Systematic Review of Treatment Staff Services for Patients with Cardiovascular Problems with Covid-19 based on Radiological Images

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Abstract

In this review study, pulmonary and cardiovascular complications caused by Covid-19 infection in the acute phase, as well as more chronic complications reported in various articles, along with their radiological manifestations, have been investigated. The emergence of the disease Covid-19 caused by infection with the new coronavirus quickly led to the declaration of a pandemic. Lung involvement has been identified as the main cause of death. Complications such as lung fibrosis, secondary bacterial or fungal infections, cardiac involvement (myocarditis and pericarditis) and vascular complications such as pulmonary embolism have been reported frequently. Different imaging methods, especially CT scan of the chest, play an important role in the early diagnosis of the disease. Although the symptoms of heart failure, in the form of heart enlargement and typical bilateral alveolar opacities and pleural effusion, are well recognized on a plain chest CT scan, myocardial injuries are best recognized on MRI. Considering the relatively high prevalence of cardiac complications secondary to Covid-19, especially when there are clinical or para clinical symptoms such as increased troponin levels, the use of special heart imaging techniques by MRI is recommended.

Keywords: *Covid-19, Radiology, Pulmonary Complications, Cardiovascular Complications.*

Tob Regul Sci.™ 2022;8(1): 3317-3338
DOI: doi.org/10.18001/TRS.8.1.251

Introduction

The Covid-19 disease caused by infection with the new SARS virus has quickly become a pandemic and despite many efforts, it continues to cause many deaths. Lung is the main organ involved in Covid-19 infection [1-3]. The reason for the high prevalence of lung involvement in patients is the presence of large amounts of angiotensin-converting enzyme (ACE2) 2 in the lung parenchyma, especially in the pneumocystis' in the alveoli, which facilitates the entry of the virus. However, the corona virus has the ability to cause complications in any body system. Although reverse transcription polymerase chain reaction (RT-PCR) laboratory test is used as the gold standard for disease diagnosis, various imaging methods such as chest X-ray, CT scan and ultrasound are used for initial diagnosis, especially in cases of false negative PCR, as well as follow-up of the treatment process and diagnosis of possible complications are used. Many of the radiological findings of Covid-19 are non-specific and can be seen in a wide range of other lung diseases, but the presence of a significant radiological appearance, especially along with clinical findings or a positive history of contact with an infected person, strongly suggests a viral infection. The most common radiological findings reported in corona pulmonary infection include lesions (Ground Glass Opacity; GGO) with or without pulmonary consolidation, preferably involving the sub pleural areas and the base of the lungs. Other significant radiological findings include crazy paving sign, halo and reticular infiltrates. Although in many patients, the complete recovery of pulmonary findings is seen, however, complications due to Covid-19 are seen in another group of patients, even after clinical recovery (Figure 1) [4-6]. The new corona virus has the ability to cause complications in any body system. Respiratory complications are one of the most well-known manifestations and can affect the course of the disease and prognosis of the patient. Involvement of the cardiovascular system has also been reported in various studies and can manifest as arrhythmia, pericarditis, acute myocarditis, cardiomyopathy, vascular embolism, and even shock. In this review study, pulmonary and cardiovascular complications caused by Covid-19 infection in the acute phase, as well as more chronic complications reported in various articles, along with their radiological manifestations, have been investigated [7].

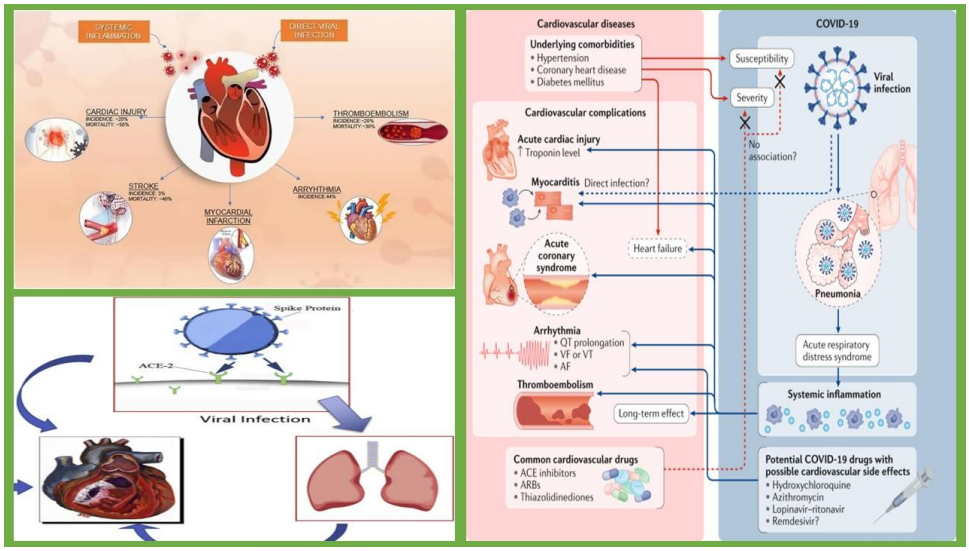

Figure 1. Severe COVID-19 is a multisystem disease, in which the lung–heart axis has an essential role. Lung infection causes systemic inflammation, predisposition to micro-thrombosis and hypoxia, which can damage the myocardium.

Patients with Covid-19 infection have symptoms such as fever, cough and shortness of breath. In this disease, people usually feel tired but do not have symptoms such as runny nose, sore throat and diarrhea. A recent report published in the Lancet journal examined pneumonia caused by the Covid-19 coronavirus in 41 patients. Based on imaging data in this study, lung abnormalities were observed bilaterally in 40 patients. In early imaging reports of NCIP patients with severe symptoms, bilateral lung involvement with consolidation was observed [8-10].

In intensive care patients, lung involvement with dense masses and ground-glass appearance was common. Chest radiographs of a 61-year-old woman who died of coronavirus showed severe invasion of dense masses over a 7-day period. Also, in a separate report of 99 patients with coronavirus, similar imaging findings were obtained. These findings showed bilateral lung abnormalities in 75% of patients and unilateral lung abnormalities in the other 25%. In another study that was conducted among 5 members of a family with corona virus, glass opacities or bilateral ground glass appearance were observed in the lung. This involvement was more extensive in the lung parenchyma tissue of people who were older. The imaging reports were very close to the findings of SARS and MERS. Another study, on the blood samples of 1099 patients infected with Covid-19 from different provinces of China, showed that in 83.2% of patients, the level of lymphocytes was lower than normal, in 36.2% of patients, platelets were lower than normal and the level Leukocytes were lower than normal in 33.7% of infected patients [11-13].

CRP level was very high in most patients and also alanine aminotransferase (ALT), aspartate aminotransferase (AST), kinase and D-dimer increased in patients. Another study conducted on clinical serological factors in 140 patients infected with Covid-19 in Wuhan showed that 68.1% of the patients had normal leukocyte levels, and 75.4% of the patients had lower levels of lymphocytes. In 52.9% of patients, the number of eosinophils decreased [14-16].

Also, in the examination of blood factors, the level of CRP and serum amyloid was increased in 90% of patients, and in 43.2% of them D-dimer, serum procalcitonin and creatine kinase were also increased. In another study that was conducted on 138 patients, it was determined that the serology parameters of these patients have undergone certain changes [17-19].
The amount of white blood cells and neutrophils in these patients increased and the number of lymphocytes and platelets decreased. Also, an increase in D-dimer, keratin kinase, keratin and LDH was seen in the blood factors of these patients. The study, on the blood samples of 24 asymptomatic carriers with confirmed Covid-19, showed that in 16.7% of patients, the number of lymphocytes was reduced, and in most of the patients, the amount of ALT, AST, CPR, D-dimer and keratin kinase was increased [20].

Search strategy and selection of articles

A study on 41 patients showed that 63% of them had the number of lymphocytes below the normal level and their ALT, AST, D-dimer, bilirubin, creatinine and LDH increased. These studies show that a primary way to diagnose this disease is to check changes in cells and blood factors. Although no case of pleural effusion has been reported in the pneumonias of the coronavirus Covid-19, pneumothorax has been seen in one percent of cases (one person out of 99 patients). In general, imaging findings in coronaviruses are very nonspecific and may overlap with symptoms of H1N1 influenza, cytomegalovirus pneumonia, or certain pneumonias. Severe clinical symptoms, history of contact with a patient with Covid-19 or travel to Southeast Asian countries (such as China, South Korea or Japan) are considered in the diagnosis of NCIP. Although more research is being done on the clinical and radiological aspects of Covid-19, imaging is considered an important component in patient management [21].
Search in Scopus, Google scholar, PubMed databases and by searching with keywords such as "Scanning Electron Microscope Analysis" and "Investigation of Shear Bond Strength of Two Types of Two-Stage Orthodontic Adhesive" and "Fluoride to Human Tooth Enamel" to obtain articles related to the selected keywords [19-21]. Case report articles, editorials, and articles that were not published or only an introduction of them were available, as well as summaries of congresses and meetings that were in languages other than English, were ignored. Only the original research articles that evaluated the effectiveness of different drugs in the treatment of COVID-19 using standard methods were studied (figure 2) [22].

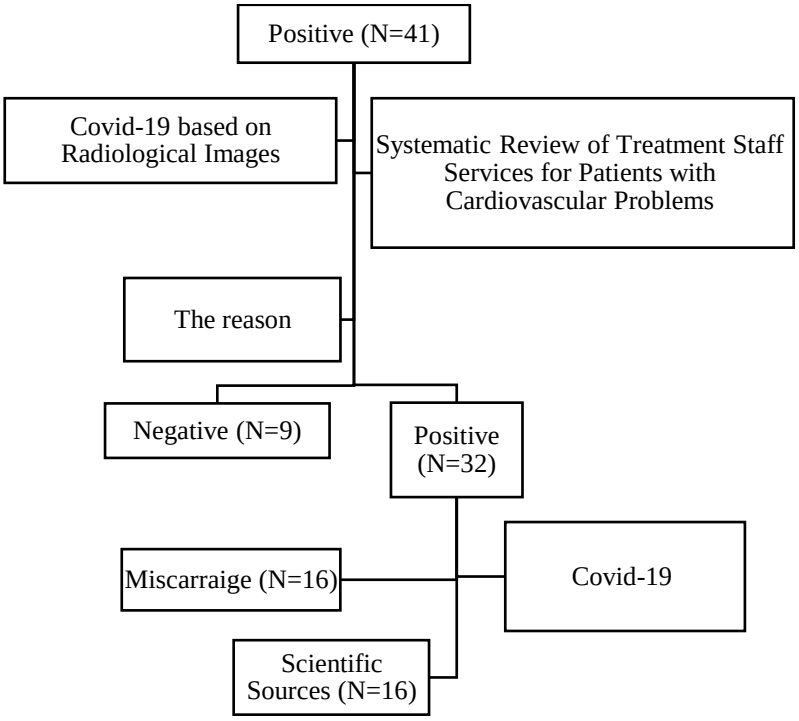

Figure 2. Flow chart of included subjects

Requirements for radiology department staff in dealing with suspected coronavirus patients

The personnel of the radiology department are on the front line of dealing with patients suspected of Covid-19. Imaging centers should have protocols in place to manage their staff in front of patients with suspected Covid-19. The new coronavirus, Covid-19, is highly contagious. Researchers believe that this new coronavirus is transmitted through respiratory droplets. However, full certainty about how this virus is transmitted from surfaces to humans is still being studied. A thorough understanding of the routes of virus transmission is essential for the safety of patients and healthcare professionals. Large droplets pose a risk of transmission up to 3 feet (91.44 cm), but virus transmission may also occur up to 6 feet (183 cm) [23].

Based on the researchers' experience with SARS, using a satellite radiography center and dedicated radiography equipment can reduce the risk of transmission of individual infections. If it is necessary to transfer the patient to the radiology department, a surgical mask should be used while transporting him. As of March 4, 2020, the World Health Organization recommended the use of a standard medical mask to protect the respiratory system. Other guidelines from the centers for disease control and prevention recommend the use of N95 masks for people who are in direct contact with corona patients. Other guidelines recommend the use of liquid-resistant, disposable insulating clothing to protect personnel. In these instructions, to prevent contact with respiratory droplets of patients with Covid-19, in addition to wearing a gown; It is recommended to use a pair of disposable gloves over the clothing, cover the eyes with goggles and put a face shield on it [24].

In a study that was conducted on 254 people from the treatment staff caring for patients with SARS coronavirus, the implementation of safety and protective measures led to a clear reduction of the disease in them. The tunnel (gantry) of CT scan and MRI machines, probes of ultrasound machines, blood pressure bracelets, keyboard and computer mouse related to radiology image reporting should be disinfected after contact with each patient. According to the Spaulding classification of the centers for disease control and prevention and the US food and drug administration (FDA), these surfaces should either be washed with soap and water or with a low- or medium-level disinfectant such as iodophor ethyl alcohol or isopropyl to be disinfected [25].

Materials and methods

In this review, the validity of keywords related to pulmonary and cardiovascular complications of Covid-19 were searched in reliable scientific databases including Pubmed, Embase, Scopus, Web of science, and Google scholar in the period from December 2019 to 2022, and articles related to the radiological findings of the said complications were included in the study.

Complications of lung parenchyma

Pulmonary fibrosis

In the acute phase of the disease and in the first few days, GGO can be seen as a dominant finding in plain radiographs and CT scans. These changes are especially prevalent in the lower parts of the lung and tend to involve the lung environment in the sub pleural areas. In the second week of the disease, the appearance of GGO mainly goes towards consolidation, and then, with the start of the recovery process, the amount of consolidation is reduced again, and finally, in many patients, lung parenchymal changes are completely resolved (table 1).

Table 1. Important radiological findings of Covid-19 in the investigation by CT scan of the lung based on different phases of the patient [26].

The initial phase, day 0-4			
Absorption phase Day 14 and after	Peak phase Day 9-13	Progressive phase Day 5-8	
Recovery of consolidation foci and GGO and return of parenchymal changes to normal state in most cases The possibility of remaining fibrotic changes and scars	Changing the predominant pattern from GGO to consolidation and the possibility of the formation of transient fibrotic parenchymal bands	Multi lobe and two-way conflict with GGO release changes, crazy paving view and consolidation	Environmental GGO changes with preference in the lower lobes of the lung and unilateral or bilateral involvement

In a cohort study on 103 patients recovered from Covid-19, parenchymal changes in the CT scan of the patients were investigated after 3 months of follow-up. In 25% of patients, some degree of residual radiological changes, mainly in the form of GGO areas, in 20% of cases, fibrotic

parenchymal bands were seen. In another study, 12 patients with severe pulmonary involvement who needed hospitalization in the intensive care unit were examined [27]. The average time for examining radiological findings in this patient was about 56 days from the onset of symptoms. In the CT scan of the lungs of the patients, despite the partial improvement of the lesions of the acute period such as GGO and consolidation, lung parenchymal changes, mainly in the form of fibrotic findings, were still visible. In another study by Yun et al., it was found that in people with more severe primary disease, the radiological healing process of lesions is slower and the possibility of developing pulmonary fibrosis is higher than in patients with less severe symptoms. Such findings can be established early in patients who have recovered from the acute phase of Covid-19 [28].
On the other hand, the continuation of pulmonary fibrosis findings in longer follow-ups confirms the slow process of their recovery and in some cases the possibility of their remaining stable. Pulmonary fibrosis can be caused as an idiopathic process depending on genetics or due to age. However, chronic inflammatory processes in the field of lung infections can also be the cause of fibrosis. Also, lung fibrosis can be caused as a known complication following acute respiratory distress syndrome (ARDS). In such cases, abnormal immune mechanisms secondary to cytokine storm are involved in the development and progression of lung fibrosis. Although the virus is eradicated in recovered patients, probably the effective mechanisms in causing fibrosis remain active and can lead to irreversible changes in a minority of patients. Even a small amount of non-progressive fibrosis alone can increase complications and mortality, especially in elderly patients and in people with a previous history of cardiovascular diseases [29].

Secondary pulmonary infections

Secondary infections following viral pulmonary infections are important known complications that are caused by facilitating the colonization and proliferation of bacteria in the respiratory tract. Accordingly, secondary infections following Covid-19 have also been reported. In studies on 19 Covid-19 patients hospitalized in ICU, secondary bacterial infection, mainly by Staphylococcus aureus and Acinetobacter baumannii, was reported in 100% of patients. In addition to secondary bacterial infections, fungal infections such as different species of Aspergillus, especially Aspergillus fumigatus, can also affect the course of the disease. Findings of an increase in the prevalence of pulmonary aspergillus in patients with Covid-19 have been reported. The pathophysiology of such findings is still unclear [30].
Changes in the immune system following ARDS or the use of immunosuppressive and anti-inflammatory drugs such as corticosteroids used in the treatment of some patients, especially people with severe disease or ARDS, can be considered as a risk factor for secondary fungal infection. Old age, lymphopenia, concurrent chronic respiratory diseases and cytokine storm are other possible causes [31].

Lung collapse

The presence of gelatinous mucoid secretions, especially in the areas of the lung that have been affected by consolidation, can lead to bronchial obstruction and finally lung parenchyma collapse. Examining the enhancement pattern after contrast injection; It is helpful to differentiate the areas of pneumonia from collapse caused by airway obstruction. In 10-20% of patients, changes in the walls of the bronchioles in the form of an increase in wall thickness have also been reported.

Acute respiratory distress syndrome (ARDS)

ARDS is one of the important and common complications of Covid-19 and is seen in 20-40% of patients with severe respiratory symptoms, especially on the 6-8 day after infection. Although ARDS is often a clinical diagnosis, radiological methods are also essential for diagnosis and treatment. In the acute phase of ARDS, the findings are bilateral alveolar opacities. And as clinical manifestations worsen, lung consolidations also become more severe. In the late stages, fibrotic changes and disorder of the lung parenchymal structure and reticular shadows and tractional bronchiectasis are also observed. In fact, the typical presentation of ARDS includes bilateral pulmonary infiltrates without cardiac abnormalities or hydrostatic pressure changes [32].

Cavity

Despite the fact that pulmonary manifestations in the form of cavitation are not among the radiological findings of Covid-19, and even based on the criteria of the American Radiological Society (RSNA), in the presence of cavity lesions, other differential diagnoses are more likely than Covid-19. There are case reports regarding the creation of caveats in the context of Covid-19. The exact mechanism of creating such lesions is not yet known, but histopathological studies have introduced the existence of foci of bleeding and necrosis in the lung tissue as possible effective factors in causing cavitation. Obstruction of small terminal bronchioles by mucus and excessive expansion of alveoli distal to the site of obstruction are other possible mechanisms [33-35].

Pneumothorax and pneumomediastinum

Due to the presence of pathological changes including the accumulation of exudate in the alveolar space, the presence of inflammation in the inter alveolar septa and interstitial space, and ARDS secondary to diffuse alveolar damage and cytokine storm, patients with Covid-19 are prone to develop pneumothorax and pneumomediastinum. These side effects are more common especially in people with an underlying disease such as COPD or those who are being treated with an artificial respiration device, which can be caused by a decrease in the capacity of the involved lung and a tendency to cause baro trauma caused by artificial respiration. Timely diagnosis and appropriate treatment of such complications play a significant role in reducing morbidity and mortality.

Cardiac complications

The severity of cardiovascular involvement following Covid-19 includes a wide spectrum and varies from subclinical myocardial involvement to obvious clinical findings. Cardiac findings observed due to Covid-19 may be primary or secondary, or may be caused by the deterioration of the manifestations of cardiovascular diseases. Arrhythmia, cardiomyopathy, acute myocarditis and shock have all been reported. Myocardial injuries are seen in 20-30% of hospitalized patients, and such complications are more common in people with heart disease (55%). Severe myocarditis is reported in 7% of patients, which often leads to death. Various mechanisms are involved in causing myocardial damage. Severe viral infection can increase the chance of rupture of atherosclerotic plaques in the coronary arteries and thus cause a heart attack (Figure 3) [36-38].

Also, hypoxia and vasoconstriction, which occurs in cases of severe and severe infection, can lead to a decrease in the supply of oxygen needed by tissues, followed by ischemia of the myocardium, especially in people with atherosclerosis changes. Cardiomyopathy is also a common complication of corona infection and can be caused by myocarditis or severe systemic inflammation. In a study on patients with severe infection, positive findings of cardiomyopathy were seen in 33% of patients.

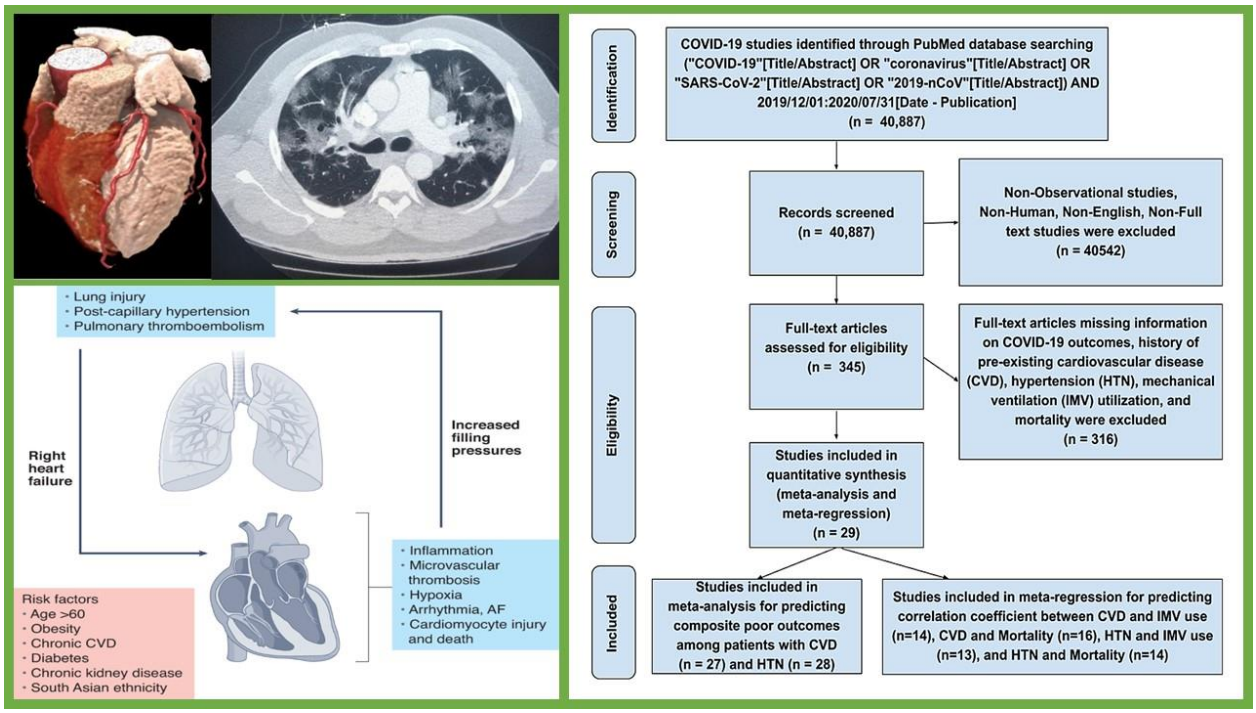

Figure 3. Cardiac complications base on Covid-19

Cardiomegaly, cephalization, pleural effusion, and curly lines may be seen in the chest X-ray. In CT scan or MRI of the heart, widening of ventricles, reduction of ejection fraction and radiological signs of myocarditis mentioned above are observed. Tamponade has rarely been reported following myocarditis due to Covid-19. The presence of pericardial effusion is well visible in the CT scan of patients. Also, pericardial changes can be seen in the form of increased thickness in cases of pericarditis [39].

Vascular complications

There is increasing evidence that coagulation disorders associated with Covid-19 predispose patients to venous and arterial thromboembolism. Although the complete and exact pathogenesis of this phenomenon is not yet known, thrombotic complications are among the causes of poor prognosis and are associated with high mortality. Pulmonary venous embolism is common in people with severe diseases. This risk is especially high when the disease is caused by the corona virus. The molecular changes caused by Covid-19 are similar to the changes seen in pulmonary vascular patients and can lead to vascular endothelial dysfunction, increase the risk of coagula ability in the lung and cause micro thrombosis and problems in lung hemodynamics [40].

On the other hand, secondary pulmonary embolism is another known vascular complication due to the increased risk of coagulation and the possibility of clot formation in peripheral veins. Pulmonary venous embolism has been reported in many studies in the context of Covid-19, which is mainly secondary to increased thrombosis in peripheral veins. In various studies, the presence of venous thrombosis has been reported in 25-49% of patients. Pulmonary angiography is a suitable diagnostic method to investigate the possible presence of pulmonary embolism, especially in patients with sudden exacerbation of respiratory symptoms or positive D-dimer marker. The most common cases of thrombosis occur in the segmental and lobar branches of the lung, and the presence of thrombosis in the central vessels of the lung is less reported [41-43].

In the CT scan of the lungs of 51 patients with severe Covid-19 infection, a high prevalence of pulmonary artery thrombosis and wedge-shaped areas due to reduced tissue blood supply was observed. Despite the fact that in a number of patients in these areas, there was obvious thrombosis in the proximal vessels, in about half of the patients, no obvious thrombosis was identified in the CT scan, which can confirm the presence of micro thrombi that cannot be detected by conventional imaging methods.

Diagnosis of Covid-19 based on the symptoms of the disease

Patients with infection with positive clinical signs and symptoms who are usually suspected of this disease and go to medical centers with symptoms such as fever above 38.5 °C, dry cough, shortness of breath and diarrhea, which should be examined in terms of respiratory examination. become in the study by Chen et al., on patients from a Wuhan hospital in China, out of 99 patients with Covid-19 infection, 51% had chronic diseases with symptoms of fever (83%), cough (82%), shortness of breath (31%), pain muscle (11%), fatigue (9%), headache (8%), sore throat (5%), runny nose (4%), chest pain (2%), diarrhea (2%), and nausea and vomiting (1%) were.

In another study conducted by Huang and his colleagues, it was found that in nine pregnant women with Covid-19 infection, symptoms included fever (in seven of nine patients), cough (in four of nine patients), muscle pain (in three 1 out of 9 patients), sore throat (in 2 out of 9 patients), diarrhea (in 1 out of 9 patients) and shortness of breath (in 2 out of 9 patients). When their babies were sampled and examined, the babies had no symptoms of the coronavirus, indicating no evidence of direct mother-to-child transmission of the infection.

Another study of 41 hospitalized patients in Wuhan with confirmed Covid-19 infection showed that 32% of the patients had underlying diseases such as diabetes, hypertension and cardiovascular diseases, and clinical symptoms such as fever (98%), cough (76%), fatigue (44%), sputum production (28%), headache (8%), bloody sputum (5%) and diarrhea (3%). In addition, the results of examining the clinical symptoms of four Covid-19 patients who visited the Public Health Clinic Center, China and were confirmed to be infected with Covid-19 showed that most of them had fever, fatigue and dry cough, and some of them had nasal congestion. They had runny nose and diarrhea. In another study conducted by Zhang and his colleagues on 138 patients confirmed to be infected with Covid-19 in Wuhan Hospital, it shows that the most common symptoms of infected patients are fever, fatigue, dry cough, anorexia, runny nose, shortness of breath, phlegm, diarrhea, nausea, dizziness, headache, vomiting and abdominal pain [44].

Diagnostic methods of Covid-19 based on serological techniques

Compared to other diagnostic methods, serological techniques are the most used to diagnose infections. The number of different blood cells, including leukocytes, lymphocytes, neutrophils, platelets, and hemoglobin, undergo changes that can indicate the type and severity of the disease. Covid-19 also causes changes in the level of blood cells in patients. For example, in the study by Chen et al., on 99 hospitalized patients with Covid-19 infection, the level of leukocytes was lower than normal in 9% of patients and higher than normal in 24% of patients; 38% of patients had higher than normal levels of neutrophils; 12% of patients had decreased platelets and 4% of patients had higher platelets and decreased hemoglobin and lymphocytes. Albumin decreased in 98% of patients and glucose and lactate dehydrogenase (LDH) increased in more than half of patients. Also, a significant increase was seen in the biomarkers associated with the infection of patients such as interleukin 6, serum ferritin, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [45].

Nowadays, serum CRP value is determined and measured by different methods such as capillary tube precipitation, hemagglutination immunodiffusion, and latex agglutination method, but among them, latex-agglutination method is more common than other methods. To measure lactate dehydrogenase in blood samples, kinetic methods such as "lactate to pyruvate" or "pyruvate to lactate" conversion are usually used. Different iso enzymes of lactate dehydrogenase are also separated using electrophoresis method. Also, by using chemiluminescence, chromatography, ultraviolet light absorption and fluorescence methods, changes in ALT and AST enzymes in blood samples can be measured. In order to measure CK enzyme, various methods such as immune electrophoresis and chromatography can be used; But these methods are time-consuming and are not useful for quick and emergency diagnosis.

Other methods that are used are immunological methods such as the use of anti-enzyme labeled antibody, which is also a bit time-consuming. Another method that is preferred over other methods is the safety harness method. For serological analysis of Covid-19, ELISA kits containing viral nucleoproteins can also be used to detect immunoglobulins such as IgM and IgG. In Zhang et al.'s

study, on patients with Covid-19, the amount of antibodies was low or undetectable in the first days, but in the following days, the infection caused by this disease leads to an increase in the amount of IgM and IgG antibodies, which can be useful in diagnosing the infection. Apart from the designed methods and kits based on ELISA, turbidometry, nephlometry, immune electrophoresis, chemiluminescence, ELFA, CLIA, IFA and RIA serology methods are another application for measuring IgM and IgG produced in this disease [46].

Covid-19 diagnostic methods based on PCR-based molecular methods

The molecular study of Covid-19 is based on PCR, an enzymatic method to produce a large number of target genes. This method is widely used to amplify small amounts of genetic material in order to provide a sufficient sample for laboratory studies. Due to the existence of a wide range of applications, as well as the high sensitivity and specificity of this technique, the PCR-based diagnostic method has become a common and reliable method for detecting the corona virus. In general, the RNA of the coronavirus is transferred to cDNA by reverse transcription. After that, PCR is performed and the PCR product is identified through specific diagnostic methods or tools. Meanwhile, gel electrophoresis and gene sequencing are the conventional methods after PCR to detect coronaviruses; But due to the time-consuming process and high cost, these methods are not usually used in clinical samples [47].

Currently, RT-PCR is a popular method for detecting coronaviruses due to its high specificity. In addition, Real-Time RT-PCR is much more sensitive than conventional RT-PCR methods and can help in rapid diagnosis of infection. Some patients show unusual symptoms of Covid-19 in the early stages of infection or disease, therefore, molecular studies are needed to identify the causative agent in order to confirm the transmission of the virus through respiratory, mouth and feces. For the molecular study of Covid-19, different samples such as throat and rectal swabs are used to perform Real-Time RT-PCR. In Zhang et al.'s study on patients with Covid-19, the results of throat and rectal swab tests from these patients show that the virus was detected in both samples. In this study, 50% of throat swabs and 25% of rectal swabs were positive for diagnosis in the initial samplings.

During the following days, the rate of positive rectal swabs (75%) versus positive throat swabs (50%) increased, suggesting that the higher number of positive throat swabs in the early days of infection is indicative of Covid-19 infection. In the initial stages, it is more in the throat, and with the passage of time of the disease, the rate of infection is seen more in the rectal swabs.

In Qian et al.'s study, rectal and throat swabs were prepared from 91 patients with confirmed Covid-19, who had no symptoms, and it was found that in these patients, the number of positive anal swabs is more than that of throat swabs. It was even observed that some of these people have negative throat swabs, but their anal samples are positive. After repeating various tests, it was found that anal swab samples play a more important role in detecting the virus in asymptomatic patients than throat samples. In the RT-PCR test conducted by Peng and his colleagues on various patient samples, including blood, urine, anal and throat swabs, the presence of the Covid-19 virus was

observed in all samples, indicating the presence of the virus in all samples, this is the point that this virus can infect people through the respiratory, digestive, urinary and blood systems. For this reason, it is recommended to evaluate different individual samples to diagnose Covid-19, especially in people who have no symptoms.

In the study conducted by Chu and his colleagues on sputum and throat swab samples from 2 suspected patients, both samples were positive for the presence of the virus, which indicates that in addition to respiratory droplets, transmission also occurs through sputum. (LAMP) is a unique technique for high-efficiency isothermal nucleic acid amplification. This method is used for the amplification of DNA and RNA with considerable sensitivity and specificity. Normally, 4 different primers are used to identify 6 distinct regions in the target gene, which greatly increases the specificity of the method. The LAMP method is fast and does not require expensive equipment. As a result, using the LAMP test helps to reduce the cost of diagnosing the coronavirus.

Discuss

Diagnostic method of Covid-19 based on microarray technique

Microarray is a rapid detection method with very high throughput. For this purpose, the cDNA related to the coronavirus genome is produced with the help of special probes through reverse transcription from the RNA of the coronavirus. Then, the labeled cDNAs are adjacent to the solid phase oligonucleotides fixed on the slide for hybridization, and then washing is performed to remove unbound cDNAs. If the sample prepared from the patient is positive, the RNA of the coronavirus can be detected through special probes located on the kit. Due to the superiority of the microarray method to detect the virus, this method can be widely used in the diagnosis of the corona virus. In the study conducted in the field of microarray design for the detection of Covid-19, Guo and his colleagues succeeded in designing a 60 bp oligonucleotide according to the TOR2 sequence of the Covid-19 virus genome, which is effectively used to detect the coronavirus in medical samples.

The remarkable thing about the kits designed on the basis of microarray is that because this virus is mutable, it is very important to design a kit that fits these mutations. In this regard, Guo and his colleagues succeeded in designing a special microarray in this field. This group succeeded in building an advanced microarray to detect 24 single nucleotide polymorphisms (SNPs) that detect mutations on the S gene of the coronavirus. This group managed to identify the different patterns of the coronavirus with 100% accuracy. The radiological technique called computed tomography of the chest or CT scan (CT) is one of the effective ways to diagnose viral infection in suspected people, which can be helpful in diagnosing infection, especially in people without clinical symptoms. Radiological images of the lungs of patients with confirmed Covid-19 can provide comprehensive information about the severity of infection [48].

The images taken from the lungs of different patients show various abnormalities in the lungs, such as ground glass opacity (GGO), consolidation, nodules, structural changes, bronchial wall thickening, vascular dilation, bronchial enlargement, reticulation, crazy cobblestone pattern, and

lymphadenopathy. The study by Bernheim et al., on chest CT scans of 121 patients with confirmed Covid-19, showed that in 60% of patients both lungs were affected and in 10.7% of patients only the right lung was involved. Only the left lung was involved in 5.7% of patients.
The most common abnormalities of these patients included GGO, consolidation, bronchial wall thickening and lung peripheral changes. Covid-19 can infect different lobes of the lung depending on the severity of the disease, for example, a study by Chung et al. in 21 patients infected with Covid-19 showed that in 5% of patients one lobe was involved, 10% two lobes were involved, 14% three lobes involved, 19% had four lobes involved and 38% had all five lobes involved. GGO is defined as hazy areas with a slight increase in density in the lungs, obscuration of the bronchi and peripheral vessels. In the initial review of 21 patients by Chung et al., GGO was seen in 57% of patients, which was the first CT observation of Covid-19 patients. The conducted studies showed that GGO as the most common radiographic method shows the presence of the disease at a rate of over 98%. The reticular pattern is defined as the thickness of the interstitial space of the lung in the interlobular space and interlobular lines. This pattern can increase in patients with Covid-19 whose disease period is longer. A crazy cobblestone pattern is a pattern of interlobular space and interlobular lines that look like irregular cobblestones. In recent studies in patients with Covid-19, 5-36% of the patients had a crazy cobblestone pattern in their lungs.
Nodule refers to a round or irregular nodule or pit-shaped nodule that is less than 3 cm in diameter. According to the studies, 3-13% of patients can show multifocal solid irregular nodes. Lymphadenopathy is actually swelling of lymph nodes in which one or some or all lymph nodes are swollen. Lymphadenopathy has been observed in 4-8% of patients with Covid-19. Pericardial fluid accumulation is actually fluid accumulation between the heart and the pericardium, which has been seen in 5% of people with Covid-19 with inflammation. Caltra drug, which is an anti-AIDS drug, has been used by the Chinese Ministry of Health to treat the disease of Covid-19. The drugs lopinavir and ritonavir, which have recently been used in South Korea to treat patients with Covid-19, have significantly reduced the virus titer and improved the patients' conditions.
Remdesivir is an adenosine nucleotide analog with antiviral activity against a wide range of RNA viruses, which has recently attracted the attention of many researchers and is being investigated and passed tests as a treatment option for treating patients with Covid-19. It is clinical. Recent results show that remdesivir along with chloroquine are effective in controlling Covid-19 disease in laboratory conditions and can be evaluated in the treatment of Covid-19 disease. In addition to the drug combinations mentioned above, other different drugs such as chloroquine phosphate, redesivir, favovir, etc. are also being investigated as therapeutic candidates. Plasma therapy is another treatment option for treating patients with Covid-19, which has been used in some countries, including Iran. In this method, the plasma of recovered patients is extracted and used for passive immunization (Figure 4 & 5) [49].
The first study in Iran and one of the five studies in the world was published by Hasanvand et al. In this study, in order to check whether this virus is airborne, standard air sampling equipment was installed at a distance of at least two to five meters from the beds of patients with Covid-19

and at a height of about one and a half meters from the floor. Also, other side parameters such as the number of airborne particles, humidity level and carbon dioxide were also measured.
According to the results of this research, the Covid-19 virus was not observed in any of the air samples of the rooms of corona patients, and the findings of this study were the same as the results of the studies conducted in Singapore, Hong Kong, etc. Although in this study, the Covid-19 virus was not observed in any of the air samples inside the hospitalization rooms of Covid-19 patients; But due to the fact that so far limited evidence has been published in the world in this field, it is very necessary to conduct more studies and consider different conditions. This research was one of the first studies in the world regarding the investigation of the transmission of Covid-19 through the air. In another study conducted by Moradi et al., by estimating and evaluating based on the GAM model parameters of time-dependent transmission rate, time-dependent recovery rate, and time-dependent mortality rate of the outbreak of Covid-19 in China, and using from the number of Covid-19 infections in Iran, the number of patients for the next month in Iran was estimated.

1	Liu et al.	**2015**						0.47	**[0.39 – 1.06]**	1.60
2	Backer et al.	**2015**						0.95	**[0.94 – 1.02]**	1.32
3	Barzideh et al.	**2012**						0.93	**[0.53 – 1.01]**	4.32
4	Schuh	**2014**						0.51	**[0.55 – 1.08]**	1.61
Heterogeneity t^2=0.9, I^2= 0.02, H^2=0.50								0.38	**[0.62 – 1.07]**	2.33
Test of Θ= Θ, Q (4) =1.15, P= 0.14										
1	Afkar et al.,	**2022**						0.14	**[0.27 – 1.08]**	1.32
2	Tanaka et al.,	**2014**						0.56	**[0.52 – 0.22]**	2.15
3	Karimzadeh et al.,	**2021**						0.61	**[0.54 – 0.89]**	1.32
4	Furuta et al.,	**2013**						0.79	**[0.12 – 0.99]**	3.87
Heterogeneity t^2=0.22, I^2= 0.14, H^2=0.19								0.97	**[0.19 – 1.00]**	1.15
Test of Θ= Θ, Q (4) =1.25, P= 0.21										

Figure 4. Systematic Review of Treatment Staff Services for Patients with Cardiovascular Problems

Figure 5. Systematic Review of Treatment Staff Services with Cardiovascular Problems with Covid-19 based on Radiological Images

The value and importance predicted and estimated in this study is to emphasize the peak time of the epidemic, hospital preparedness, government measures and public preparedness to reduce social contacts. In a study conducted by Eshrati and his colleagues, the factors affecting the mortality rate of Covid-19 patients admitted to the ICU were investigated. Based on the findings of this study, the mortality rate in Covid-19 patients admitted to the intensive care unit with underlying diseases such as chronic obstructive pulmonary disease, diabetes and kidney diseases is higher than other patients. Therefore, in order to reduce the death rate, more attention should be paid to these patients and people who have underlying diseases.

In a study conducted by Nikoubakht and his colleagues, the importance of designing remote counseling services in the field of Covid-19 disease has been pointed out. In this way, by minimizing the presence of specialist doctors and other colleagues in the field of treatment in the face of high-risk conditions, the possibility of infection for the treatment staff on the one hand and the waiting period and the need for protective equipment on the other hand will be minimized. In a study that was conducted at the request of the medical care monitoring center of the ministry of health, treatment and medical education of Iran, all hospitals were required to register hospitalized patients with a confirmed or suspected Covid-19 diagnosis. In this study, which was conducted by Jalili et al., the characteristics and mortality rates of people infected with this virus in Iran were investigated and analyzed. The high mortality rate corresponds to the hospitalized population. In accordance with other studies, hypoxemia, fever, and cough were common symptoms recorded as common complications in these patients.

Conclusion

Different diagnostic methods such as serological, molecular and radiological can help health centers in diagnosing Covid-19; Today, molecular and radiographic methods are used as the main methods for diagnosing the disease of Covid-19. Radiology technique is known as one of the most suitable methods for detecting viral infection due to its high speed and accuracy and less false negative answer in this field. Therefore, due to the high prevalence of Covid-19 and taking into account the incubation period of 2 to 14 days for this disease, correct and timely diagnosis of this disease in the early stages of the disease will play an important role in controlling the spread of the disease and treating patients. Therefore, it is very important to use effective methods in diagnosing the infection of Covid-19 and it is very vital in saving the lives of patients and preventing the transmission of the infection to other people and its widespread spread in human societies. Due to the fact that sometimes the virus is detected in blood and anal swabs, but not found in throat swabs, as a result, these patients can act as carriers and transmit the infection to other people, so it is suggested that for correct and timely diagnosis Several diagnostic methods should be used for this disease, especially in asymptomatic patients, and different samples of the patient should be evaluated.

It is also recommended that due to the lack of effective treatment and vaccine, the best way to deal with this disease is to avoid contamination and prevent its spread through protective measures and personal hygiene for people who already have high blood pressure, heart disease, and heart failure. Corona virus can aggravate their heart disease and can create a new problem for them.

ACE2 is found everywhere in the body, more than 80% of which is found in the lung tissue and the remaining 20% in the heart, kidney and even the brain. The same mechanism that causes damage to the lungs can also cause damage to the heart. In addition to the role of ACE, inflammation occurs after any viral and microbial disease, which can cause the rupture of fatty plaque in the heart vessels and cause heart attacks. On the other hand, the reduction of oxygen supply (hypoxia) due to pulmonary involvement can play a role in aggravating and creating new heart problems for these patients.

Therefore, ACE and inflammation and hypoxia caused by coronavirus can affect the heart. Studies have shown that those who have underlying diseases such as cancer, heart diseases, blood pressure, lung diseases and diabetes, as well as those who are older (especially over 70 years old) will have a higher risk of contracting and dying; Therefore, those who have underlying diseases should be more careful than other people. Those who already have heart disease such as coronary artery occlusion, heart failure and high blood pressure, the corona virus can aggravate this disease in them and can also cause heart failure or heart attack or new heart rhythm disorders for the person. Some of those who visit us now come with heart symptoms such as heart palpitations, chest pain, and shortness of breath, which may have nothing to do with their lungs and may be related to heart diseases that people already have or due to the Covid-19 disease. They are created to be relevant. Those who have heart disease should take their medicines regularly and go to medical centers whenever they have symptoms. Considering that 80% of those who get infected with corona have

a mild illness and are treated with home care, we recommend that they do not go to medical centers until their symptoms worsen. Because in addition to the overcrowding of medical centers and the reduction of the medical staff's ability to treat acute patients, their illness may be something else and they mistakenly attribute it to Covid-19, and when they go to medical centers due to the population density, they are diagnosed with this disease. Many different complications have been reported following the Covid-19 disease, however, pulmonary involvement is still the most important cause of death.

Although the disease often improves after going through different clinical phases, short-term or long-term complications are observed in some patients. Persistent fibrotic changes following clinical improvement, bacterial and fungal lung infections, ARDS, pneumomediastinum and pneumothorax, heart injuries in the form of myocardial and pericardial involvement, and pulmonary artery embolism are all important complications reported following infection with the coronavirus. Different imaging methods, especially CT scan of the chest, not only play an important role in the initial diagnosis of the disease, but are widely used in order to follow the treatment process and detect possible secondary complications. Therefore, it is necessary to be familiar with the common radiological findings of the disease as well as the radiological manifestations of secondary complications in order to perform appropriate treatment measures. Reducing or stopping the process of developing pulmonary complications following Covid-19 infection will be of significant importance in reducing mortality and improving the quality of life of those who have recovered.

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