making it the most reliable method for detecting SARS-CoV-2 [8]. However, PCR requires specialized laboratory equipment, making it less accessible for large-scale screening, especially in remote or overburdened regions.

Antigen tests detect viral proteins (antigens) through an enzyme-linked immunosorbent assay (ELISA) of a nasopharyngeal or nasal swab. Their main advantage is speed: the result is available within 15-30 minutes, making them useful for mass testing and emergency use. However, the sensitivity of antigen tests is significantly lower, especially at low viral loads or in the early stages of the disease. According to a study, the sensitivity of antigen tests ranges from 88.2% to 89.6% [9]. This means that they are more suitable for screening in populations with a high probability of disease or in cases where a quick result is needed.

Serum immunoglobulin M (IgM) and immunoglobulin G (IgG) concentrations, quantified through standard serological assays, reflect the humoral immune response to pathogens; although these measurements are informative for confirming prior exposure and assessing immune status, they lack the temporal sensitivity required for early-stage diagnosis or definitive confirmation of an active infection. Following infection, the immune system initiates antibody production. Typically, IgM class antibodies appear first, often approximately 5-10 days after infection, whereas IgG class antibodies usually reach detectable levels later, typically from day 7-14. This inherent delay in the antibody response means that serological tests are less suitable for diagnosing acute infection at very early stages (e.g., during the first week) compared to methods that directly detect the virus or its components. Furthermore, their prognostic value regarding the duration of protection remains a subject of active research, as evidenced by findings from 2023–2024 [10-12].

The development of automated approaches to the diagnosis of infectious diseases has become particularly important after the emergence of highly pathogenic coronaviruses, such as SARS-CoV, MERS-CoV, and SARS-CoV-2. For example, to combat MERS-CoV, methods for predicting immune response and creating potential vaccines using computational modeling are being actively investigated [13]. Similar approaches to analyzing viral infections can also be applied in the development of automated COVID-19 diagnostic systems and digital medicine.

Chest radiography is often used to assess the condition of the lungs in patients with COVID-19 symptoms. X-ray images can reveal signs characteristic of viral and bacterial pneumonia, including bilateral lung lesions. Although chest radiography is not as sensitive as CT, it remains a useful method for detecting severe forms of pneumonia, especially in settings with limited access to CT. According to studies, chest radiography detects abnormalities in 63% of patients with moderate to severe COVID-19 [14].

Chest CT is a more sensitive method for detecting lung lesions caused by COVID-19 compared to chest radiography. CT allows the detection of characteristic changes in the lungs, such as ground-glass opacities, consolidations, and fibrosis, which are typical of viral pneumonia. This makes CT an indispensable tool for monitoring severe forms of disease. The sensitivity of CT for detecting lung lesions in patients with COVID-19 ranges from 76.25% to 90% [15], making this method valuable for assessing disease progression and planning treatment [16].

Table 1 compares the diagnostic methods discussed based on sensitivity, specificity, turnaround time, cost, and key advantages/disadvantages.

While diagnostic methods such as PCR or antigen tests directly detect the presence of the virus, CT offers the unique advantage of allowing assessment of the extent of lung damage. The high sensitivity of CT, combined with the ability to obtain images in real-time, makes it an important tool in clinical decision-making. In some patients with low viral load, the initial PCR test may be false-negative, whereas CT already captures typical signs of COVID-19 pneumonia [17, 18]. Although CT sensitivity is generally high [18-20], its specificity varies significantly and is typically lower than that of PCR [21] and approved SARS-CoV-2 rapid antigen tests [22]. Thus, it is advisable to use CT as an adjunct to laboratory diagnostics and as a means of monitoring the course of the disease.

As research indicates [23, 24], chest CT is the most informative method for diagnosing alterations in lung architecture in COVID-19 viral pneumonia. Serial CT findings demonstrate that the radiological evolution of pneumonia in COVID-19 correlates with the clinical course of the disease [25].

With the application of machine learning and deep learning methods, the potential of CT as a diagnostic tool significantly increases. Studies have shown that such algorithms can detect and quantify abnormalities on CT images with an accuracy exceeding 90% [26]. Convolutional neural networks (CNNs), as one type of deep learning algorithm, have proven effective in recognizing COVID-19-specific signs, such as ground-glass opacities and consolidations [27]. This not only improves diagnostic accuracy but also significantly reduces physician workload.

The authors of reference [28] believe that artificial intelligence systems, particularly machine learning, are capable of revolutionizing radiological diagnostics, improving detection, increasing diagnostic accuracy, and reducing the time spent on developing diagnostic conclusions.

## 2. Methodologies and Applications of Machine Learning in COVID-19 CT Analysis

The rapid progression of the COVID-19 pandemic necessitated the development of automated tools to aid in diagnosis. Machine learning and deep learning have become central to this effort, offering powerful methods for analyzing chest CT images, which are rich in diagnostic information. The literature reflects progression from foundational techniques to highly specialized deep learning models for various diagnostic tasks.

**Table 1:** Overview and comparison of key diagnostic approaches in COVID-19

| Category | Specific method | What it detects | Sensitivity | Specificity | Advantages | Disadvantages |
|---|---|---|---|---|---|---|
| Molecular genetic methods | RT-PCR | SARS-CoV-2 RNA | High (up to 95-98%) | High (>98%) | "Gold standard" for diagnosis<br>Early detection | Requires a laboratory<br>High cost<br>Long turnaround time (4-72h) |
| Immunological methods (based on antigen-antibody reaction) | Antigen (Ag) test | Viral proteins (antigens) | Moderate (highly variable, 50-95%) | High (>99%) | Speed (15-30 min)<br>Low cost<br>Suitable for mass screening | Risk of false-negative results with low viral load |
| | Antibody (Ab) test | Antibodies (IgM, IgG) to the virus | High (>90% after day 14) | High (>95%) | Identifies past infection<br>Important for epidemiological studies | Not suitable for early diagnosis<br>Antibodies appear late |
| Imaging methods | Chest radiography (CXR) | Pathological lung changes (signs of pneumonia) | Moderate (~60-80%) | Low (~25-80%) | Wide availability<br>Speed<br>Low cost | Low informativeness in early stages<br>Non-specific changes |
| | CT | Characteristic lung changes (GGO, consolidation) | High (80-99%) | Low (~25-90%) | High sensitivity to lesions<br>Detailed assessment of damage extent | High cost and radiation dose<br>Non-specific (changes similar to other viral pneumonias)<br>Cannot confirm active infection |

### 2.1. Early Detection and Lesion Classification

Initial research focused on identifying and classifying the characteristic lesions (Fig. 1) of COVID-19 pneumonia, such as GGO, crazy-paving patterns, and consolidation.

A common strategy involves combining traditional machine learning with deep learning features. For instance, Ukrainian researchers developed hybrid approaches that utilized texture analysis, specifically the gray level co-occurrence matrix (GLCM), to extract quantitative features from regions of interest, which were then fed into a custom seven-layer convolutional neural network for classification [29]. While this method proved effective, particularly for GGO identification, the authors noted limitations related to small patient cohorts and variable accuracy across different lesion types, underscoring the need for model refinement.

Building on this, more sophisticated multi-level diagnostic pipelines were proposed. Davydko et al. [30, 31] designed a system that integrated convolutional neural networks with other machine learning classifiers, such as logistic self-organizing forests (LSOF) and the group method of data handling (GMDH). This pipeline performed a sequence of tasks: first filtering images for signs of COVID-19, then segmenting the affected lung areas with a U-Net model and finally classifying the specific lesion types. The authors reported high classification efficacy, especially for GGO, but highlighted that segmentation accuracy and the system's computational complexity remained areas for future improvement [31].

### 2.2. The Biological Significance of CT Texture Biomarkers

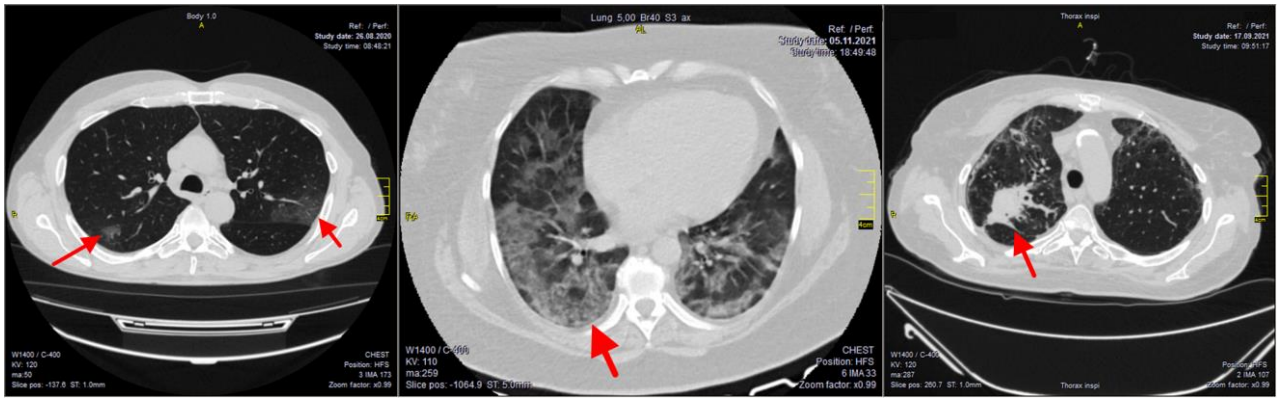
The machine learning models discussed in this review rely on classifying radiological patterns whose texture features are not arbitrary mathematical constructs; rather, they are quantitative descriptors of underlying biological processes at the tissue and cellular level. Understanding this link is fundamental to appreciating their clinical and scientific value [32].

*2.2.1. Ground-Glass Opacity as a Marker of Early Alveolar Injury*

GGO is radiologically defined as a hazy increase in lung attenuation that does not obscure the underlying pulmonary vessels. From a biological standpoint, GGO represents an early and often reversible stage of lung injury. The specific pathophysiology includes the partial filling of alveolar spaces with proteinaceous fluid, inflammatory cells (exudate), or blood, combined with a thickening of the lung interstitium due to edema and cellular infiltration [32]. Texture analysis quantifies this state with high precision. Features like increased homogeneity and low contrast reflect the relatively uniform nature of the fluid-filled alveoli compared to the air-tissue interface of healthy lungs. Therefore, a texture-based GGO classifier does not merely identify a pattern; it quantifies the extent of initial diffuse alveolar damage, providing a sensitive biomarker for the onset of viral pneumonia.

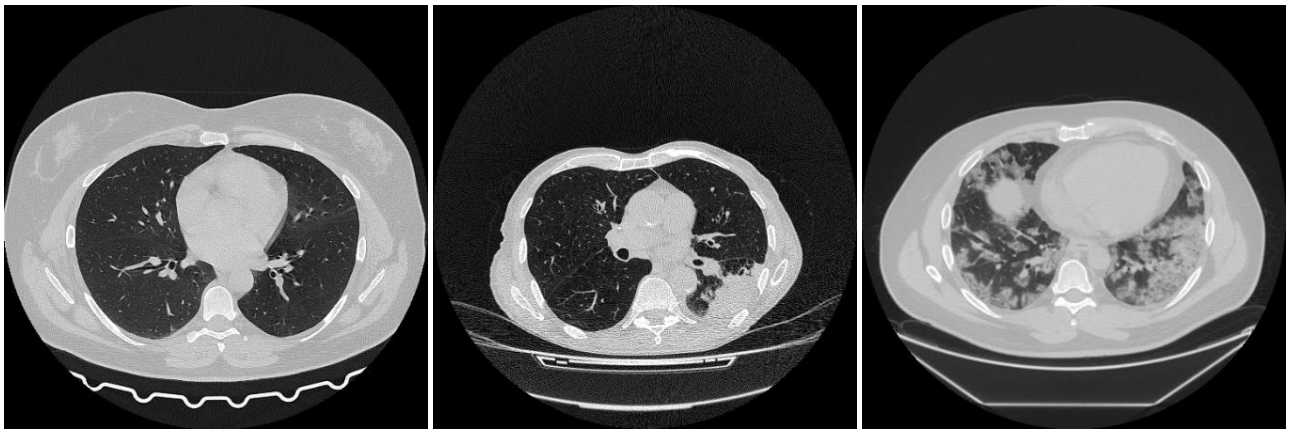
*2.2.2. Consolidation and Crazy-Paving as Indicators of Disease Progression*

As the disease progresses, GGO can evolve into consolidation or a crazy-paving pattern. Consolidation appears as a dense, uniform opacification that completely obscures the underlying lung architecture. This signifies a more severe stage of injury where the alveolar air has been entirely replaced by inflammatory exudate, corresponding to advanced diffuse alveolar damage (DAD) [32]. Texture algorithms detect this as a highly homogeneous region with very low internal contrast. The crazy-paving pattern, consisting of GGO superimposed with thickened interlobular septa, reflects a dual pathology: the GGO signifies alveolar filling, while the linear septal thickening indicates pronounced interstitial edema. Computationally, this is a highly heterogeneous pattern, captured by texture



**a)** **b)** **c)**

**Figure 1:** Examples of chest CT slices with: a – ground-glass opacity; b – crazy-paving pattern; c – consolidation. Original images from the authors' institutional archive (de-identified); not reproduced or adapted from any published source.



**a)** **b)** **c)**

**Figure 2:** Examples of chest CT slices: a – normal; b – with pneumonia; c – with COVID-19. Original images from the authors' institutional archive (de-identified); not reproduced or adapted from any published source.

features like high entropy and contrast. A model that differentiates these patterns is thus distinguishing between stages of inflammatory progression, from partial alveolar flooding (GGO) to complete flooding (consolidation) and combined alveolar-interstitial edema (crazy-paving).

*2.2.3. Fibrotic-like Changes as Signatures of Tissue Remodeling and Scarring*

In the post-acute phase, particularly in Long COVID, the lung can undergo a process of mal-adaptive repair, leading to permanent fibrotic-like changes [33]. These include reticulations, traction bronchiectasis, and honeycombing, which represent irreversible architectural distortion. Biologically, this is driven by the persistent activation of fibroblasts, leading to excessive deposition of collagen and other extracellular matrix proteins, which results in lung scarring and stiffening [34]. This process is often accompanied by microvascular injury and remodeling, impairing gas exchange. Texture analysis excels at quantifying this structural disarray. Features that measure heterogeneity, randomness (entropy), and the presence of sharp edges and lines are highly sensitive to these changes. Consequently, machine learning models trained on these texture biomarkers can objectively measure the degree of established fibrosis, offering a powerful tool for prognostication and monitoring the long-term sequelae of severe COVID-19.

### 2.3. Differential Diagnosis

A critical clinical task is the differentiation of COVID-19 from other respiratory conditions with similar radiological presentations. To address this, Yukhymiuk et al. [35] conducted a comparative analysis using both CNNs and autoencoders to distinguish between normal, bacterial pneumonia, and COVID-19 chest CT scans (Fig. 2). Their work demonstrated the superior classification performance of convolutional neural networks over autoencoders for this task, while also acknowledging the potential for model overfitting and the need for more robust data handling, for instance by incorporating segmentation.

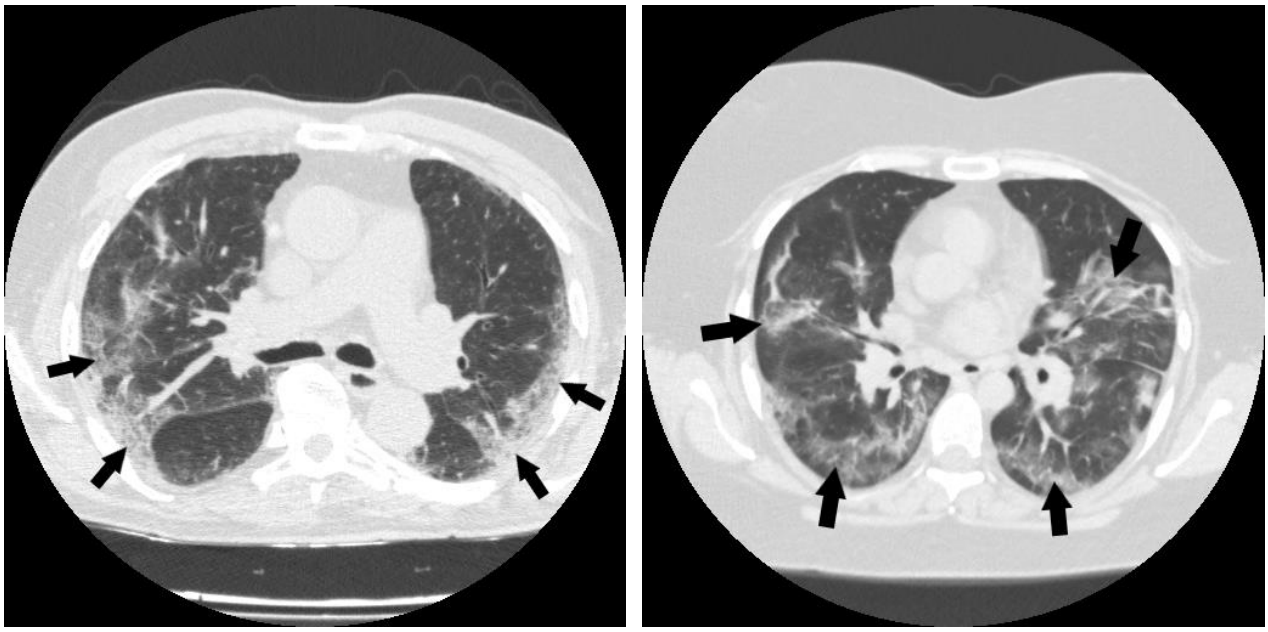
This line of research is well-represented in international literature. Mishra et al. [27] applied transfer learning using established convolutional neural network architectures, VGG16 and ResNet50, to classify CT scans as normal, pneumonia, or COVID-19. They achieved excellent results, particularly in the binary task of distinguishing COVID-19 from normal scans and used techniques like data augmentation and cross-validation to ensure model robustness. Similarly, Gupta and Bajaj [36] evaluated pre-trained models like MobileNetV2 and DarkNet19, finding that DarkNet19 was exceptionally accurate for COVID-19 screening. They also proposed a novel lightweight model that could reduce training time while maintaining high performance, a crucial factor for clinical deployment.

### 2.4. Tracking Disease Progression and Long COVID

Beyond initial diagnosis, machine learning offers tools to monitor disease progression and identify long-term sequelae, or "Long COVID." Lutchenko et al. [37] specifically focused on creating models to distinguish between the acute phase of COVID-19 and the persistent changes of Long COVID on CT images (Fig. 3).

Their methodology involved U-Net-based lung segmentation followed by texture analysis and classification with various ensemble machine learning algorithms [38]. Among the tested methods, the random forest of optimal complexity trees (RFOCT) [39] was identified as highly effective, showcasing the potential of machine learning to quantify subtle, persistent structural lung changes [37].

The clinical relevance of this research is supported by systematic reviews and meta-analyses. For example, a review by Babar et al. [33] of short- and long-term CT findings confirmed that while abnormalities



**a)** **b)**

**Figure 3:** Examples of chest CT slices: a – with signs of COVID-19; b – with signs of Long COVID. Original images from the authors' institutional archive (de-identified); not reproduced or adapted from any published source.

like GGO decrease over time, fibrotic-like changes can persist for two or more years post-infection, especially in patients who had severe disease. This provides a strong clinical basis for developing computational tools to track and manage post-COVID pathology.

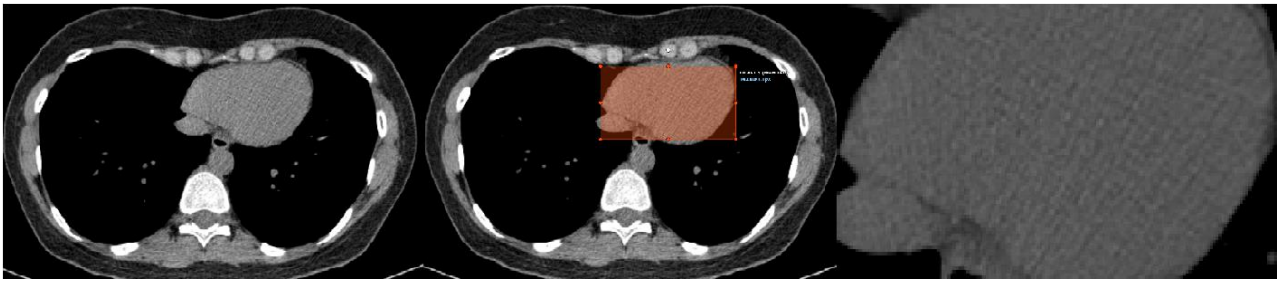
### 2.5. Advanced Architectures and Novel Approaches

Researchers have also explored beyond standard convolutional neural networks to improve performance and efficiency. Godbin and Jasmine [40] demonstrated that strong results could be achieved using only GLCM-derived texture features (contrast, homogeneity, etc.) coupled with ensemble classifiers like random forest, XGBoost, and LightGBM. Their random forest model reached near-perfect classification accuracy on a public dataset, highlighting the power of well-engineered features.

In a move towards more computationally efficient hardware, Garain et al. [41] proposed a novel approach using a deep convolutional spiking neural network (SNN). SNNs mimic biological neurons more closely and can operate on low-power neuromorphic chips. Their potential-dependent SNN model outperformed traditional deep learning models like VGG16 and ResNet on a COVID-19 detection task, suggesting a promising future direction for energy-efficient medical image analysis, though the authors noted the significant training time required for such models.

### 2.6. Diagnosis of Extrapulmonary Pathologies

Finally, the application of these methods is not limited to the lungs. COVID-19 is a systemic disease, and associated pathologies like myocarditis are a serious concern. Nastenko et al. [42] developed a methodology to aid in the diagnosis of myocarditis by analyzing structural changes in the heart visible on chest CT scans (Fig. 4).



**a)** **b)** **c)**

**Figure 4:** An example of an annotated chest CT slice: a – input image; b – a rectangular region of interest; c – output image. Original images from the authors' institutional archive (de-identified); not reproduced or adapted from any published source.

Using a public dataset [43], their work focused on texture analysis to build classification models that could support clinical decision-making for this serious complication.

### 2.7. Integration with Virology, Immunology, and Health Economics

The clinical utility of machine learning in analyzing COVID-19 CT images extends far beyond simple diagnosis, offering powerful translational bridges to virology, immunology, and health economics. Quantitative metrics derived from CT scans, such as the percentage of affected lung volume or the texture features of lesions, can serve as non-invasive surrogate endpoints in clinical trials for novel antiviral or immunomodulatory therapies. For instance, a measurable reduction in computationally defined lung injury could provide early evidence of a drug's efficacy, helping to stratify patient cohorts and accelerate therapeutic development.

Furthermore, these automated analyses provide a crucial link to immunology. The radiological patterns of severe COVID-19 are manifestations of the host's immune response, with features like extensive consolidation often correlating with hyperinflammation and elevated biomarkers like C-reactive protein and interleukins. Machine learning models can quantify this immune-mediated damage, offering objective tools to study disease immunopathology and identify patients who might benefit from targeted anti-inflammatory treatments. This aligns with the broader search for reliable "correlates of protection" and response, a central theme in modern virology and vaccine research [10, 12].

From a health-economics perspective, the impact is equally significant. Automated, rapid CT severity scoring enables more efficient resource allocation – a critical factor during pandemic surges. By providing objective data for triage, these systems can help hospitals prioritize intensive care unit (ICU) beds, ventilators, and specialized staff for patients with the highest predicted risk of adverse outcomes [26], thereby optimizing patient care and mitigating the economic burden on healthcare systems.

### 2.8. Vision–Language and Multimodal Integration of CT and Textual Data

This theme of integration is now extending from the combination of different scientific fields to the fusion of different data types, heralding the next frontier in artificial intelligence development. A significant trend in medical artificial intelligence is the development of multimodal models that integrate medical imaging with associated textual information, such as electronic health records (EHR) and radiology reports. In radiology, large vision–language models (VLMs) trained on paired image-text data are emerging as a powerful new paradigm. For instance, Li et al. [44] recently introduced "BrainGPT," a multimodal large language model designed for 3D brain CT report generation. By creating a dedicated dataset of CT volumes with corresponding reports and employing instruction tuning, their proof-of-concept model generated narrative findings that were indistinguishable from human-written reports in approximately 74% of cases during a Turing test. This work demonstrated the feasibility of applying VLM architectures to volumetric medical imaging.

Building on such foundational work, research is expanding to other anatomical regions and larger-scale models. The development of 3D vision–language foundation models, exemplified by the Merlin model for abdominal CT [45], has shown the viability of training on massive datasets comprising millions of CT slices paired with EHR text. These models learn joint representations of imaging and text, enabling a range of downstream applications, including automated radiology report generation, visual question answering (VQA), and cross-modal retrieval.

The clinical utility of multimodal integration has been particularly evident in the context of COVID-19, where combining imaging with clinical data enhances prognostic accuracy. A study in Nature Communications [46] demonstrated that a deep learning analysis of admission chest CT scans, when fused with patients' clinical variables and laboratory results, significantly improved the prediction of severe outcomes. This multimodal approach, termed "artificial intelligence-severity," outperformed models relying on clinical data alone, underscoring the complementary prognostic value of imaging data. Following this principle, other researchers have developed hybrid pipelines wherein a convolutional neural network processes the CT scan while a separate model ingests textual or tabular inputs (e.g., symptoms, lab values). The extracted features are then fused for tasks such as risk stratification. One such hybrid model, designed to predict ICU admission or mortality using both CT and clinical biomarkers, achieved high accuracy in discriminating between patient cohorts [47]. These findings consistently show that multimodal designs yield more robust COVID-19 severity predictions than single-modality approaches.

The field continues to advance rapidly, with recent reviews noting substantial progress in radiology-specific report generation models and medical VQA systems that leverage both visual and linguistic features [48]. Concurrently, there is growing interest in adapting general-purpose VLMs like GPT-4V for medical applications. While preliminary investigations suggest potential, rigorous quantitative evaluations of their performance in nuanced CT interpretation tasks

are still forthcoming [49]. In summary, the fusion of imaging and textual data through vision–language and other multimodal architectures represents a significant advancement, aiming to create more contextually aware and clinically integrated decision support systems.

## 3. Potential Directions for Further Research Using Machine Learning

The key findings from the reviewed literature are consolidated in Table 2, which compares the technical approaches and clinical impact of notable studies in the field.

The rapid progress in applying machine learning to COVID-19 CT analysis has not only addressed immediate clinical needs but has also illuminated a clear path for future innovation. The limitations of current models and the emergence of new technologies define the critical frontiers for the next generation of research.

### 3.1. Towards Generalization and Out-of-Distribution Detection

A primary limitation of many models reviewed here is their narrow training on specific COVID-19 datasets. The next crucial step is to develop more robust and generalizable systems. This involves training models on massive, diverse datasets that include not only COVID-19 but also a wide array of other viral and bacterial pneumonias, interstitial lung diseases, and acute respiratory distress syndrome from various causes. A key research direction is the development of reliable out-of-distribution (OOD) detection – creating intelligent systems that can recognize when a case presents features, they were not trained on (i.e., those "previously unseen") and flag it for human expert review. This capability is essential for building trustworthy artificial intelligence tools that can be safely deployed in real-world clinical environments where pathologies are varied and unpredictable.

### 3.2. Longitudinal Modeling for Long COVID and Extrapulmonary Complications

While our review has highlighted models for detecting Long COVID and myocarditis at single time points, the true clinical value lies in longitudinal analysis. Future work should focus on developing models that can process serial CT scans from the same patient over months or years. Such systems could quantify the rate of progression or resolution of pulmonary fibrosis, track subtle changes in myocardial texture indicative of chronic inflammation, and provide objective, non-invasive biomarkers for disease activity. This would represent a paradigm shift in managing the long-term sequelae of COVID-19, enabling personalized follow-up and timely therapeutic intervention.

### 3.3. Predictive Modeling for Post-Infection Malignancy Risk

Given that chronic inflammation is a well-established risk factor for carcinogenesis, and severe COVID-19 involves profound pulmonary inflammation, a compelling long-term research avenue is the development of predictive models for Long COVID complications like broncho-alveolar lung cancer. Based on the initial severity and specific texture features of a patient's CT scan during the acute phase, machine learning models could be trained to identify cohorts at the highest risk for future malignant transformation. This research would require large-scale, long-term follow-up data but holds immense potential for creating early-warning systems and guiding surveillance strategies in high-risk COVID-19 survivors.

### 3.4. Advancing Multimodal and Foundation Models

As we have discussed, multimodal models represent a cutting-edge frontier. The future in this domain involves moving beyond simple data fusion to creating truly synergistic systems. Key directions include:

- Refining vision-language models to not only generate reports but also to highlight discrepancies between their findings and the official radiologist's report, acting as an intelligent second reader.
- Developing VQA systems that can answer complex, context-aware clinical questions (e.g., "Is the fibrosis more prominent in the upper lobes compared to the scan from six months ago?").
- Building foundation models that can natively integrate and reason across imaging (CT), pathology reports, genomic data, and clinical time-series data to provide a holistic, patient-specific diagnostic and prognostic summary.
- A critical challenge for these massive models is their "black box" nature. Future research must focus on developing robust explainability (XAI) methods to make their reasoning transparent and trustworthy to clinicians.

**Table 2:** Summary of key published studies on machine learning for COVID-19 ct analysis

| Task | Machine learning approach | Key performance metric | Biological endpoint and clinical impact | Ref. |
|---|---|---|---|---|
| Classify COVID-19 lesion types (GGO, crazy-paving, consolidation) | Hybrid classifier: convolutional neural network + LSOF + GMDH + texture features | F1-score: 0.96 | *Endpoint:* differentiating stages of alveolar/interstitial inflammation. *Impact:* aiding early diagnosis (via GGO) and objective severity assessment. | [30, 31] |
| Differentiate Normal vs. COVID-19 and Pneumonia vs. COVID-19 | Convolutional neural network, Autoencoder | Accuracy: 1.00 (convolutional neural network, Pneumonia vs. COVID-19) | *Endpoint:* distinguishing viral (SARS-CoV-2) vs. other causes of lung injury. *Impact:* improving diagnostic specificity; guiding appropriate therapy selection. | [35] |
| Classify Normal vs. Pneumonia vs. COVID-19 | Transfer Learning (VGG16, ResNet50) | Accuracy: 94.76% (VGG16) | *Endpoint:* automated detection of viral pneumonia patterns. *Impact:* enabling high-throughput screening and reducing radiologist workload. | [27] |
| Automated screening of COVID-19 vs. non-COVID | Pre-trained networks (DarkNet19) and lightweight convolutional neural network | Accuracy: 98.91% (DarkNet19) | *Endpoint:* high-fidelity identification of SARS-CoV-2 lung pathology. *Impact:* enabling rapid, accurate screening with computationally efficient models. | [36] |
| Differentiate acute COVID-19 vs. Long COVID lung changes | Ensemble methods (RFOCT) with texture analysis | Accuracy: 0.89 (RFOCT) | *Endpoint:* quantifying persistent fibrotic-like changes vs. acute inflammation. *Impact:* identifying patients Long COVID for targeted follow-up. | [37] |
| Screen for COVID-19 using only texture features | GLCM texture features + Ensemble methods (Random Forest) | Accuracy: 100% (Random Forest) | *Endpoint:* demonstrating that macroscopic tissue texture robustly signatures viral lung injury. *Impact:* validating texture analysis as a powerful standalone diagnostic approach. | [40] |
| Detect COVID-19 using a biologically inspired model | Spiking Neural Network (SNN) | F1-score: 0.99 | *Endpoint:* mimicking biological neural processing for image recognition. *Impact:* proof-of-concept for ultra-low-power, energy-efficient diagnostic hardware. | [41] |
| Aid in the diagnosis of COVID-19-associated myocarditis from chest CT | Texture analysis + classification algorithms | Accuracy: ~0.74 | *Endpoint:* detecting structural changes in myocardial tissue. *Impact:* supporting early detection of a major extrapulmonary complication. | [42] |
| Predict severe outcomes in COVID-19 patients | Multimodal artificial intelligence: Deep learning (CT) + clinical/lab variables | AUC: 0.79 | *Endpoint:* fusing imaging biomarkers with systemic biological data. *Impact:* enhanced prognostic accuracy for better patient risk stratification. | [46] |
| Predict ICU admission or death in COVID-19 patients | Hybrid DL/machine learning: convolutional neural network (CT) + clinical biomarker model | AUC: 0.94 | *Endpoint:* integrated assessment of lung damage and systemic response. *Impact:* more robust severity prediction to guide critical care resource allocation. | [47] |
| Assess general-purpose VLM (GPT-4V) on radiology tasks | Quantitative evaluation of GPT-4V on multi-region imaging | While GPT-4V can identify what an image is, it cannot reliably interpret what is wrong within it | *Endpoint:* probing the zero-shot reasoning capabilities of general artificial intelligence on medical images. *Impact:* establishes a baseline for applying general foundation models in radiology. | [49] |

## Conclusions

This review has demonstrated that machine learning has provided a powerful and indispensable set of tools for navigating the diagnostic challenges of the COVID-19 pandemic. Across a spectrum of approaches – from quantitative texture analysis to deep convolutional neural networks and advanced multimodal systems – a clear conclusion emerges: the most effective diagnostic models are those that integrate data and techniques. Whether by combining deep learning features with handcrafted texture biomarkers or by fusing computed tomography data with clinical text, these hybrid strategies yield more robust and clinically relevant insights than single modality approaches alone.

Crucially, this review underscores that these computational methods are not mere pattern classifiers but sophisticated bioengineering tools capable of quantifying the underlying pathophysiology of viral lung injury, from initial alveolar exudate to chronic fibrotic remodeling. While significant challenges in model generalization, explainability, and seamless clinical integration remain, the trajectory of the field is clear. The ongoing development of foundation models and multimodal artificial intelligence promises to create more holistic, context-aware systems that will not only redefine diagnostics for future pandemics but also become integral to routine clinical decision support.

## Interests' disclosure

The authors declare no competing interests related to this study.

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## ДІАГНОСТИКА COVID-19-АСОЦІЙОВАНОЇ КАРДІОПУЛЬМОНАЛЬНОЇ ПАТОЛОГІЇ ЗА ДАНИМИ КТ ІЗ ЗАСТОСУВАННЯМ ШТУЧНОГО ІНТЕЛЕКТУ: ОГЛЯД МЕТОДІВ І НАПРЯМИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Пандемія COVID-19 підкреслила вирішальну роль комп'ютерної томографії (КТ) у діагностиці та лікуванні вірусної пневмонії, водночас створивши надмірне навантаження на радіологів. Машинне навчання (МН) стало потужним вирішенням цієї проблеми. Ця стаття представляє комплексний огляд методів МН для автоматизованого аналізу COVID-19-асоційованої кардіопульмональної патології за даними КТ-зображень.

Ми узагальнюємо ключові результати фундаментальних та передових досліджень. Останні досягнення показують, що моделі МН, особливо ті, що поєднують глибоке навчання з кількісним текстурним аналізом, здатні точно класифікувати характерні ураження (наприклад, матове скло, консолідацію), диференціювати гостру та постковідну фази захворювання та відрізняти вірусну пневмонію від інших станів. Ці текстурні біомаркери забезпечують об'єктивну оцінку базових біологічних процесів, таких як альвеолярне запалення та інтерстиціальний фіброз.

У статті розкрито зв’язок між радіологічними патернами КТ (матове скло, бруківка, консолідація, фібротичні зміни) та відповідними біологічними процесами – альвеолярним ексудатом, інтерстиціальним набряком і ремоделюванням тканини. Їхня кількісна репрезентація текстурними та морфометричними ознаками в моделях МН створює неінвазивні біомаркери, що поглиблюють розуміння патофізіології COVID-19 і підсилюють клінічні рішення щодо стратифікації та моніторингу. Майбутні дослідження мають бути спрямовані на розробку більш надійних, ефективних моделей та їх інтеграцію в клінічну практику. Існує також значний потенціал у використанні цих кількісних інструментів для створення неінвазивних біомаркерів для моніторингу прогресування хвороби, стратифікації пацієнтів у клінічних випробуваннях нових терапевтичних засобів та прийняття рішень у сфері економіки охорони здоров'я.

**Ключові слова:** штучний інтелект; COVID-19; комп’ютеризована діагностика; дифузне альвеолярне запалення; прогресування захворювання; машинне навчання; вірусна пневмонія; легеневий фіброз; комп’ютерна томографія.