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Respiratory Failure in COVID-19 Condition

Olalekan Bukunmi Ogunro and Oluwaseun Ruth Olasehinde

Abstract

Respiratory failure, characterized as the unsuccessful maintenance of adequate gas exchange, is associated with abnormalities of arterial blood gas tensions. The coronavirus disease-2019 (COVID-19) is majorly a respiratory disease capable of causing infection caused by the newly discovered coronavirus (SARS-CoV-2) with a consequential effect on respiratory failure. Simply put, respiratory failure is the major clinical demonstration of COVID-19 and the frontline cause of the associated mortality. Respiratory failure instigated by COVID-19 has some clinical features in affected patients. Disorders of the respiratory neuromuscular, airway, pulmonary vesicles, and lung parenchyma all manifest in COVID-19. These features are heterogeneous and categorized into progressive respiratory distress and unique “silent hypoxemia” as two phenotypes. Knowing the exact phenotype in patients with COVID-19 has been of important clinical significance in seeking the right treatment strategies for treating respiratory failure. The chapter will, therefore, provide more insights into the pathophysiology, clinical attributes, pathogenesis, and treatment approach of respiratory failure in COVID-19 conditions, as well as evaluate any similarities and differences that may exist.

Keywords: COVID-19, respiratory insufficiency, breathing difficulty, ventilation, oxygenation, respiratory dysfunction, respiratory failure, SARS-CoV-2

1. Introduction

Breathing is an indispensable requirement in life. Ideally, in humans and all mammals, oxygen (O₂) from the air is breathed into the lungs, while carbon dioxide (CO₂) is breathed out as a waste product made by cells of the body. Oxygen utilization and carbon dioxide production are, therefore, essential to life. The proper function of tissues and organs requires adequate oxygen from the lungs into the blood. The respiratory system allows the entry of O₂ and the parting of CO₂ in the body. Accumulated carbon dioxide causes severe damage and injury to these tissues and organs and slows the rate of delivery of oxygen to the body.

Respiratory failure is a grave condition that makes breathing difficult without any aid and usually sets in when the lungs are unable to get adequate oxygen (hypoxic respiratory failure) into the blood or the difficulty of the lungs to get rid of carbon dioxide (ventilator failure) to meet metabolic requirements. Acute respiratory failure may be quick and happens without prior notice. In most cases, it is associated with

breathing diseases/injuries such as pneumonia, stroke, opioid overdose, or even injury of the spinal cord or lungs.

Patients with respiratory issues can have illness from a family of viruses known as coronavirus. The term “corona” refers to the surface of the virus, which is coated in spikes like crowns. Examples of coronaviruses that infect humans include the common cold and severe acute respiratory syndrome (SARS). A new coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the cause of the infectious disease known as coronavirus disease-2019 (COVID-19) [1, 2]. The coronavirus disease 2019 (COVID-19) pandemic is caused by the novel coronavirus regarded as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 was identified initially in December 2019 in Wuhan, China, by several patients. Since then, COVID-19 has raised myriad global concerns [1]. One of the resultant effects of COVID-19 is lung damage with gradual declination may result in acute hypoxic respiratory failure and, in the worst scenario, results in acute respiratory distress syndrome (ARDS). Acute hypoxemic respiratory failure is a major clinical feature of COVID-19 during inflammation of the lungs. COVID-19-related respiratory failure has features of injury to the alveolar epithelium cells, while the endothelium cells may be less damaged [3].

Apart from meeting the Berlin definition of ARDS, COVID-19 has uniqueness in both pathological and pathophysiological characteristics, not limited to endothelial injury, pulmonary capillary hyperplasia, and extensive microthrombus [4]. COVID-19 can, therefore, be regarded as a preponderantly respiratory infectious disease with respiratory failure as the principal clinical outcome and the pre-eminent cause of mortality [5].

As in patients who battle with respiratory failure instigated by other means, heterogeneity of clinical features exists in persons with respiratory failure instigated by COVID-19. The gradually advancing respiratory distress and distinct silent hypoxemia are the two phenotypes. Recognition of the exact phenotypes in patients with COVID-19 will be of immense value for the best treatment options. In most cases recorded, respiratory failure due to COVID-19 develops very quickly because this disease affects the respiratory system primarily while damage to other organs may be secondary [6]. Since there is still no major cure treatment for COVID-19, it is therefore important that the key therapeutic intervention focuses on symptomatic treatment of respiratory failure. This chapter is focused on providing scientific insights into the epidemiology, pathophysiology, and clinical features of respiratory failure in COVID-19 conditions to help healthcare professionals manage patients with COVID-19.

2. Respiratory failure

The system for taking in oxygen and releasing carbon dioxide commences at the nose and mouth and goes through the airways and the lungs. Air usually comes in through the respiratory system via the nose and mouth and is then taken down the pharynx through the larynx. A cartilaginous structure known as epiglottis usually covers the entrance to the larynx. The epiglottis prevents food from getting into the airways by closing automatically during food intake [7].

Respiratory failure sets in when the respiratory system fails to meet the oxygen and ventilatory demands of an individual/patient. Respiratory failure, therefore, is a clinical term that defines the failure of the respiratory system to preserve its physiological role of gas exchange such that PaO₂ maintained is not beyond 60 mmHg and/or PaCO₂

greater than 50 mmHg. Respiratory failure happens when the breathing system cannot sustain enough levels of blood oxygen, as well as difficulties in eliminating carbon dioxide in the blood [8]. Respiratory failure can be a slow development with symptoms not limited to shortness of breath, distress in breathing, extreme tiredness, restlessness, and drowsiness (when the low oxygen level is low), as well as headaches, blurry sight, disarray, speedy breathing (carbon dioxide levels is high). In newborns, symptoms of respiratory failure may include inward pull of the ribs' muscles, speedy breath, nostrils broadening with the breath, grunting, and bluish skin and lips tone. Respiratory failure poses a serious threat to the lungs and other vital organs [9].

Diagnosis of respiratory failure may be determined by the blood levels of oxygen and carbon dioxide levels apart from a physical examination. Generally, factors such as the blood levels of oxygen and carbon dioxide, causative factors, and rate of development determine the symptoms associated with respiratory failure. Acute respiratory failure can result in a life-threatening emergency that necessitates additional oxygen through nasal tubes or a breathing-aided machine (ventilator) [10].

Factors such as age, environment, medical condition, lifestyle habits, or drugs increase the risk of respiratory failure. For instance, infants with neonatal respiratory distress because of the under-developed lung, certain lung birth defects, or

S/N	Circumstances	Conditions	Outcome
1	Difficulty in breathing	Weakness following collapsed airways and stroke	Blockage of the windpipe
2	Difficulty exhaling	Asthma condition and conditions of chronic obstructive pulmonary disease	Narrowing of airways; accumulation of mucus and narrowing of the airways
3	The difficulty of air entry to the lungs	Weak muscles, severe pains, airway blockage by mucus, fractured or broken ribs, and pneumothorax	respiratory failure
4	Retention of fluid in the lungs	Lack of oxygen passage from the air sacs into the blood makes it difficult for the blood's carbon dioxide to enter the air sacs to be exhaled	Accumulation of fluid in the lungs associated with the condition such as ARDS, pneumonia, drowning, heart failure, and head injury or trauma
5	Breathing muscles difficulties	Spinal cord trauma or condition of many diseases of the muscular system (occurring among members of a family) due to inadequate oxygen-rich blood in reaching the diaphragm and other breathing muscles or condition of cardiogenic shock and sepsis	Non-vitality and muscle wasting (muscular dystrophy)
6	Situations that affect the brain's control over breathing, usually when there is an overdose of drugs like an opioid overdose	High concentrations of carbon dioxide in the blood detected by the brain	Accumulation of carbon dioxide in the body while the concentration of oxygen fall

Table 1.
Circumstances, conditions, and the resultant effect of respiratory failure.

pulmonary hypertension are more vulnerable to respiratory failure, while aged persons with weak breathing muscles or with a common cold or allergies are more prone to respiratory failure [11]. Also, breathing lung irritants (such as dust, chemical fumes, dyes and paints, asbestos, aniline, or smoke) from the environment for a long period of time can lead to lung damage and pose a risk of severe lung diseases [12]. There is also more danger of respiratory failure with some medical conditions such as disorders of the muscles and nerve (like Guillain-Barre syndrome, amyotrophic lateral sclerosis, and myasthenia); diseases of the airways and lungs (cystic fibrosis, interstitial lung diseases, asthma, and COPD); congestive heart failure or pulmonary embolism; spinal cord or brain infections; meningitis; pneumonia; bronchiolitis; obstructed airway; chest or back injuries; severe scoliosis; and food or drug allergies [13, 14]. Moreover, life habits like smoking can instigate diseases of the lungs and potentiate vulnerability to respiratory failure. Indiscriminate alcohol or drugs affects the area of the brain that controls breathing by making breathing becomes slow and shallow and may ultimately give rise to acute respiratory failure. In addition, some sedatives used during surgery raise the risk of respiratory failure [15]. Respiratory failure may be a resultant effect of many factors described in **Table 1**.

Respiratory failure can be classified as hypoxemic (Type 1) and hypercapnic (Type 2). Hypercapnia often results from a failed respiratory, leading to PaCO₂ greater than 50 mmHg. In the hypoxemic respiratory failure associated with COVID-19, ARDs, severe pneumonia, and edema, PaO₂ is lesser than 60 mmHg with normal or subnormal PaCO₂ [16].

3. Pathogenesis and pathology of ARDS-associated and non-associated COVID-19

In contrast to the conventional ARDS, the pathogen of COVID-19 is obvious; SARS-CoV-2 causes it, a beta-coronavirus that gains entry into the cells by binding the angiotensin-converting enzyme 2 (ACE2) receptor *via* the viral structural spike (S) protein. Alveoli (II) epithelial cells, small intestine, bronchia, vesicle, and numerous types of immune cells, such as macrophages, monocytes, and dendritic cells, all contain ACE2 receptors in varying degrees. As a result of attacking the lung immune cells, SARS-CoV-2 can cause a lower respiratory infection and trigger an inflammatory reaction [17].

Comparing COVID-19 to a typical case of ARDS, the pathophysiology is more complex and varied. Some patients with acute COVID-19 proceeded to well-known ARDS, although a sizable portion of these patients did not exhibit the “reduced lung capacity and impaired compliance” that are typical of classical ARDS. In contrast to how severe the hypoxemia is, their pulmonary compliance is almost normal. Additionally, intrapulmonary shunt, along with dead space ventilation, is the primary cause of ARDS-related hypoxemia [4, 18]. Hypoxemia caused by COVID-19 can be understood by dysfunctional hypoxic pulmonary vasoconstriction, which impairs lung perfusion regulation, and microthrombus of the lung alveoli, which simultaneously increases dead space and causes intrapulmonary shunt. Reports have shown that patients with COVID-19 experience hypoxemia for a variety of reasons, including vascular dysfunction, dead space, and intrapulmonary shunt [19].

Gattinoni et al. classified the COVID-19 phenotype as type H and type L. The following were the key L-type symptoms: (1) Low elastance, almost normal compliance, and nearly normal lung gas content are indicators of low elastance. (2) Low ventilation

to perfusion ratio. (3) Lightweight lungs and (4) Limited lung recruitment. Although there is significant hypoxemia in these patients, respiratory compliance is beyond 50 ml/cm H₂O. The lung is not very recruitable and contains a lot of gas. The main cause of severe hypoxia is the impaired ventilation-to-perfusion ratio [20].

High PEEP and prone positioning are used to increase oxygenation, but not by encouraging the enlargement of the collapsed alveolar region, but rather by

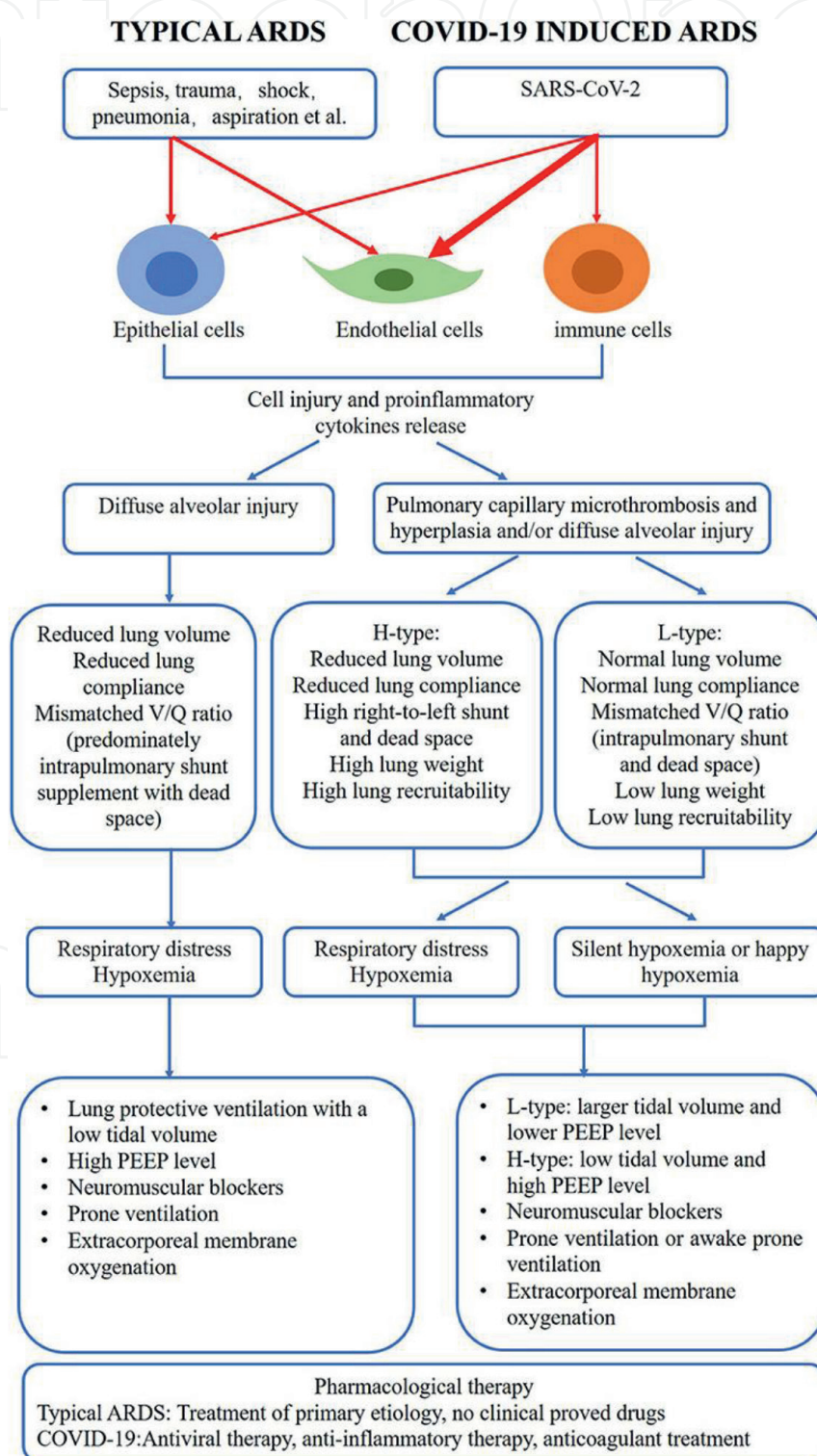


Figure 1. Comparison of ARDS-associated and non-associated COVID-19. Source: Lu [4].

redistributing pulmonary perfusion and boosting the ratio of ventilation to perfusion. Although the venous blood mixing from right to left shunt is apparent in these individuals, about 50% of computerized tomographic scans of the two lungs have shown no notable alveolar region in these individuals [21]. The primary symptoms of H-type COVID-19 include worsening of edema of the lungs and a reduction in pulmonary gas volume, which causes an increase in stretching resistance and a reduction in pulmonary compliance, high right-to-left shunt that is brought on by the alveolar collapse in gravity-dependent areas, large lung mass, high recruit ability of the lungs. H-type and conventional severe ARDS are comparable [22]. It has been reported that 20–30% of COVID-19 patients who are hospitalized in the intensive care unit (ICU) show severe hypoxemia and lung compliance below 4 ml/cmH₂O, which may indicate the existence of severe ARDS [23]. Individuals with serious hypoxemia who were hospitalized in ICU had non-invasive ventilation initiated; these patients also exhibited robust spontaneous inspiratory efforts and significant chest negative pressure. Thus, these individuals also suffer patient self-induced lung injury (P-SILI) and viral infection [24]. Many COVID-19 patients exhibited L-type in the early stages. L-type can change into H-type in the late stages of the disease due to the progression of the condition and lung damage brought on by high-stress breathing [25].

The pathophysiology of conventional ARDS and COVID-19-induced ARDS differ significantly, with the L-type of COVID-19 being the most notable variation. There are numerous explanations that could apply (**Figure 1**). Considering the etiology of ARDS, typically, shock, sepsis, transfusion, trauma, and other insults result in endothelial and epithelial damage as well as disruption of the blood-gas barrier, which increases permeability and causes the flooding of the alveolar and interstitial spaces by protein-rich fluid, resulting in low compliance, decreased lung volume, and an improper ratio of ventilation to perfusion [4]. COVID-19 pathogen is nonetheless known to be SARS-CoV-2 and the associated variations, which primarily target the endothelium *via* the ACE2 receptor with only little effects on the epithelial cell. As a result, lung compliance and volume are practically normal. Additionally, COVID-19's damaged pulmonary endothelium lost its ability to regulate lung perfusion due to hypoxic vasoconstriction, which ultimately led to the development of an intrapulmonary shunt [26, 27]. Furthermore, the COVID-19-damaged pulmonary endothelium changes from a typical anti-inflammation condition to an “active” phenotype defined by pro-adhesive qualities, inflammatory mediators production, and the development of microthrombi, which causes the amount of dead space to increase [28].

4. Hypoxemic respiratory failure in COVID-19 condition

A better understanding of the pathophysiological aspects of COVID-19 continues to ensue with the discovery of different variants of SARS-CoV-2. Viral pneumonia remains the principal complication of COVID-19 simply because it is associated with fluid retention in cells, tissues, or serous cavities of the interstices of the lungs, usually situated in the sub-pleural areas [29]. Severe hypoxemia probably occurs during the phase whereby a relative amount of lung parenchyma is involved, but the exact mechanism is not fully understood. A perturbed control of pulmonary vascular tone (vasoplegia) is, however, suggested to be the cause whereby vascular tone is not constricted despite alveolar hypoxia (**Figure 2**) [31].

The mouth, nose, or eyes are the main entry points for COVID-19 causative virus, SARS-CoV-2, into the body. The mucous membrane in the back of the throat and the

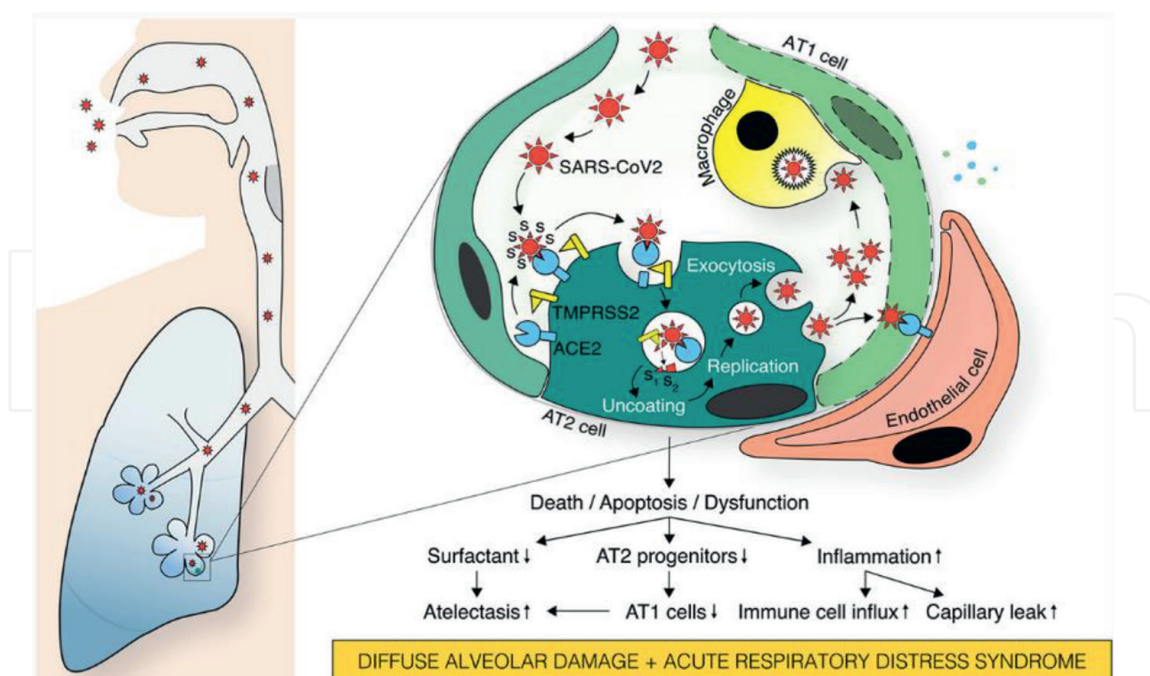


Figure 2.
 Severe hypoxemia probably occurs during the phase whereby a relative amount of lung parenchyma. Source: Brosnahan [30].

rear of the nasal passages are the next places it travels. It attaches to the cells there, reproduces, and enters the lung tissue. The virus might then move on to infect further bodily tissues [32].

People who have respiratory issues can become ill from COVID-19 caused by SARS-CoV-2. The most common clinical symptom and fatality factor of COVID-19 is respiratory failure. Asymptomatic to severe respiratory failure are all possible clinical demonstrations of COVID-19. People with COVID-19-related respiratory failure may deteriorate to the point where they need invasive mechanical ventilation or may not survive [33].

Respiratory illness from mild to severe is usually experienced by most patients with virus infection who may recover without special care, while serious ailments and demand medical attention may develop in others. Serious illness is more likely to affect the elderly and people with underlying medical conditions, including cardiovascular disease, diabetes, chronic respiratory diseases, or cancer. COVID-19 has the potential to cause serious illness or kill anyone at any age [34]. Acute respiratory distress syndrome, also known as ARDS, is a serious side effect of COVID-19, and lung problems include pneumonia. There could be long-term harm to the lungs and other organs because of sepsis, another potential COVID-19 side effect. More serious respiratory diseases like bronchitis that can necessitate hospitalization may also be brought on by more recent coronavirus strains.

Lung inflammation and fluid accumulation are symptoms of pneumonia. Respiratory difficulties in certain patients can be so severe that they require medical care, oxygen therapy, and perhaps a ventilator. Pneumonia due to COVID-19 usually affects both lungs. Coughing, shortness of breath, and other symptoms appear when the fluid-filled air sacs in the lungs' ability to absorb oxygen are blocked. Despite the fact that most patients recover from COVID-19-induced pneumonia without any long-term lung damage, pneumonia can be rather severe. Lung damage may result in breathing issues even after the illness has stopped; these issues may improve over several months [34].

Bronchitis in COVID-19 conditions is associated with excessive production of sputum in the airways. The excessive sputum leads to cough and chest congestion and constricts the airways, making breathing more difficult. Even after recovery from COVID-19 infection, inflammation of the membranes lining the bronchial tubes may continue to stimulate coughing with consequential effects on the quality of life [35]. Furthermore, the alveoli are filled with fluid from the lungs' tiny blood veins as COVID-19 pneumonia advances. The resultant outcome is the development of acute respiratory distress syndrome (ARDS), which is the term for lung failure that may occur as a result of shortness of breath. In order to assist the body in circulating oxygen, many ARDS patients are unable to breathe on their own and may require ventilator support. Recovery from COVID-19 and ARDS may result in lung scarring that lasts a lifetime [36].

Severe COVID-19 infection complications include sepsis. When an infection gets into the bloodstream and circulates throughout it, causing tissue damage, sepsis starts to take hold. The collaboration between the organs breaks down in sepsis. The lungs and heart are only two examples of the many organ systems that can begin to shut down one after the other. Even in cases where sepsis is successfully treated, the patient may experience long-term lung and other organ damage [37]. In the COVID-19 condition, the immune system is actively battling the invader. This could make the body more susceptible to a superinfection—the simultaneous infection of the body with two viruses or bacteria—on top of COVID-19. Additional infections may cause more lung damage. There is a startling observation that one in four patients who get severe COVID-19 also have a superinfection, which means that their recovery will be slower [38, 39].

5. Hypoxemic respiratory failure in COVID-19

The causes of respiratory failure in COVID-19 conditions can be intrapulmonary shunting, lung perfusion regulation loss, intravascular microthrombi, impaired diffusion capacity, preservation of lung mechanics, and rapid deterioration [40].

V/Q mismatch principally causes arterial hypoxemia at the initial state of SARS-CoV-2 infection. Therefore, continuous flow of pulmonary arterial blood to the non-ventilated alveoli manifests a significant increment in $P(A-a)O_2$ gradient, which eventually results in local interstitial edema domiciled mainly at the interface that can be termed intrapulmonary shunting [14, 30].

A proportional failure of the hypoxic pulmonary vasoconstriction mechanism or constriction of intrapulmonary arteries in alveolar hypoxia in COVID-19 condition usually causes a never-ceasing increase in the pulmonary flow of blood to nonaerated alveoli of the lung [3]. This cascade of events leads to the loss of control over lung perfusion. The resultant effect is a decreased concentration of angiotensin-converting enzyme 2 (ACE2) associated with an increased level of angiotensin II (Ang II), leading to arbitration of pulmonary vasoconstriction *via* agonist effect at the Ang II receptor, while being antagonized by Ang 1–7 [41].

Furthermore, the imbalance between fibrinolytic activity and procoagulant majorly results in intravascular microthrombi when there is severe inflammation and endothelial injury (a hallmark of COVID-19 pathogenesis). Endothelial injury can be a result affect infection of the lung capillary endothelial cells by a cytopathic virus that directly affects the expression of ACE2 [42].

It is also possible that the lung diffusion capacity is impaired due to the loss of alveolar epithelial cells from COVID-19. This results in the propagation within the

alveolar cells (type II cells). In this situation, the production of many viral particles that are being released leads to an immune response that mediates the death of infected cells. This increases $P(A-a)O_2$ gradient and arterial hypoxemia in the COVID-19 condition [12, 43].

It has also been known that there is a peak of COVID-19 challenge in patients on mechanical ventilation, signifying probably low respiratory system compliance. On the contrary, an increased airway resistance or increase in physiological and anatomical inactive ventilation usually does not occur at the onset of infection. There is also a steady breathing rate maintained at a low frequency as much as there is normality in lung compliance in patients having no underlining lung disease [44].

There can be a rapid deterioration in patients with COVID-19 that has an impact on the cortical response obtained from respiratory points. Consequently, the disease advances with a concomitant increase in dyspnea [45].

6. Clinical manifestation of respiratory failure in COVID-19

An 8- to 12-day incubation period was usually experienced by persons having COVID-19. The symptoms of COVID-19 might range from being asymptomatic and having minor symptoms to having severe ARDS. The most prevalent symptoms in patients with severe COVID-19 who needed to be admitted to the hospital were cough, fever, and dyspnea [46]. Patients with COVID-19 frequently experience extrapulmonary organ symptoms, including gastrointestinal ones like vomiting, nausea, and diarrhea, as well as taste and smell loss, headaches, bone pain, muscular aches, and other similar ones [47].

Some patients with cases of COVID-19 do not exhibit evident dyspnea while having significant hypoxemia, with oxygen saturation below 70% and partial pressure of arterial oxygen below 40 mmHg, a condition known as “silent hypoxemia” or “happy hypoxemia.” The predominant partial pressure of CO_2 inhibits the reaction of the brain to hypoxia, abnormal chemoreceptor function of the carotid body caused by virus attacks, inaccurate oxygen in arterial blood at low saturations, shifts in the oxygen dissociation curve, and distinct permissiveness of low oxygen concentrations [45, 48]. Another possibility for “silent hypoxia” is a cardiorespiratory adaptation to hypoxemia. Tachycardia and increased cardiac output are the typical reactions. However, these reactions are constrained by aging, genetics, and concurrent diseases. Lactic acidosis, bradycardia, and a lower cardiac output are signs that the body is unable to make up for the reduced oxygen transfer. The latter could appear suddenly, and they are all warning signs of impending tissue damage or hypoxemia-induced mortality [49].

Because there are so many blood vessels in lung tissues, SARS-CoV-2 can directly instigate severe harm to the vascular endothelium of the lung. Variable degrees of damage are also exhibited by the airway and alveolar epithelium [50]. Endothelial cell activation potentiates inflammatory reactions and coagulation apart from participating in the adhesion, rolling, and migration of inflammatory cells. This cascade of events eventually results in coagulation activation, diffusion dysfunction, and barrier degradation [51].

Edema, infiltration of inflammatory cells, fibrinous exudation, congestion of alveolar septal vesicle, vascular thrombi, and hemorrhagic necrosis are some of the pathological symptoms of COVID-19 [52]. On postmortem, these patients had a diffuse alveolar injury (DAD) recorded in 67–100% of them, which is consistent with the usual ARDS. The COVID-19 patients did, however, exhibit specific vascular characteristics,

such as microthrombosis and hyperplasia, as a result of the severe endothelium destruction. SARS-CoV-2 infection directly contributes to the development of endotheliitis in a number of organs as a result of viral participation (distinguished by the involvement of viral bodies) and the response of inflammation of the host (**Figure 3**) [4].

Studies have shown distinctive vascular features in the lungs of COVID-19 fatality patients. Capillary microthrombi of the lungs were nine times higher in COVID-19 patients than in influenza patients. It was complemented by capillary hyperplasia *via* intussusceptive angiogenesis, together with interrupted cell membranes and severe endothelial injury with an intracellular virus [53, 54]. A pulmonary embolism represented one-third of the patients' primary causes of death in an autopsy analysis of 12 consecutive COVID-19 patients. The frequency of deep thrombosis in the veins was up to 58%. These findings imply that the primary vascular alterations in COVID-19 patients, including microthrombosis of the lung capillary, damage of the epithelial cells, and hyperplasia are what distinguish them from ARDS patients and result in a distinct pathophysiological action and therapeutic feedback [55, 56]. Although the majority of patients had DAD, these data came from autopsies of people who had COVID-19-related deaths. DAD is most likely a late-stage manifestation of this illness rather than an early indicator [57].

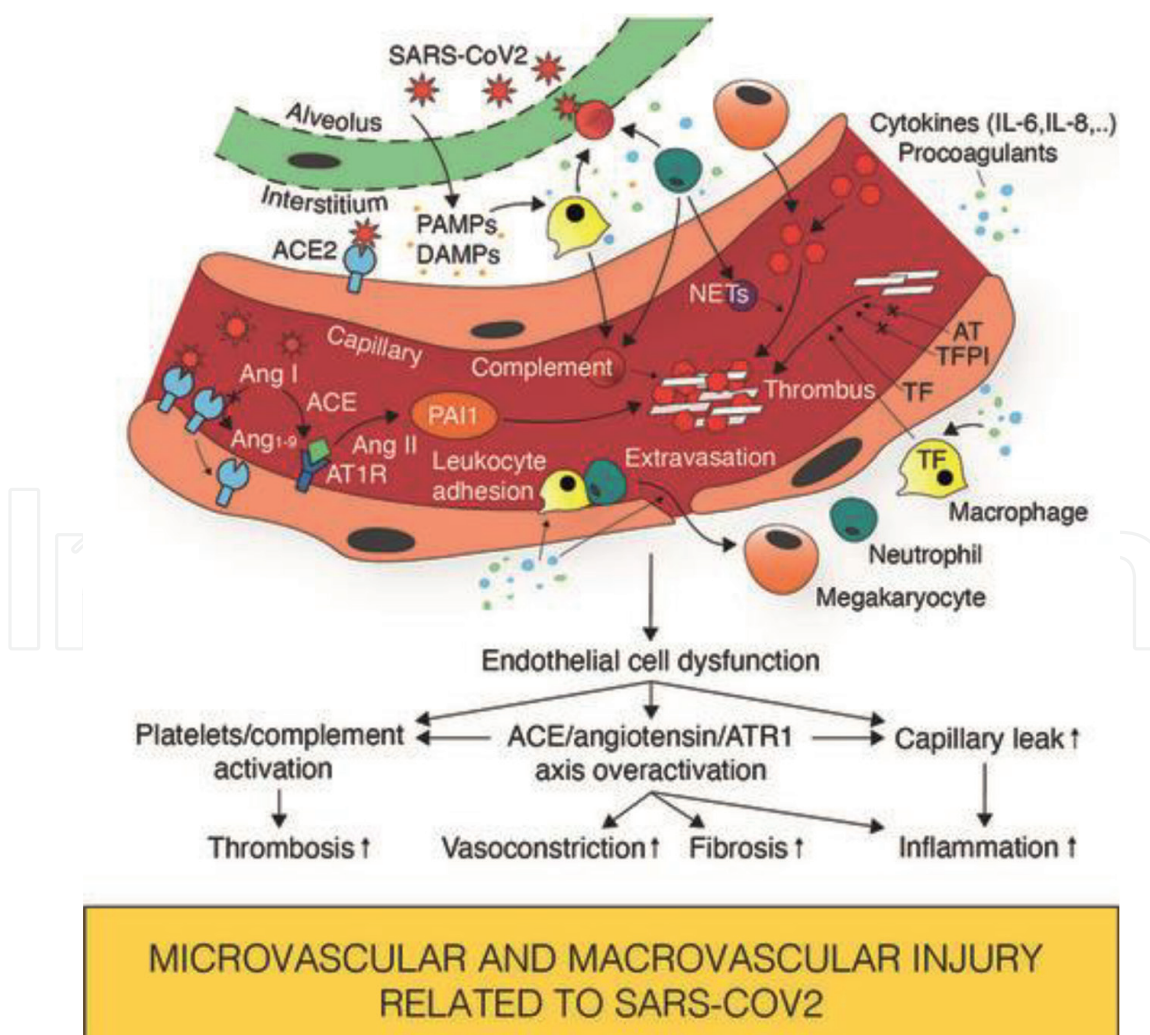


Figure 3. Pathobiological effects of epithelial injury tiny air sacs of the lungs by acute respiratory syndrome coronavirus-2 (SARS-CoV2) infection. Source: Brosnahan [30].

7. Management of respiratory failure in COVID-19 condition

The pathology and management of hypoxemic respiratory failure in the COVID-19 condition have similarities with acute respiratory distress syndrome. Acute hypoxemic respiratory failure, often manifested as hemoglobinopathies, pulmonary edema, or vascular occlusion, is considered a grave complication of COVID-19 and requires mechanical ventilation [19].

Mechanisms (including include vascular occlusion, hemoglobinopathies, pulmonary edema, and a mismatch between ventilation and perfusion) have been proposed for the substantial hypoxemic condition in patients. However, histopathological evaluation reveals the similarity between diffuse alveolar damage or related etiologies and ARDS [58]. Also, many comparable features exist between the variable pulmonary compliance in COVID-19 and pulmonary compliance values in ARDS. As a whole, patients with COVID-19 have similar pathology to ARDS [19]. Oxygen therapy, non-invasive ventilation, and intubation are ways of managing respiratory failure in COVID-19 condition. However, there may be some factors to consider for the best management choice [59]. For instance, there is controversy about choosing between a high-flow nasal cannula (HFNC), early intubation, or non-invasive positive pressure ventilation because there are patients who may need support beyond supplemental oxygen. Protecting healthcare workers from being exposed to viral aerosols while rendering care to patients may also be another issue. Also, non-invasive positive pressure ventilation (NIPPV) usually renders ventilatory support out the requirement of the endotracheal airway, which keeps the patients awake. This management option is non-invasive, but it is not entirely benign. It has been shown that ventilation protection having minimal volumes and pressures of tide improves results in ARDS patients. By and large, management options for respiratory failure in COVID-19 range from optimized oxygenation, respiratory support availability, necessary intubation, and of course, orienting ventilatory pressure with the needs of patients [31, 60].

8. Conclusion

COVID-19, caused by SARS-CoV-2, is highly infectious that leads to the fatal coexistence of two or more related medical conditions, especially ARDS. People with respiratory issues can be vulnerable to COVID-19. Therefore, for patients with COVID-19 condition, severe hypoxemia associated with ARDS is the frontline cause of acute respiratory failure. The most prominent clinical symptom and human death factor of COVID-19 is respiratory failure. Symptomless or mild- to life-threatening respiratory failure are possible clinical manifestations of COVID-19 condition. In individuals with severe COVID-19, critical hypoxemia related to ARDS is the major causative factor of acute respiratory failure. COVID-19-associated ARDS have similarities with other causes of ARDS in relation to pathology and respiratory physiology. In this regard, patients with respiratory failure in COVID-19 conditions are usually managed as in the condition of ARDS. Since there is no clear-cut treatment for COVID-19, supportive treatment is crucial. Sound knowledge of the features of respiratory failure in COVID-19-related ARDS is crucial for accurate treatment. This review provides more scientific information on the pathophysiologic mechanisms linked with ARDS and severe COVID-19 pneumonia with emphasis on respiratory failure related to COVID-19 associated with acute hypoxemia. This will help to improve the prognosis.

Conflict of interest

The authors declare no conflict of interest.

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References

- [1] Gyebi GA, Adegunloye AP, Ibrahim IM, Ogunyemi OM, Afolabi SO, Ogunro OB. Prevention of SARS-CoV-2 cell entry: Insight from in silico interaction of drug-like alkaloids with spike glycoprotein, human ACE2, and TMPRSS2. *Journal of Biomolecular Structure and Dynamics*. 2020;**40**(5):2121-2145. DOI: 10.1080/07391102.2020.1835726
- [2] Gyebi GA, Ogunro OB, Adegunloye AP, Ogunyemi OM, Afolabi SO. Potential inhibitors of coronavirus 3-chymotrypsin-like protease (3CLpro): An in silico screening of alkaloids and terpenoids from African medicinal plants. *Journal of Biomolecular Structure and Dynamics*. 2021;**39**(9):3396-3408. DOI: 10.1080/07391102.2020.1764868
- [3] Czajkowska-Malinowska M, Kania A, Kuca P, Nasiłowski J, Skoczyński S, Sokołowski R, et al. Treatment of acute respiratory failure in the course of covid-19. Practical hints from the expert panel of the assembly of intensive care and rehabilitation of the polish respiratory society. *Advances. Respiratory Medicine*. 2020;**88**(3):245-266
- [4] Lu S, Huang X, Liu R, Lan Y, Lei Y, Zeng F, et al. Comparison of COVID-19 induced respiratory failure and typical ARDS: Similarities and differences. *Frontiers in Medicine*. 2022;**9**(5):1-11
- [5] Oldani S, Ravaglia C, Bensai S, Bertolovic L, Ghirotti C, Puglisi S, et al. Pathophysiology of light phenotype SARS-CoV-2 interstitial pneumonia: From histopathological features to clinical presentations. *Pulmonology*. 2022;**28**(5):333-344. DOI: 10.1016/j.pulmoe.2021.03.003
- [6] Ball L, Silva PL, Giacobbe DR, Bassetti M, Zubieta-Calleja GR, Rocco PRM, et al. Understanding the pathophysiology of typical acute respiratory distress syndrome and severe COVID-19. *Expert Review of Respiratory Medicine*. 2022;**16**(4):437-446. DOI: 10.1080/17476348.2022.2057300
- [7] Harless J, Ramaiah R, Bhananker SM. Pediatric airway management. *International Journal of Critical Illness and Injury Science*. 2014;**4**(1):65-71
- [8] Wallbridge P, Steinfort D, Tay TR, Irving L, Hew M. Diagnostic chest ultrasound for acute respiratory failure. *Respiratory Medicine*. 2018;**141**(2):26-36. DOI: 10.1016/j.rmed.2018.06.018
- [9] Piraino T. Noninvasive respiratory support in acute hypoxemic respiratory failure. *Respiratory Care*. 2019;**64**(6):638-646
- [10] Kempker JA, Abril MK, Chen Y, Kramer MR, Waller LA, Martin GS. The epidemiology of respiratory failure in the United States 2002-2017: A serial cross-sectional study. *Critical Care Explorations*. 2020;**2**(6):e0128. DOI: 10.1097/CCE.0000000000000128
- [11] Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: Noninvasive ventilation for acute respiratory failure. *European Respiratory Journal*. 2017;**50**(4):1-20. DOI: 10.1183/13993003.02426-2016
- [12] Clementi N, Ghosh S, De Santis M, Castelli M, Criscuolo E, Zanoni I, et al. Viral respiratory pathogens and lung injury. *Clinical Microbiology Reviews*. 2021;**34**(3):e00103-e00120. DOI: 10.1128/CMR.00103-20

- [13] Laghi F, Tobin MJ. Disorders of the respiratory muscles. *American Journal of Respiratory and Critical Care Medicine*. 2003;**168**(1):10-48
- [14] Sarkar M, Niranjana N, Banyal PK. Mechanisms of hypoxemia. *Lung India*. 2017;**34**(1):47-60
- [15] Kershaw CD, Guidot DM. Alcoholic lung disease. *Alcohol Research and Health*. 2008;**31**(1):66-75
- [16] Gottlieb J, Capetian P, Hamsen U, Janssens U, Karagiannidis C, Kluge S, et al. German S3 guideline: Oxygen therapy in the acute care of adult patients. *Respiration*. 2022;**101**(2):214-252
- [17] Li C, He Q, Qian H, Liu J. Overview of the pathogenesis of COVID-19 (Review). *Experimental and Therapeutic Medicine*. 2021;**22**(3):1-10
- [18] Pfortmueller CA, Spinetti T, Urman RD, Luedi MM, Schefold JC. COVID-19-associated acute respiratory distress syndrome (CARDS): Current knowledge on pathophysiology and ICU treatment - a narrative review. *Best Practice & Research Clinical Anaesthesiology*. 2021;**35**(3):351-368. DOI: 10.1016/j.bpa.2020.12.011
- [19] Swenson KE, Ruoss SJ, Swenson ER. The pathophysiology and dangers of silent hypoxemia in COVID-19 lung injury. *Annals of the American Thoracic Society*. 2021;**18**(7):1098-1105
- [20] Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Critical Care*. 2020;**24**(1):1-3
- [21] Marini JJ, Hotchkiss JR, Broccard AF. Bench-to-bedside review: Microvascular and airspace linkage in ventilator-induced lung injury. *Clinical Review & Education*. 2020;**323**(22):2329-2330
- [22] Karbing DS, Panigada M, Bottino N, Spinelli E, Protti A, Rees SE, et al. Changes in shunt, ventilation/perfusion mismatch, and lung aeration with PEEP in patients with ARDS: A prospective single-arm interventional study. *Critical Care*. 2020;**24**(1):1-13
- [23] Krynytska I, Marushchak M, Birchenko I, Dovgalyuk A, Tokarskyy O. COVID-19-associated acute respiratory distress syndrome versus classical acute respiratory distress syndrome (a narrative review). *Iranian Journal of Microbiology*. 2021;**13**(6):737-747
- [24] Fernando SM, Ferreyro BL, Urner M, Munshi L, Fan E. Diagnosis and management of acute respiratory distress syndrome. *CMAJ*. 2021;**193**(21):E761-E768
- [25] Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. *Clinical interventions in Aging*. 2006;**1**(3):253-260
- [26] Barbosa LC, Gonçalves TL, de Araujo LP, de Rosario LV, Ferrer VP. Endothelial cells and SARS-CoV-2: An intimate relationship. *Vascular Pharmacology*. 2021;**137**(1):106829. DOI: 10.1016/j.vph.2021.106829
- [27] Kumar A, Singh R, Kaur J, Pandey S, Sharma V, Thakur L, et al. Wuhan to world: The COVID-19 pandemic. *Frontiers in Cellular and Infection Microbiology*. 2021;**11**(3):1-21
- [28] Smadja DM, Mentzer SJ, Fontenay M, Laffan MA, Ackermann M, Helms J, et al. COVID-19 Is a Systemic Vascular Hemopathy: Insight for Mechanistic and Clinical Aspects. Vol. 24. Netherlands: Springer; 2021. pp. 755-788. DOI: 10.1007/s10456-021-09805-6
- [29] Alipour SD, Jamaati H, Tabarsi P, Mortaz E. Immunopathogenesis of

pneumonia in covid-19. *Tanaffos*. 2020;**19**(2):79-82

[30] Brosnahan SB, Jonkman AH, Kugler MC, Munger JS, Kaufman DA. COVID-19 and respiratory system disorders: Current knowledge, future clinical and translational research questions. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2020;**40**(11):2586-2597

[31] Raoof S, Nava S, Carpati C, Hill NS. High-flow, noninvasive ventilation and awake (nonintubation) Prone in patients with coronavirus disease 2019 with respiratory failure. *Chest*. 2020;**158**(5):1992-2002. DOI: 10.1016/j.chest.2020.07.013

[32] Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. *JAMA - Journal of the American Medical Association*. 2020;**324**(8):782-793

[33] Lotfi M, Hamblin MR, Rezaei N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. *Clinica Chimica Acta*. 2020;**508**(4):254-266

[34] Attaway AH, Scheraga RG, Bhimraj A, Biehl M, Hatipođ LU. Severe covid-19 pneumonia: Pathogenesis and clinical management. *The BMJ*. 2021;**372**:n436. DOI: 10.1136/bmj.n436

[35] Goyal D, Inada-Kim M, Mansab F, Iqbal A, McKinstry B, Naasan AP, et al. Improving the early identification of COVID-19 pneumonia: A narrative review. *BMJ Open Respiratory Research*. 2021;**8**(1):1-9

[36] Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): Clinical features and

differences from typical pre-COVID-19 ARDS. *Medical Journal of Australia*. 2020;**213**(2):54-56.e1

[37] Olwal CO, Nganyewo NN, Tapela K, Djomkam Zune AL, Owoicho O, Bediako Y, et al. Parallels in sepsis and COVID-19 conditions: Implications for managing severe COVID-19. *Frontiers in Immunology*. 2021;**12**(2):1-6

[38] Hoque MN, Akter S, Dilruba I, Islam MR. Microbial co-infections in COVID-19: Associated microbiota and underlying mechanisms of pathogenesis. *Microbial Pathogenesis*. 2021;**156**:104941. DOI: 10.1016/j.micpath.2021.104941

[39] Schultze JL, Aschenbrenner AC. COVID-19 and the human innate immune system. *Cell*. 2021;**184**(7):1671-1692. DOI: 10.1016/j.cell.2021.02.029

[40] Yuan S, Jiang SC, Zhang ZW, Fu YF, Hu J, Li ZL. The role of alveolar edema in covid-19. *Cell*. 2021;**10**(8):1-15

[41] Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. *Critical Care*. 2020;**24**(1):1-10

[42] Prasad M, Leon M, Lerman LO, Lerman A. Viral endothelial dysfunction: A unifying mechanism for COVID-19. *Mayo Clinic Proceedings*. 2021;**9**(12):3099-3108. A

[43] Fuschillo S, Ambrosino P, Motta A, Maniscalco M. COVID-19 and diffusing capacity of the lungs for carbon monoxide: A clinical biomarker in care settings. *Biomarkers in Medicine*. 2021;**15**(8):2-4

[44] Haudebourg AF, Perier F, Tuffet S, De Prost N, Razazi K, Dessap AM, et al. Respiratory mechanics of COVID-19-versus non-COVID-19-associated acute

respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*. 2020;**202**(2):287-290

[45] Dhont S, Derom E, Van Braeckel E, Depuydt P, Lambrecht BN. Conceptions of the pathophysiology of happy hypoxemia in COVID-19. *Respiratory Research*. 2021;**22**(1):1-9

[46] Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. *Annals of Internal Medicine*. 2020;**172**(9):577-582

[47] Sarkesh A, Sorkhabi AD, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. Extrapulmonary clinical manifestations in COVID-19 patients. *American Journal of Tropical Medicine and Hygiene*. 2020;**103**(5):1783-1796

[48] Bickler PE, Feiner JR, Lipnick MS, McKleroy W. "Silent" presentation of hypoxemia and cardiorespiratory compensation in COVID-19. *Anesthesiology*. 2021;**134**(2):262-269. DOI: 10.1097/ALN.0000000000003578

[49] Stawicki S, Jeanmonod R, Miller A, Paladino L, Gaieski D, Yaffee A, et al. The 2019-2020 novel coronavirus (severe acute respiratory syndrome coronavirus 2) pandemic: A joint american college of academic international medicine-world academic council of emergency medicine multidisciplinary COVID-19 working group consensus paper. *Journal of Global Infectious Diseases*. 2020;**12**(2):47-93

[50] Jin Y, Ji W, Yang H, Chen S, Zhang W, Duan G. Endothelial activation and dysfunction in COVID-19: From basic mechanisms to potential therapeutic approaches. *Signal Transduction and Targeted Therapy*. 2020;**5**(1):1-13. DOI: 10.1038/s41392-020-00454-7

[51] Stenmark KR, Frid MG, Gerasimovskaya E, Zhang H, McCarthy MK, Thurman JM, et al. Mechanisms of SARS-CoV-2-induced lung vascular disease: potential role of complement. *Pulmonary Circulation*. 2021;**11**(2):1-14. DOI: 10.1177/20458940211015799

[52] Mondello C, Rocuzzo S, Malfa O, Sapienza D, Gualniera P, Ventura Spagnolo E, et al. Pathological findings in COVID-19 as a tool to define SARS-CoV-2 pathogenesis. A systematic review. *Frontiers in Pharmacology*. 2021;**12**(4):614586. DOI: 10.3389/fphar.2021.614586

[53] Bösmüller H, Matter M, Fend F, Tzankov A. The pulmonary pathology of COVID-19. *Virchows Archives*. 2021;**478**(1):137-150

[54] Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary vascular Endothelialitis, thrombosis, and angiogenesis in Covid-19. *New England Journal of Medicine*. 2020;**383**(2):120-128

[55] Deshpande C. Thromboembolic findings in COVID-19 autopsies: Pulmonary thrombosis or embolism? *Annals of Internal Medicine*. 2020;**173**(5):394-395

[56] Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: A prospective cohort study. *Annals of Internal Medicine*. 2020;**173**(4):268-277

[57] Elsoukkary SS, Mostyka M, Dillard A, Berman DR, Ma LX, Chadburn A, et al. Autopsy findings in 32 patients with COVID-19: A single-institution experience. *Pathobiology*. 2021;**88**(1):56-68

[58] Wilcox SR. Management of respiratory failure due to covid-19. *The BMJ*. 2020;**369**(5):2-3. DOI: 10.1136/bmj.m1786

[59] Bonnesen B, Jensen JUS, Jeschke KN, Mathioudakis AG, Corlateanu A, Hansen EF, et al. Management of covid-19-associated acute respiratory failure with alternatives to invasive mechanical ventilation: High-flow oxygen, continuous positive airway pressure, and noninvasive ventilation. *Diagnostics*. 2021;**11**(12):1-12

[60] Mina B, Newton A, Hadda V. Noninvasive ventilation in treatment of respiratory failure-related COVID-19 infection: Review of the literature. *Canadian Respiratory Journal*. 2022;**9914081**(8):1-8. DOI: 10.1155/2022/9914081