

Advantages and limitations of artificial intelligence tools in the analysis of thoracic computed tomography images in patients with COVID-19 pneumonia – a review

Nina Mrvoš¹, Melita Kukuljan^{1,2}, Maja Karić^{1,2}, Klaudija Višković^{1,3}

¹ Faculty of Health Studies, University of Rijeka, Rijeka, Croatia

² Clinical Hospital Center Rijeka, Department of Diagnostic and Interventional Radiology, Rijeka, Croatia

³ University Hospital for Infectious Diseases „Dr. Fran Mihaljević“, Department of Radiology and Ultrasound, Zagreb, Croatia

Corresponding author: Nina Mrvoš, email: ninamrvos@gmail.com

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Abstract

Coronavirus disease 2019 (COVID-19) is a systemic viral infection caused by the highly infectious SARS-CoV-2 virus, which can lead to pneumonia and other complications. It first appeared at the end of 2019 in China and spread rapidly around the world causing authorities to declare a pandemic at the start of 2020. People infected with this virus usually present with symptoms such as cough, fever and shortness of breath. This respiratory disease causes changes in lung parenchyma that can be analysed on a CT scan. CT became one of the most accurate diagnostic methods for confirmation of COVID-19 in patients as well as a tool for estimating the stage of infection. Since identifying the disease from radiological scans is quite time-consuming and complex, the development of artificial intelligence (AI) models has emerged as a potential solution to enhance diagnostic speed and accuracy. Most common AI models were based on deep learning and machine learning and were able to correctly identify COVID-19 pneumonia on CT scans. The main problem in developing these models proved to be the lack of databases on which these models could be trained. This review analysed the results of twenty-one papers published on the topic of AI use in detecting COVID-19 on CT scans. The results of analysis show that AI is significantly accurate in detecting COVID-19 pneumonia, but it still needs to be developed further.

Key words: COVID-19, SARS-CoV-2, computed tomography of the chest, artificial intelligence, deep learning, machine learning

Introduction

As of February 2, 2025, the World Health Organization (WHO) has published a report according to which there have been 777,368,929 recorded cases of COVID-19 in the world since December 2019 (1). Since its beginning in Wuhan, China, this severe respiratory disease has spread rapidly globally, leading to the declaration of a pandemic on March 11, 2020 (1).

The high speed of expansion and the growing number of patients have created enormous pressure on the healthcare system and its employees. One of the main health specialties that actively worked on the early detection and control of the development of COVID-19 was radiology. Radiological methods used in the diagnosis of COVID-19 are: chest radiographs, computed tomography (CT) of the chest, thorax ultrasound and magnetic

resonance imaging (MRI) of the chest (2, 3, 4). Given that patients infected with COVID-19 required urgent hospital admission, there was a shift in long waiting lists for examinations of patients not infected with COVID and an additional workload of radiology department employees.

In order to perform examinations as quickly and efficiently as possible and make a diagnosis, the idea of introducing new systems and technologies in healthcare appeared. One of the most commonly implemented technologies was artificial intelligence (AI) (2). At the starting stages of the pandemic, AI models were still under development, so their precision and accuracy were low. In order to achieve better results, it was necessary to create large databases with numerous radiological images, especially CT scans of patients who had proven disease by PCR (Polymerase Chain Reaction) test (5).

The goal of this review paper is to determine the advantages in the application of artificial intelligence tools i.e. machine learning and deep learning, in the analysis of images of patients with COVID-19 pneumonia using computed tomography compared to the analysis of images read exclusively by radiologists.

Methods

Databases Google Scholar, MedRix, IEEE, PubMed and Scopus were searched using the following keywords: artificial intelligence, computed tomography of the chest, COVID-19, deep learning, machine learning, SARS-CoV-2.

Study inclusion criteria was set that included review articles and original scientific papers according to the above keywords published from January 1, 2020 to December 31, 2024. In addition, all articles had to be published in English. Articles without peer review, duplicate articles, articles that dealt with other radiological diagnostic methods except CT (X-ray, ultrasound, MR), case reports and studies which involved CT protocols of the thorax with contrast were not included in the analysis.

Articles selected for further analysis, after separating those that met exclusion criteria, were divided into review articles and original scientific articles. The next step was to group articles that deal with the use of AI tools in CT and thorax in patients with COVID-19 pneumonia by the deep learning method and by the machine learning method. The articles highlighted in the previous step were reviewed, with a focus on the title and abstract to ensure the relevance of the topic. After that, the selected articles

were analysed in detail in their entirety with an assessment of whether the research goals were clearly stated, whether the research methodology was elaborated in detail, and whether the research results were presented in accordance with the research question. In the last phase of filtering, in accordance with the hypotheses, studies were separated into two groups, one which showed that the use of AI tools such as machine learning and deep learning in the diagnosis of COVID-19 using CT, allow for faster detection of diseases compared to images read exclusively by radiologists and the group with studies that showed that AI tools did not contribute to faster and more accurate detection of diseases.

A total of 59 papers on the application of artificial intelligence in the diagnosis of COVID-19 using computed tomography of the thorax were reviewed. Out of 59 reviewed papers, 40 articles were excluded according to the given criteria, and 12 review papers and 9 original scientific papers were included.

Papers that were finally selected for detailed analysis were divided into several thematic groups: pathophysiology and epidemiology of COVID-19 infection, CT-scan protocols, opacification and other radiological signs of COVID-19 infection on CT, the significance of the use of AI tools in COVID-19 pneumonia in CT of thorax, the advantages and limitations of the use of deep learning tools, the advantages and limitations of the use of machine learning tools, guidelines for further research of artificial intelligence tools.

Finally, the limitations of the study were listed, and in the conclusion, the supporting arguments of the study highlighted with a summary of key evidence.

Table 1. Review articles included in the analysis on the application of artificial intelligence in the diagnosis of COVID-19 disease using computed tomography of the thorax

Article no.	Name of the first author and year of publication	Methodology explored	Imaging method	Research goals	Research results	Limitations of the study
1.	Serena Low W.C. et al., 2021 (6)	Deep learning	CT & X-ray	A review of deep learning techniques in imaging of COVID-19 pneumonia patients	The development of deep learning techniques is limited due to the limited number of databases.	Different formats, forms of archiving and quality are used in image databases so it makes comparison of images difficult
2.	Fusco R. et al., 2021 (7)	Machine learning and deep learning	CT & X-ray	Overview of deep learning and machine learning techniques in the diagnosis and treatment of COVID-19 pneumonia, comparison of sensitivity and specificity of CT and X-ray images	There was no statistically significant difference in the median value of accuracy between X-ray and CT (Chi square test; p value > 0.05).	The analysis of the images could not be performed for patients who were in critical condition, as they could not be involved in the imaging process.
3.	Alassiri R. et al., 2022 (8)	Deep learning and transferable learning	CT	Retrospective analysis of deep learning algorithms to improve the results of pre-trained models with and without data augmentation	The rate of improvement in the accuracy of pre-trained models after data augmentation was 3%.	A small number of CT studies of patients were used (349, of which only 10% were used for validation). Clinical patient data were not considered.

Article no.	Name of the first author and year of publication	Methodology explored	Imaging method	Research goals	Research results	Limitations of the study
4.	Heidari A. et al., 2022 (9)	Deep learning	CT & X-ray	Comparison of modern systems that use deep learning for the detection of COVID-19 disease by systematic review of the literature.	The effectiveness of different models varies.	Unavailability of non-English articles, and articles published by certain publications, insufficiently clear description of the algorithms used.
5.	Roberts M. et al., 2021 (10)	Machine learning	CT & X-ray	To compare the quality of the methodology and the possibility of repeating the use of methods of different machine learning models for the detection of COVID-19 disease.	None of the included machine learning models is good enough to be used in diagnosis of COVID-19.	Lack of documentation on proposed algorithmic approaches, high risk of model bias due to training on a small number of COVID-19 positive images
6.	Aggarwal P. et al., 2022. (11)	Deep learning	CT & X-ray	Summarize significant deep learning-based studies that can help in the future of developing models for the rapid and accurate diagnosis of COVID-19	Summary of the latest achievements (state of art) of deep learning techniques used in CT and X-ray technology. Most of the studies used smaller datasets, and there is a lack of comparison with existing studies, and there are no codes and data available to verify clinical use.	They are not highlighted.
7.	Komolafe T. E. et al., 2021 (12)	Deep learning	CT	Summarize all available evidence through systematic review and meta-analysis to quantitatively assess the accuracy of the diagnostic test (DTA) of the deep learning algorithm for detecting COVID-19 disease on chest CT scans.	Three studies reported higher accuracy of the deep learning algorithm's diagnostic test (DTA) compared to the radiologist's interpretation, 4 studies showed that the deep learning algorithm helped DTA performance, 6 studies showed that sensitivity was higher than specificity, 9 studies showed that specificity was higher than sensitivity.	They are not highlighted.
8.	Ozsahin I. et al., 2020 (3)	Deep learning and machine learning	CT	To review studies that address the use of AI in the diagnosis of COVID-19 using CT.	Widely trained networks can be very successful at every stage of CT scan classification.	The data used in the studies could come from different institutions and different devices. Lack of demographic and clinical information about patients.

Article no.	Name of the first author and year of publication	Methodology explored	Imaging method	Research goals	Research results	Limitations of the study
9.	Alzubaidi M. et al., 2021 (14)	Deep learning	CT, X-ray and UTZ	Identify and demonstrate the role of deep learning algorithms during the COVID-19 pandemic.	Most studies used a deep learning algorithm to detect COVID-19 through radiological images, but did not use the algorithm for the purpose of tracking infected cases or applications in robotics.	The number of data sets is small and uniform. The analysed studies were suggestions and have not been empirically tested.
10.	Wang Q. et al., 2022 (13)	Deep learning	CT	To analyse the performance of deep learning models in the diagnosis of COVID-19 disease from chest CT scans.	Deep learning models have great potential in accurately diagnosing COVID-19 and distinguishing them from other inflammatory lung diseases.	Source of data from different countries and from different CT machines. Too little literature is included.
11.	Kataoka Y. et al., 2024 (14)	Deep learning	CT	To examine whether the central-peripheral distributions of ground glass opacity and consolidation were associated with severe outcomes in patients with SARS-CoV-2 pneumonia independent of the whole-lung extents of these abnormal shadows.	Higher ratio of GGOs in the central regions to those in the peripheral regions was associated with severe outcomes in patients with severe SARS-CoV-2 pneumonia.	CT protocols vary among institutions, images with pleural effusion, pneumothorax, and pulmonary lung tumors were not included, associations of the CT findings with short-term outcomes, but not long-term outcomes.
12.	Bumm R. et al., 2024. (16)	Machine learning	CT	Determine the accordance of computer vs. human analysis to demonstrate the feasibility of computer analysis with Lung CT Analyzer and to elaborate on the existing differences in lung involvement between the severity-scored groups, to evaluate whether tissue affection in severe cases could be attributed to the side of lungs, lung regions or lung lobes and to predict patients requiring intensive care unit treatment.	The extent of lung involvement, particularly in the lower lobes, dorsal lungs, and lower half of the lungs, may be associated with the need for ICU admission in patients with COVID-19. Computer analysis showed a high correlation with expert rating.	An inherent component of the design in the preceding study, subjective variables.

Table 2. Original scientific articles included in the analysis on the application of artificial intelligence in the diagnosis of COVID-19 using computed tomography of the thorax

Article no.	Name of the first author and year of publication	Methodology explored	Imaging method	Research goals	Research results	Limitations of the study
1.	Abdulsalam Hamwi W., et al 2022 (17)	Machine learning (convolutional neural network)	CT & X-ray	Develop an integrated machine learning model to reduce misdiagnosis and late diagnosis of COVID-19, and compare research with other research.	An overall accuracy and an F1 score of 99.73% was achieved by applying meshes in the analysis of CT scans in PNG format. Most of the scans are accurately diagnosed.	They are not highlighted.
2.	Türk V. et al., 2022 (18)	Deep learning	CT	To compare four models of a deep learning algorithm for classifying positive and negative COVID-19 findings.	The best result and the highest accuracy were achieved by the MobileNet architecture.	Limited number of COVID-19 patients, different sizes and resolutions of CT scans.
3.	Vaidyanathan A. et al., 2022 (19)	Deep learning	CT	Propose an artificial intelligence framework based on a three-dimensional convolutional neural network intended for the classification of CT scans of patients with COVID-19 disease, influenza/pneumonia acquired in the community and without infection.	The tested model showed excellent results in an external validation system with an area under the curve of 0.90, 0.92 and 0.92 for COVID-19 disease, community-acquired influenza/pneumonia and no infection.	The presence of only cases of community-acquired pneumonia in the division for influenza/community-acquired pneumonia, the origin of shots from only two different suppliers.
4.	Yousefzadeh M. et al., 2021 (20)	Deep learning	CT	Present and evaluate the diagnostic performance of the <i>ai-corona</i> model on multiple databases, and compare it with the findings of radiologists, RT - PCR tests and two other scientific studies.	The <i>ai-corona</i> model has learned to diagnose COVID-19, and distinguish it from other lung diseases from CT scans. It also showed better performance compared to the other two models.	The model was built to be as powerful and accurate as possible, but on a simpler database. They did not separate other types of pneumonia separately to make the model as accurate as possible. They did not enter data on cases that were RT-PCR negative and CT positive.
5.	Anwar T. et al., 2021 (21)	Deep learning	CT	Test the EfficientNet model using a five-fold cross-check strategy to verify the accuracy of the model and compare the performance with other articles.	An accuracy score and an F1 score of 0.90 were obtained on the same database where the other articles received an accuracy score of 0.86 and an F1 score of 0.85.	They are not highlighted.

Article no.	Name of the first author and year of publication	Methodology explored	Imaging method	Research goals	Research results	Limitations of the study
6.	Chamberlin J. H. et al., 2022 (22)	Deep learning	CT	To assess the ability of a deep convolutional neural network to predict the outcome of COVID-19 disease, and to analyse the success of an algorithm for grading disease progression.	The tested algorithm proved to be a precise and diagnostically accurate tool in the assessment of COVID-19 disease.	A single institution source of data, the retrospective nature of this study that includes repeated waves of COVID-19, vaccines, and strains, the study did not include current demographics and comorbidities as risk factors in scope.
7.	Chrzan R. et al., 2022 (23)	Deep learning	CT (High Resolution HRCT)	To analyse the performance of artificial intelligence models in estimating the degree of COVID - 19 disease progression on CT scans with high resolution.	Artificial intelligence has proven to be a simple and reliable way to diagnose COVID-19, as for prediction of the degree of advancement of the disease.	Retrospective design, no specific estimate was used to measure the volume of inflammation therefore the model cannot estimate the volume of inflammation, it could not distinguish between inflammatory consolidations and changes in the lungs caused by diseases other than COVID-19.
8.	Gunraj H. et al., 2022 (24)	Deep learning (deep neural network)	CT	To present the new COVID - Net CT - 2 algorithm intended for the diagnosis of diseases COVID-19 from CT scans.	This algorithm has been trained on a large, diverse and multinational group of patients and provides precise and accurate quantitative results.	The algorithm is not entirely ready for widespread use, but it can be used as a basis for new research.
9.	Nguyen D. et al., 2021 (25)	Deep learning	CT (3D)	To evaluate deep learning classification models trained to identify COVID-19 disease based on 3D CT data from different countries.	Deep learning models correctly identify patients who are COVID-19 positive with high accuracy, but only when the model was used on the database on which it was trained.	Models fail when applied to an unknown database (possible consequence of different protocols and methods of data collection from different countries and different patient demographics), lack of generalization in patient identification.

Respiratory disease COVID-19

COVID-19 is one of the inflammatory diseases of the respiratory system caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This type of virus causes diseases in animals in most cases, but through mutations in wild animals, it can come into contact with humans and infect them. This is how the SARS-CoV-2 virus was transmitted from bats to humans, giving rise to a new respiratory disease, COVID-19, transmitted by aerosol from person to person in close contact and presenting with symptoms such as high body temperature, cough and respiratory difficulties (26).

Structure of the SARS-CoV-2 virus

The SARS-CoV-2 virus belongs to the coronavirus family *Coronaviridae*, its particle size ranges from 60 to 140 nm, and it contains single-stranded ribonucleic acid (RNA). It contains 14 open-read frameworks encoding 16 non-structural, 9 auxiliary, and 4 structural proteins (27). Non-structural proteins are involved in regulating the replication and transcription of RNA viruses as enzymes. Helper proteins are not essential for coronavirus replication and transcription, but they make it easier for the virus to adapt to the host and defend against the host's immune system (Figure 1).

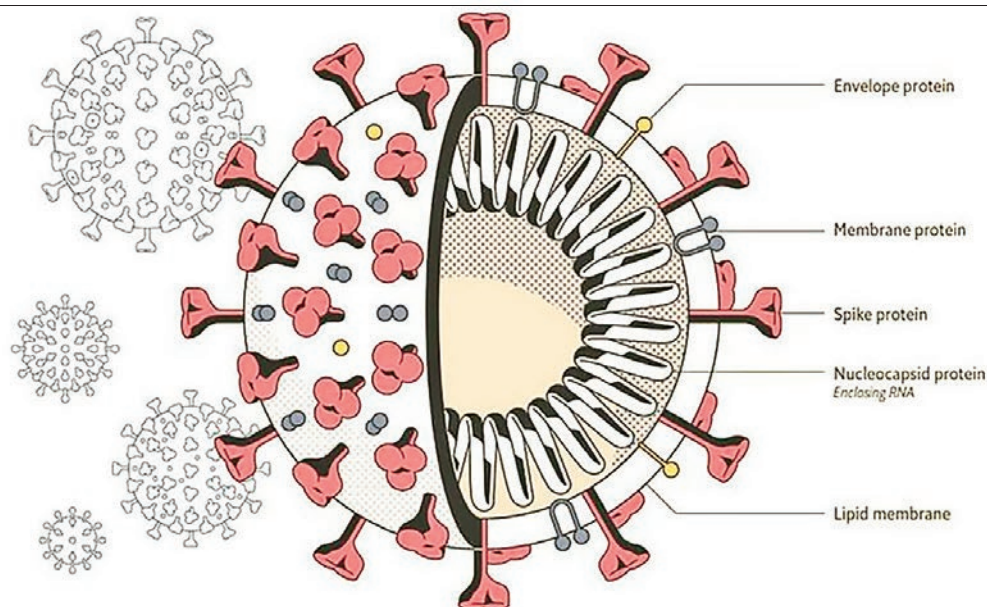


Figure 1. Structure of SARS-CoV-2 virus

Source: <https://www.researchgate.net/publication/354266318/figure/fig1/AS:1063078342950912@1630469036040/The-structure-of-COVID-19.jpg>

Transmission of SARS-CoV-2 virus and protection measures

After the virus mutated enough to be able to jump from animal to human, it became highly infectious to humans. Infected people are most contagious before they develop the first symptoms (approximately 2 days before the onset of symptoms) and in the early stages of the disease. The disease caused by this virus can be transmitted between people in different ways (1).

It is most often spread among people who are in close contact, at a short distance. The virus is transmitted by liquid particles, i.e. aerosol from the mouth or nose of an infected person when the person speaks, breathes or coughs. A person can become infected this way if the particles come into contact with the mucous membranes of the eyes, mouth or nose (1). Infection can also occur if people touch their mouth, nose, or eyes after touching a contaminated surface or object. It is also possible to be infected in poorly ventilated rooms or in closed spaces where there are many people where the aerosol full of infectious particles lingers for a long time (1).

During the pandemic, the WHO gave detailed guidelines for adherence to the population to reduce the spread of the disease (1). To reduce the possibility of infection with the virus, it is important to keep a physical distance of at least one meter from others. It is desirable to avoid crowds, but if it is unavoidable, it is necessary to wear medical face masks properly. Frequent washing and disinfecting of hands also reduces the likelihood of transmission of infection.

Preventive action is achieved by vaccination. With the rapid development of the disease, scientists tried to develop vaccines that would be successful in defending against the disease. At the very beginning of the disease, over 100 types of vaccines were developed based on previous knowledge of *Coronaviruses* (28). The use of vaccines was primarily recommended for the elderly population and people with comorbidities or immunocompromised, in order to protect them from infection or to mitigate the se-

verity of the disease if infection occurs. Today, it is recommended that the entire population should be vaccinated with at least one dose of the vaccine in order to alleviate possible symptoms and to reduce mortality (1).

Symptomatology and clinical picture of COVID-19

The incubation period of COVID-19, the period of time from exposure to the virus to the manifestation of the first symptoms, lasts on average 5 to 6 days, but can last up to 14 days (29). This period is also called the presymptomatic period, it is characterized by high contagiousness of people who can easily transmit the virus to other healthy individuals.

The age group most often affected by this disease is from 40 to 70 years of age (30). The main symptoms include fever, body aches, shortness of breath, dry cough and sometimes gastrointestinal symptoms such as abdominal pain, vomiting and changes in stool. The severity of the disease can vary from asymptomatic so that patients do not even notice that they are infected, through a mild form to very severe disease (30).

Initially, it may be an infection of the upper respiratory system, but in some patients the disease can develop into a more severe form such as pneumonia with shortness of breath and can progress to acute respiratory distress syndrome (ARDS) and in the most severe cases can lead to death (31). The at-risk part of the population consists of elderly people with comorbidities, pregnant and premature babies, newborns and people who are immunocompromised (30).

Methods of diagnosing COVID-19

Timely detection of the SARS-CoV-2 virus is important to help control the spread and progression of COVID-19. Thanks to modern molecular medicine techniques, there

are several ways and tests that can detect the SARS-CoV-2 virus. One of the tests that has become the gold standard in the diagnosis of COVID-19 is reverse transcriptase-polymerase chain reaction (RT-PCR) (32). This infectious disease of the lungs can also be detected by radiological methods, the most accurate of which is the CT method (32).

RT-PCR test

RT-PCR is the most commonly used test to determine COVID-19 disease. It is mainly used to quickly diagnose patients who have developed symptoms of the disease, or to screen asymptomatic patients. It works on the principle of highly sensitive technology that detects the presence of genetic material of the virus in a sample. A sample for analysis is taken with a swab of the nasal or nasopharyngeal area (33).

Once the sample is taken for analysis, it is treated with several chemical solutions to extract the RNA and remove other substances such as proteins and fats. The RNA extracted in this way is a mixture of the patient's genetic material and the RNA of the virus, if present (33). In the next step, RNA is converted into DNA through a reverse transcription process with the help of enzymes. Then, the mixture with DNA is placed in an RT-PCR machine that works on the principle of heating and cooling the mixture in order to initiate chemical processes that create copies of certain parts of the viral DNA (33). In addition to the process of creating copies of viral DNA, marker tags are attached to the new parts, which release a fluorescent dye. The computer measures the release of fluorescent dye and displays the result on the screen (33).

The result is positive, i.e. the presence of the virus is confirmed, when the fluorescence level exceeds a certain measure (33). Scientists also track how many cycles of viral DNA copy formation it took for fluorescence to occur, as this is how they determine the severity of the disease and how advanced it is. The fewer cycles it takes, the more severe the disease is (33).

This test is accurate in most cases, but false negative and false positive results can also occur. This is due to sampling at different times from the onset of symptoms. Ideally, the patient should be tested on the third or fourth day after the onset of the first symptoms (33).

Computed tomography (CT) of the thorax

CT is a layering imaging technique that uses a collimated X-ray beam directed perpendicular to the longitudinal axis of the body resulting in an axial cross-section of the selected layer thickness. The image is obtained in such a way that the detectors measure the intensity of attenuated radiation after passing through the body. Due to its high sensitivity, this radiological method is used to confirm the presence of COVID-19 disease and determine the stage of advancement (3).

The chosen protocol for imaging a patient suspected of having COVID-19 disease is the standard protocol for imaging the thorax, but it can also be recorded using a high-resolution protocol (HRCT) (34). The topogram determines the field of view, usually from the apex of the lungs

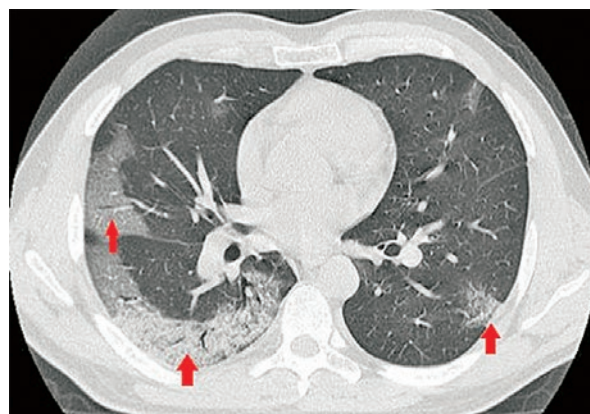


Figure 2. Chest CT in a patient with COVID-19 pneumonia on the third day of illness. Visible peripherally located ground glass opacifications (red arrows).

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to the base of the lungs, without including the adrenal glands. The use of a contrast agent is not necessary for this examination because COVID-19 pneumonia is mainly localized in the lungs and does not spread to the pleura and mediastinum. It is desirable that the imaging is done when the patient takes a deep breath in order to have a better view of the lungs. However, given that COVID-19 is a lung disease that causes coughing and breathing difficulties, it is necessary for the imaging protocol to last as short as possible to avoid artefacts. Therefore, single-phase CT imaging is suggested – with a faster case rotation time (0.5 s or less) and a higher value *pitch* (more than 1:1) (34).

Radiomorphological signs of COVID-19 disease that are presented on CT scans are consolidations, air bronchogram, ground-glass opacities (GGO), crazy-paving, reverse halo sign and peribronchovascular pattern (3). Observing these radiomorphological signs, it can be roughly concluded at what stage of development the disease is.

In the early stage, which lasts from the onset of the disease to four days, GGO can be seen on CT scans (Figure 2). The next, progressive phase, which lasts five to eight days, is presented on CT scans by opacification of crazy paving, GGO and minor consolidations. The peak phase lasts for nine to thirteen days, which is manifested on CT scans by consolidations of the lung parenchyma surrounded by a halo or GGO sign (Figure 3). The last or absorption phase occurs after the fourteenth day of the disease when the lung parenchyma begins to recover, which is seen on CT scans as GGO and linear consolidation (35).

The most common sign of COVID-19 pneumonia are multifocal GGO that are located bilaterally. The lesions are most often located in the basal, peripheral and posterior parts of the lungs. The signs of COVID-19 that are presented on CT scans can be quite similar to the signs of other viral pneumonia. What distinguishes COVID-19 from some viral pneumonia (e.g., caused by adenovirus or influenza virus) is the peripheral localization of the lesions, the permeation of all five lung lobes, and the presence of narrow reticulations and peribronchovascular thickenings (36).

It is also possible that COVID-19 pneumonia is atypically presented on CT scans, in which case pseudonodular consolidations can be seen on the scans, and an inverted

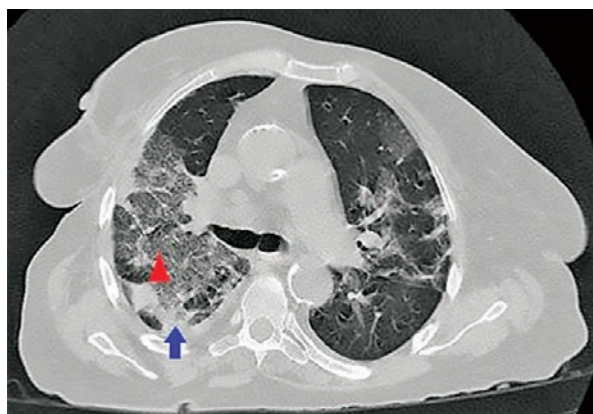


Figure 3. Chest CT in a patient with COVID-19 pneumonia on the tenth day of illness. Ground glass opacifications (red triangle) and peripheral consolidations are visible in the lung parenchyma of the right lung (blue arrow).

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halo sign. If the disease is in its early stages, i.e. there is no involvement of both lungs, signs may be visible only unilaterally (usually for the first four days from the onset of symptoms). The localization of pathological patterns in the pulmonary tips or peribronchovascular can also be highlighted (37).

Artificial intelligence (AI)

AI is a field of science that is classified as a branch of computer science that aims to imitate human behavior by copying human thinking and intelligence and thus solving complex tasks (38). This domain of computer science builds systems that have the ability to receive, analyze, and respond to various stimuli that are presented to them in the form of data. Based on the data entered, the program based on AI technology can learn from the given data and act independently. The two main tools by which an AI-based program can update its database are machine learning and deep learning (38).

Machine learning

In a similar way to humans, AI systems can learn from past experiences and thus improve. This is made possible by a concept of work called machine learning. Namely, machine learning is a domain of artificial intelligence that deals with the construction of algorithms by which a computer independently studies given databases and learns from them and builds experience (38). With this method, the computer studies the available database (usually a training database) and uses the given algorithms to analyse it and decide what the outcome might be. The accuracy of predictions and better performance of the computer itself are the result of training on databases as large as possible (38). This model is advantageous in industries that process large amounts of complex data, as it makes people's work easier and reduces the time required to process data (38).

Machine learning can be divided into three main categories depending on what kind of learning signal or

response the computer received (38). The categories are supervised, unsupervised and reinforcement learning (38).

Supervised learning works in such a way that algorithms are trained using annotated data (38). This approach provides the system with a database that contains both a known input and output dataset, and the analysis trains the model for prediction. In this way, the algorithm compares its actual output with the given correct outputs and is thus actualized to achieve sufficiently good results. According to this way of learning, algorithms can be divided into two categories, regression and classification (38).

Unsupervised learning is a method in which a computer trains itself without a supervisor (38). The system is provided with a database that is not labelled or classified. The algorithm must independently analyse the data and determine the degree of similarity between them in order to be able to conclude and lead to an accurate output for a given problem. In this way of learning, algorithms can use two techniques, grouping and association (38).

Reinforcement learning is a learning method based on the feedback that an algorithm receives after solving a given problem (38). It works by analysing previous performances. For each correct result, the computer receives a reward, and for each incorrect result, it is punished. In this way, the algorithm is set the goal of collecting as many rewards as possible, and thus improving correctness (38).

The main advantage of this method is the ability to repeat the process until it finds the correct output and thus builds on its own. But on the other hand, the problem with the machine learning method is that training requires a heterogeneous database with a large number of data (38).

Algorithms that are upgraded and learned by the machine learning method have a wide range of applications, most often in medical diagnostics, photo processing, in the marketing and financial sectors, and many others.

Deep learning

Deep learning is categorized as a subgroup of machine learning that is more advanced than others because the system by which it works is similar to the human nervous system and tries to mimic the work of neurons (38). This model works based on the architecture of neural networks that are inspired by the human brain. Neural networks consist of numerous nodes that are located in hidden layers whose task is to connect the input and output layers (38). The number of hidden layers varies from network to network, and because of their number, which is usually large, it comes from the name deep learning (Figure 4). The "deeper" the network, i.e. the more hidden layers there are, the greater the possibility of better display and processing of data. The deep learning process begins with the computer understanding the given problem and identifying the data and selecting the correct algorithm, after which the training and testing of the model begins (38).

The advantage of this learning model is that it can learn without predefined data and does not require detailed programming like machine learning. The biggest challenge faced by this model is the collection of large amounts of data and their accurate classification (38).

AI has found application in medicine in various parts of the healthcare system, from data storage to aid in di-

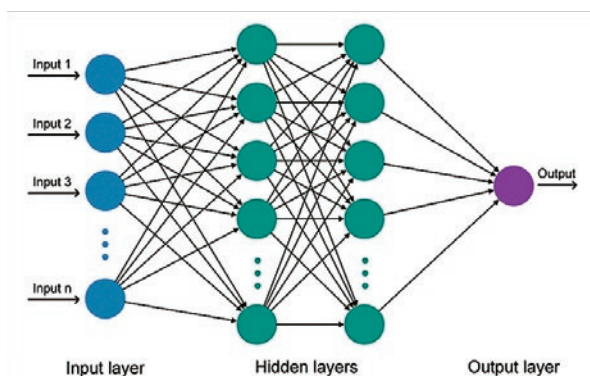


Figure 4. Structure of deep neural network

Source: <https://www.researchgate.net/publication/352111703/figure/fig4/AS:1030797767237634@1622772747886/Schematic-diagram-of-an-Artificial-Neural-Network-ANN.png>

agnosis. The branch of medicine that has always led the way in the digitalization of medicine has been radiology. Radiology is still one of the leading drivers in the introduction of AI into the healthcare system in order to work on accuracy and speed in diagnosis.

Every year, more and more radiological examinations are performed, which creates a high workload for radiologists. Regardless of the scope of knowledge and experience of the radiologist, with such a workload, inevitable errors can occur when diagnosing. Therefore, in order to help radiologists and reduce their workload, AI technology began to be introduced in radiology. The application of AI was particularly prominent during the COVID-19 pandemic, when the wide scope of work had already become extremely large (38).

Application of artificial intelligence in the diagnosis of COVID-19

With the onset of the COVID-19 pandemic, various new challenges for the healthcare system have emerged. There were difficulties with timely diagnosis due to the fact that the tests were sometimes unavailable and of

lower quality, which would lead to false results. Also, due to the high speed of the spread of the disease, many people were infected at the same time, which resulted in delays in the processing of samples. Due to the very nature of the disease, it was necessary for COVID-19 to be accurately and quickly diagnosed.

In order to address the challenges brought by the COVID-19 pandemic, AI technology has begun to be implemented in the healthcare system. The benefit of AI has been particularly highlighted by its application in diagnostic radiology in the reading of radiological images such as CT scans and digital thoracic radiographs. In this way, the accuracy and speed of the time required to process the footage is increased. Studies have shown that today's AI models are very successful in diagnosing COVID-19, and that their accuracy in predicting the diagnosis is on par with radiologists and in some cases even more accurate (39).

Healthcare professionals use AI technology to analyse radiological images as quickly and accurately as possible and reach a diagnosis without the need for long-term analysis of images. Also, when reviewing a large number of images, radiologist fatigue can occur and subjectivity in interpreting the findings, which can result in errors in diagnosis (39).

In order to reduce the rate of diagnostic errors, deep learning models are used with the aim of developing tools for image analysis that work on the principle of automatism (Figure 5). These tools lead to more accurate results and diagnoses more quickly, and ultimately reduce the workload on radiologists. It is characteristic of deep learning models that by identifying individual structures and parts, they can learn from radiological images and thus upgrade the neural network and expand the database (40).

To build software for the diagnosis of COVID-19, in most cases, deep learning models were used that function by using the transfer learning method (40). This combination has achieved high precision and accuracy of the model in distinguishing COVID-19 from other lung diseases (40). Several classification algorithms have played an important role in classification in research related to the diagnosis of COVID-19 disease (40). Some of these are neural networks, vector support machines, random forest

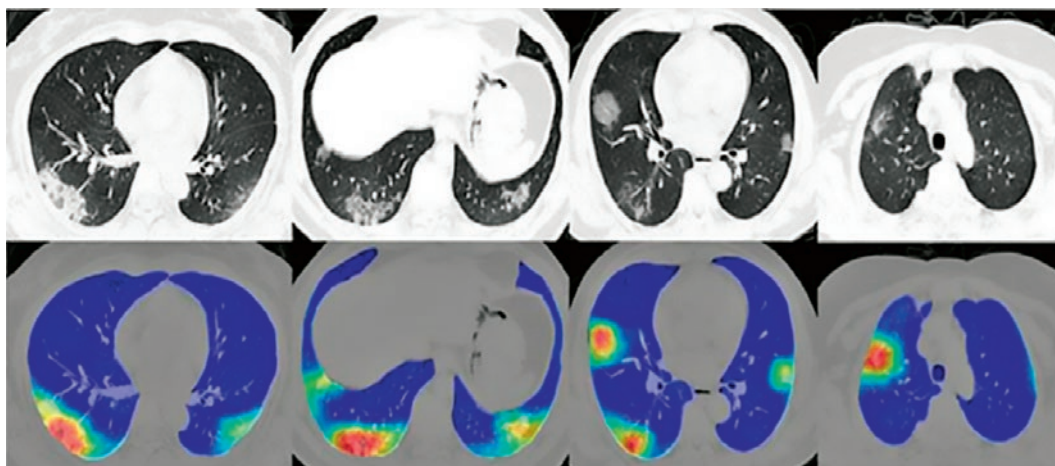


Figure 5. The top row shows unmarked CT scans of a patient with COVID-19 pneumonia, and the bottom row shows "heat maps" with marked characteristic lesions for COVID-19 pneumonia marked by an artificial intelligence algorithm.

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algorithm, and decision trees (40). These algorithms have shown high performance in performing tasks, but they still need to be optimized (40).

Radiological signs of COVID-19 infection on computed tomography and scanning protocols

The authors of all analysed papers, both review and original, listed in Tables 1 and 2, are unique in the use and classification of radiological signs that occur on CT scans in patients with COVID-19 pneumonia. In the acute phase, ground-glass opacifications (GGO), consolidation of the lung parenchyma, or combinations occur most often (7). The terminology is standardized and defined according to the Fleischner Society glossary of terms (36).

Of the 9 original scientific papers (Table 2), only three groups of authors provided a detailed protocol for scanning patients (19, 22, 23). These protocols were performed on 64 or 128-layer CTs, in the inspiratory phase, without the use of an intravenous contrast agent, during a single breath hold. The thickness of the layers ranged from 0.5 to 2 mm, and the fixed pipe voltage was set at 120 kVp with automatic tube modulation. From the raw data, CT images were reconstructed with a 512x512 matrix in axial cross-section, with iterative reconstruction. The data was then archived in a Picture Archiving and Communications System (PACS) and transferred to interfaces for different algorithms for the use of AI tools.

The authors of the other analysed scientific papers from Table 2 (17, 18, 20, 21, 24, 25) did not precisely specify the scanning protocols. Some used globally publicly available databases that they named and defined. For example, Nguyen et al. used three databases: 1) China Consortium of Chest CT Image Investigation (CC – CCII) Dataset (China), 2) COVID – CTset (Iran) and 3) MosMed-Dat (Russia) (25). Other authors did not specify the names of the databases, but only stated that they were publicly available databases (19) or data collected within their hospitals (20).

The fact that different databases of imaging data and unknown or uneven scanning protocols are used in different studies points to one of the major problems in the development and integration of AI in the process of analysing CT scans in COVID-19 patients, and that is the lack of data standardization. Therefore, the comparison of results is difficult.

Training the algorithm on high-quality data that is representative of the target population, with external validation, provides the best estimate of model performance (26).

In order to collect high-quality imaging data, researchers must be familiar with local guidelines related to the use and distribution of patient data, and protocols for anonymizing and securely storing data in PACS are also crucial. Getting large amounts of CT scans with quality images and labelled lesions that have been tagged by experienced thoracic radiologists is difficult, especially when dealing with small databases. There are discrepancies between research standards in medicine and machine learning. Researchers in the field of machine learning should be familiar with standard regulations for evaluating model

features. On the other hand, medical standards must be updated to support deep learning rules.

Significance of the application of artificial intelligence tools in COVID-19 pneumonia in computed tomography of the thorax

During the COVID-19 pandemic, numerous studies have proven that CT is the primary imaging modality and the “gold standard” in patients with suspected infection (9, 21, 23). CT scans have significantly better spatial resolution compared to X-rays and show the distribution of opacifications and their forms in more detail. High spatial resolution in three-dimensional representation is particularly important, which allows for precise quantification of opacifications (9). Given the large number of patients faced by hospitals around the world during the pandemic, the limited number of radiologists, and the time that could be devoted to readings, AI experts put a lot of effort into developing tools and implementing them to automate the diagnostic process and speed up the reporting process, which would be equivalent in quality and reliability to the findings of an experienced radiologist.

The Radiologic Society of North America (RSNA) and the Imaging COVID-19 AI Initiative in Europe have made public access to databases of imaging materials, in order to enable the training of deep learning tools on proven cases (7). If there is not enough image data, the models cannot be generalized enough. In order to eliminate this shortcoming, the data augmentation method has been introduced, which is effective in training discriminatory deep learning models (3). Examples of data augmentation techniques include rotation, color fluctuation, random cropping, elastic distortions, and Generative Adversive Networks (GAN) for synthetic data generation (3, 41). They consist of two networks that conflict with each other. The first is called a generator, and the second is called a discriminator. Traditional augmentation methods that make simple image changes are less effective than advanced ones (3). In overcoming data gaps, GAN is used to develop effective data augmentation strategies for image recognition (3). This refers to complex and specialised algorithms and deep learning systems that produce dynamic image data according to predictions and data transformation from one system to another (7).

Part of the review and original studies listed in Tables 1 and 2 showed high accuracy of deep learning methods in the analysis of CT scans in patients with COVID-19 pneumonia (8, 12, 18, 19, 20). Most of these studies divided the dataset into 70–80% for training and 30–20% for testing, while other studies divided the dataset into 50% for training and 50% for testing (14). A study that divided the dataset into 40% for training and 60% for testing achieved high sensitivity and the best results (14).

Ortiz and colleagues developed two ways to automatically extract clinically relevant features from CT of the thorax within limited data and combined these features with demographic data to develop a prognosis model for COVID-19 outcomes. With the help of MIP reconstructions (Maximum Intensity Projection) they created 3D CT volume maps, which can be used in a COVID-19 diagnostic model without the need for lesion segmentation.

The model then identified four lung lesions specific to COVID-19 infection and calculated the location and extent of each type of lesion. This approach has made it possible to identify 3D pathological imaging data that can be combined with other clinical data. In this way, the authors created a predictive approach that analysed the most relevant CT findings—combined with demographic data to accurately predict outcomes compared to models based only on intensity mapping or segmented features (42).

Advantages and limitations of using deep learning tools

Datasets

To implement convolutional neural networks, it is necessary to introduce a dataset and the necessary libraries, prepare the data, build a CNN, train it, and get the final prediction. The advantage of large, publicly available databases is the possibility that they can be used by numerous researchers indefinitely in creating and testing deep learning tools. However, it is necessary to take into account that most datasets have a limited number of clinical cases of COVID-19 infection. Before data can be analysed with a deep learning tool, most of the available datasets require “pre-processing,” such as resizing, matching image formats, and segmenting the lung parenchyma image from other body parts (18). Due to problems with “unclean” raw data, such as repetitive and unsegmented lung images, selecting the best image for a model is often very challenging (18).

The ability to ‘refine’ datasets allows repetitive images to be removed from datasets (18). In this way, it is ensured that there are no repeating images before the dataset is handed over to the model. Repetitive images will generate inaccurate results if they appear in datasets that are used for both training and testing. The test set must not “see” the data beforehand, in order to test the effectiveness of the model (18). By dividing the data into three categories of sets: training, test and validation based on patient demographics, it prevents the same patient from appearing in two sets (18).

Segmentation method

Lung segmentation is the separation of images of parts of the lungs from other parts of the chest. This initial step is required for the analysis of CT scans of the lungs and plays a key role in the performance of the classification model (7). “Raw” CT scans contain noise and vary, depending on the types of devices and variations in the constitution of patients. Segmentation also resolves the heterogeneity of data among different subsets of data, if combined into a single set. Segmentation allows the model to focus on the characteristic COVID-19 opacification of the input image. The most common and widely accepted method is to mark the boundaries of the lungs that separate them from the surrounding organs, using special tools (10).

The segmentation results are annotated and the results are controlled by at least two experienced thoracic radiologists. Compared to radiologist opacification annotations, segmentation networks achieve better results in

terms of obtaining high accuracy and sharper and clearer lesion separation boundaries (10).

Pre-Trained Deep Learning Models

Pre-trained deep learning models have shown promising results in solving many problems in various research areas, such as computer vision, pattern recognition, natural language processing, and medical image classification. The superior capabilities of pre-trained networks stem from their extensive training on large datasets. To improve the diagnostic capabilities of the COVID-19 classification model, some researchers performed pre-training using an external dataset of CT scans on a large public dataset (26). Many models of convolutional neural networks have been trained on the ImageNet dataset.

Distinguishing COVID-19 from other viral pneumonias

Opacifications that occur on CT scan in patients with COVID-19 pneumonia are similar to various forms of pneumonia caused by other viruses, such as influenza, adenovirus, syncytial respiratory virus, etc. Therefore, distinguishing COVID-19 from other viral pneumonias is a key challenge in multiclass classification studies compared to binary classification studies. A multiclass classification model is used to differentiate normal lung findings from COVID-19 pneumonia and pneumonia from the general population (26).

Advantages and limitations of using machine learning tools

The machine learning process in the detection of COVID-19 pneumonia on CT scans of the lungs consists of data collection, data preparation, model selection, model training, evaluation, parameter adjustment, and prediction or inference (26).

CapsNet is a machine learning system that represents a type of artificial neural network that can be used to better model hierarchical relationships (7). It mimics a biological neural organization. “Capsules” are added to the convolutional neural network and then the output from several “capsules” is used to form more stable representations (7).

Using CapsNet is one of the practical solutions for limited COVID-19 data sets, as it can handle small data sets. Alaoui et al. used CapsNet without applying any methods to augment the datasets or pre-train the model (26). They achieved 95.7% accuracy, 95.8% specificity, 90% sensitivity and 97% AUC (26). They modified the loss function to highlight the problem of unbalanced classes due to the lack of available images of COVID-19.

Guidelines for further research on AI tools

Advanced AI algorithms still need to be developed, especially for detection, segmentation and classification of lesions in the diagnosis of COVID-19 pneumonia by CT. Our analysis of original and review scientific papers listed in Tables 1 and 2 has highlighted the following guidelines for further research of artificial intelligence tools in the analysis of CT thorax images in patients with COVID-19 pneumonia.

Anwar et al. who used the deep learning algorithm (EfficientNet) on a set of 253 CT scans of patients with COVID-19 pneumonia and 291 scans of patients who did not have COVID-19 pneumonia, believe that its further development will be achieved by testing the model on a different dataset, since they did not use a separate validation dataset in this study (21).

Alaoui et al. believe that binary classification has reached high performance, but it is necessary to improve the model of multiclass classification of CT scans in COVID-19 pneumonia by creating high-performance matrices (26). Deep learning models can be applied in the categorization of different stages of COVID-19 infection, such as pre-symptomatic, asymptomatic, mild and severe (26).

Chamberlain et al. who tested the deep convolutional network (dCNN) algorithm in the categorization of CT opacifications in patients with COVID-19 pneumonia and used a scoring system based on the expert assessment of three thoracic radiologists as the gold standard, believe that future research must focus more on the outcomes of multivariate predictive analysis than on reconciliation among radiologists (22).

Gunray et al. used amplified deep neural networks to detect COVID-19 pneumonia in two different, large international cohorts of 4500 subjects from 16 countries (24). They concluded that future research should focus on the use of pre-trained networks for tasks such as predicting lung function, assessing the severity of the disease, and creating personalized treatments for patients with COVID-19 pneumonia (24).

In the research of Pan et al., the evaluation of new deep learning methods for quantifying COVID-19 and pacification showed a good correlation with conventional CT scoring (36). They believe that in the future, the quantification of opacification based on deep learning methods in the assessment of the severity of COVID-19 pneumonia will be applicable to other forms of viral pneumonia (36).

Turk et al. evaluated four different deep learning algorithm architectures using a publicly available database on a total of 360 images of COVID-positive patients, and found that the MobilNet algorithm had the highest accuracy (18). They believe that in order to develop deep learning algorithms in the future, much larger databases must be publicly available (18).

Vaidyanathan et al. demonstrated the excellent performance of the deep learning algorithm in distinguishing opacification in COVID-19 pneumonia from influenza pneumonia in external validation on a dataset from another healthcare institution (19). They believe that such an algorithm will be very useful in clinical practice in the near future and will be able to separate the relevant layers of CT scans that contain abnormalities and are important for the disease being investigated. Such a development requires more intensive collaboration between clinicians and computer scientists who specialise in AI (19).

Verma et al. tested a mobile application of an algorithm that has high precision (99.58%) and specificity (99.46%) in labeling opacifications in patients with COVID-19 pneumonia (41). They believe that the development of mobile applications will accelerate significantly, because they are more accessible to radiologists, especially in parts of the world with less developed health care, and will enable the assessment of disease severity, and thus

adequate treatment in a much larger number of patients (41).

Yousefzadeh and colleagues concluded that in the future, AI algorithms that combine clinical information, laboratory findings including PCR and CT-based diagnosis will have the most accurate diagnosis of COVID-19 pneumonia (20).

Conclusion

AI is taking the leading role in almost every aspect of modern life today, so it is necessary to apply this technology for the best possible purposes. Its application in medicine, particularly in radiology, can greatly help and facilitate radiologists, especially in crisis situations such as the COVID-19 pandemic. The emergence of the pandemic has created an urgent need to develop AI models that would help detect COVID-19 pneumonia on CT scans.

Greater accuracy in detecting COVID-19 pneumonia has been demonstrated by deep learning models based on convolutional neural networks. These models are of significant importance for diagnosing and monitoring the progression of the disease and allow radiologists to detect infection more quickly. In addition to the advantages in the application of AI tools, there are also certain limitations. To develop a model, large databases are needed on which algorithms train. Due to the uneven size of publicly available databases, there are variations in the success of the model. Datasets can be in different formats, standards, and different qualities, making it difficult to compare results. Some research models were only experimental, and CT scans of critically ill patients with COVID-19 pneumonia were missing from the databases, due to the severity of the medical condition and the inability to transport due to connection to various devices necessary for life support.

By overcoming these limitations, AI tools can significantly improve in their precision, speed and clinical applicability in the near future and can be an excellent tool for the analysis of thoracic CT images in patients with COVID-19 infection and thus expedite and facilitate the work of radiologists.

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Prednosti i ograničenja alata umjetne inteligencije u analizi slika torakalne kompjutorizirane tomografije u bolesnika s COVID-19 upalom pluća – pregled

Sažetak

Bolest COVID-19 je sustavna virusna infekcija uzrokovana visokoinfektivnim virusom SARS-CoV-2, koja može dovesti do upale pluća i drugih komplikacija. Prvi put se pojavljuje krajem 2019. godine u Kini i brzo se širi svijetom, zbog čega je početkom 2020. godine proglašena pandemija. Ljudi zaraženi ovim virusom obično imaju simptome kao što su kašalj, groznica i otežano disanje. Ova respiratorna infekcija uzrokuje promjene u plućnom parenhimu koje se mogu analizirati na CT-u, stoga je CT postao jedan od najtočnijih dijagnostičkih metoda za potvrdu COVID-19 kod bolesnika, kao i alat za procjenu stadija razvoja infekcije. Budući da je identifikacija bolesti iz radioloških snimaka dugotrajna i složena, pojavila se ideja da se razviju modeli umjetne inteligencije (UI) kako bi se dobio brži i točniji rezultat. Najčešći modeli UI temeljili su se na dubokom učenju i strojnom učenju i uspjeli su ispravno identificirati COVID-19 na CT snimkama. Glavni problem koji se pojavljuje pri razvoju ovih modela je nedostatak baza podataka na kojima bi se ti modeli mogli trenirati. Ovaj pregledni rad analizirao je rezultate dvadeset i jednog rada na temu korištenja umjetne inteligencije u otkrivanju COVID-19 na CT snimkama. Rezultati analize pokazuju da je umjetna inteligencija visoko precizna i točna u otkrivanju COVID-19 pneumonije, ali ju je potrebno još dodatno razviti.