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Review Article

Machine learning to predict intubation in COVID-19 patients

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Abstract

COVID-19 infection, identified in December 2019, is a severe acute respiratory syndrome, associated with high rate of mortality among infected population. In some cases, intubation may be the first respiratory support to save patient's life, and any deletion in making this decision could implicate several clinical outcomes. Machine learning is known to be the first recent technology in the realm of healthcare, that automated in algorithm, based on several clinical, laboratory and demographical predictors and parameters to help in identifying the patients at a higher risk and in need for intubation.

Keywords: COVID-19; machine learning; predictors; intubation; emergency; inflammation; symptoms

Introduction

In patients suspected to have COVID-19 infection, and severe symptoms of respiratory distress, machine learning is known to be one of the most important technologies used in our time, due to the fact that it plays a key role in the realm of healthcare [1]. Machine learning or artificial intelligence is adopted by specialists, physicians and clinicians to predict the severity of a disease, the risk of mortality, and the need for hospitalization, in order to increase the quality of patient's life [2]. The clinical spectrum of COVID-19 patients ranges from mild to critically life threatening conditions [3]. Most patients suffer from mild symptoms such as fever, myalgia, dry cough, and headache, while others develop fatal complications such as respiratory failure, shock, sepsis and could require intubation [4, 5]. Therefore, machine learning based on several relevant predictors, can be used as a model to predict intubation in patients with COVID-19 infection, by providing algorithms based on clinical, demographical, and laboratory examinations to identify patients at a higher risk, and hence preventing their mortality [1, 6].

Coronavirus disease, is an infectious disease caused by SARS-CoV-2 a virus from the family of coronaviridae, that started in Wuhan China by the end of December 2019 [7], and emerged rapidly around the world, resulting in the loss of livelihoods, and called the WHO in March 2020 to announce it as a global pandemic [8]. Alongside with the severe acute respiratory syndrome, the mutation rate of SARS-COV-2 has increased significantly, and new strains have been developed, leading to aggressive symptoms and overwhelming increase in hospitalization [9,10]. Therefore, many technologies mainly artificial intelligence, have been designed to detect patients with severe symptoms in order to prioritize them and facilitate their treatment, by collecting the main data required to manage their lifesaving process [1,3].

In this review paper, machine learning will build and automate an algorithm based and focused on specific data and predictors to evaluate the patients infected with COVID-19 who are mostly in need for intubation.

Discussion

Given the wide spectrum of clinical symptoms of COVID-19 infection, that may range from asymptomatic to severe critical illness, such as acute respiratory failure, intubation may be required to support patient's ventilation and protect the airways [11]. Machine learning was designed in a way to predict the need for intubation in COVID-19 patients, based

on few clinical features and predictors, as it helps in identifying those at high risk [12].

Currently, several risk factors have been associated with critical outcomes in patients with COVID-19 infection and have been identified from clinical, laboratory, and demographical parameters. Machine learning models have been formulated according to these parameters.

Starting with the clinical parameters, which predominantly incorporate and include these components: the airway, the breathing, the circulation and the oxygenation based on the saturation, the neurological status, the vital signs and symptoms mainly fever, cough, shortness of breath and fatigue, patients of COVID-19 infection may be exposed to a sudden decompensation, and rapid deterioration of the respiratory function, hence require emergency intubation [12, 13].

COVID-19 infection is associated with acute respiratory distress syndrome, as it causes severe alveolar damage and respiratory dysregulation [14]. In the very advanced stage of COVID-19 infection, patients will start experiencing dyspnoea, with excessive production and retention of mucus, that will lead to obstructing the airways, hence increasing the risk of intubation [15].

Hypoxia is another predictor for respiratory support in subjects with COVID-19 infection [16]. It is well known, that since hypoxia is considered to be one of the main causes leading to multiple organ dysfunction, hence death, in COVID-19 patients, aggressive oxygen therapies are being considered [17], due to the fact that hypoxia leads to hypoperfusion and hypotension, as well as severe brain damage caused by oxygen starvation [18]. However, the most challenging controversial phenomenon is the silent hypoxia, in which the physician finds himself unable to make a clear decision whether to intubate or not. A silent hypoxia is a medical term that is applied on patients who have significant hypoxia in the absence of any respiratory symptoms [19].

A silently hypoxic patient is a "not to intubate decision", unless there are complications and signs of deterioration of the patient's clinical presentation [20]. Hypoxia can reach a point of no return since it will promote hypoxaemia, a condition characterized by decrease of SpO2 saturation below 90% [21]. Hypoxaemia is a life threatening criterion, specially in COVID-19 patients with comorbidities such as hypertension, obesity, and obstructive lung disease, due to the fact that it can induce death mainly when causing severe dyspnoea [22]. Hypoxaemia will provoke hyperinflammation, by activating the cytokines storm, causing by that irreversible lung damage. However, in some patients with hypoxaemia but masked symptoms of fatigue and dyspnoea, a paradoxical condition of hypoxaemia may develop, under the name of silent or happy hypoxaemia [21, 23]. When patients with COVID-19 infection evolve happy hypoxaemia, intubation must be delayed, as long as their condition doesn't progress to a respiratory distress, due to the fact that this type of hypoxaemia is reversible [24].

On the other hand, several studies have shown lately that patients with COVID-19 infection and neurological comorbidities and illnesses such as history of prior strokes and cerebrovascular events, are more likely to be intubated, as the neurological status of these patients is considered to be a strong predictor of adverse health effects [25, 26]. Moreover, Glasgow coma scale, responsible for evaluating the degree of consciousness and brain damage in patients with COVID-19 infection, is considered to be a predictor for intubation [27]. A deviation in the Glasgow coma scale score in patients with COVID-19 infection was significantly correlated to death [28]. The cause of altered consciousness level in patients with COVID-19 infection is not fully understood, however, several case studies have suggested that it may be due to either direct brain viraemia, or demyelination secondary to pro-inflammatory cytokines storm [29], alongside to hypoxia, and pH impairment that found to cause unconscious, therefore necessitate intubation [30].

According to Stevens et al 2019, dyspnoea is defined as the "air hunger". While being presented with other symptoms such as highgrade fever and cough, patients with COVID-19 infection will be subject for intubation since they will be requiring oxygen to improve their clinical conditions [31]. Patients with dyspnoea will exert more effort to breath, which, in turns, will increase the pulmonary pressure, henceforth, enabling inadequate gas exchange [32]. When having this condition, a conservative oxygen therapy has to be taken into consideration as a rescue therapy to prevent mortality.

Crucial laboratory parameters are another predictor for intubation in COVID-19 patients [33]. This category of parameters that include mainly C- reactive protein, interleukin-6, LDH protein, white blood cells count, D-Dimer was classified into mild, progressive and severe, according to the severity of respiratory failure, where progressive and severe required intubation within the first few hours of patient's admission, whereas the mild did not [33, 34].

Elevated C- reactive protein concentration more than 100 mg/L alongside with IL-6 levels are associated with additional adverse outcomes on COVID-19 patients, due to the fact that these two predictors contribute in accelerating the magnitude of systemic and disseminated inflammation [35], which is found to be, not only, featured to COVID-19, but also to other life threatening events such as thromboembolism and myocardial injuries that could worsen the prognosis in these patients [36].

IL-6 plays an important role in the pathogenesis of COVID-19 infection, as it induces the systematic circulation of the virus, and causes alveolar damage [37]. A IL-6 concentration above 24 pg/mL could be in favor of hypoxaemia, a potential predictor of hospitalization hence intubation [38], additionally of being a hot marker for respiratory failure, due to its unique role in the cytokine storm, that destroys the lungs functions significantly [36, 39].

Moreover, lactate dehydrogenase protein, was found to be a predictive biomarker that could highly affect the clinical course of the infection and the urgent need of intubation and respiratory support [40]. Ghobrial et al and Boothpur et al identified that high level of LDH in COVID-19 patients has a negative prognosis, due to the fact that it was found to be associated with lymphoproliferative disorders, by dropping T cell immunity and increasing inflammatory cytokines [41], additionally to its association with the severity of symptoms, mainly dyspnoea, due to the fact that it was found to stage the progression of fibrosis in these patients into alveolitis stage, fibrosis stage and progressive stage that in case was attained, they will be in need of invasive procedures [37, 38, 42].

High levels of white blood cells should be given more attention in COVID-19 patients, as they can correlate with mortality [43]. Recently, several scientific studies have been exploring the link between the increased count of these laboratory parameters and the adverse outcomes of COVID-19 infection and the need for intubation, as these results were not found to be severely increased in the early stage of COVID-19 infection, but rather in the very advanced stage, where patients were found to have a higher SOFA score and poor prognosis [44]. SOFA score is a score that helps in assessing and estimating the degree of organ failure and mortality [45]. When having COVID-19 infection along with leukocytosis and neutrophilia, SOFA score will be high enough to suggest sepsis and the urgent need for intubation [46].

Finishing with the last important predictor in the laboratory parameters, D- Dimer is one finding that measures the risk of thrombosis in COVID-19 patients [47]. A value of 1.5 μg/ml of D-Dimer on admission, is the optimal cutoff value to intubate [48].

The last category of parameters is the demographical model which involves age, gender, BMI, vaccination status and comorbidities, mainly COPD, obesity and hypertension [49].

Elderly patients with COVID-19 infection were found to be at a higher risk of intubation, specially if they were suffering from chronic diseases and comorbidities [50]. Although the reason for that was not fully understood, it was found out that angiotensin-converting enzyme 2 expression increases with the age factor, in terms of alveolar damage, hence, making the disease more severe to cooperate with [51, 52, 53].

On the other hand, male gender had a higher prevalence in intubated patients [54]. Several conducted studies showed that male patients had a significant association with oxygen requirements, due to the fact that the human Leydig cells in testis may enhance the expression of ACE2 [55], leading to a viral safe harbor, moreover, facilitating the entry of SARS-CoV-2 into the host cell. Unlike female patients, male patients were more vulnerable to many bacterial, fungal and parasitic infections, as reason of missing the X chromosome which plays in important role in adaptive and innate immunity [56, 57].

The impact of BMI on the severity of the disease and the need for intubation is not surprising [58]. An increased BMI level above 30 is highly linked to obesity, which in turns, was found to be biologically associated with higher levels of inflammatory cytokines [59], and the release of IL-6 from pulmonary cells, leading by that to inadequate ventilation and lung injury [60, 61].

Vaccination status is another important predictor for intubation in COVID-19 patients [62]. Unvaccinated patients were more likely to present with hypoxaemia, respiratory failure and shock [63]. COVID-19 vaccines have shown great efficacy against the disease by inhibiting the inflammatory biomarkers such as D- Dimer and CRP, which worsen the outcomes of the infection, as well as producing high affinity of virus neutralizing antibodies to avoid undesirable effects [64, 65]. For that reason, unvaccinated population is at higher risk to be intubated.

To finalize this category of parameters, comorbidities mainly chronic obstructive lung disease, obesity and hypertension are other additional predictors that put the patients with COVID-19 infection at greater risk for intubation [66].

COPD is known to be a chronic airway disease characterized by destruction of lung tissue and hypoxaemia development. Patients with COPD and COVID-19 infection are more imposed to acute respiratory distress syndrome, pulmonary thromboembolic events hence mortality [67]. On the other hand, COPD can impair the innate immune response to virus and facilitate the propagation of SARS-COV-2 in the lung of COVID-19 patients, leading to a rapid clinical deterioration [68].

COVID-19 infection and obesity is a deadly combination. Obese patients are more prone to metabolic inflammations [69]. Studies have shown that adipose tissue may be a target site for COVID-19 infection, as it leads to increasing in the AEC-2 expression, main receptor of SARS-COV-2 for host cell entry, and which was found to be higher in adipose tissue than in lungs [70, 71]. As conclusion, obesity is considered to be a dependent risk factor for intubation, as it contributes in excessive production of pro inflammatory mediators, specially in COVID-19 patients.

Finally, hypertension is the most common comorbidity in patients with COVID-19 infection [72]. COVID-19 patients who have history of hypertension are more probably to develop acute respiratory distress syndrome, due to the fact that hypertension will lead to endothelial damage, furthermore vascular injury and hypoperfusion, promoting end organ ischaemia and dysfunction [73, 74]. Hypertension is an emergency for intubation in COVID-19 subjects with poor clinical assessment, as it can activate ACE-2 production in lungs and leading to pulmonary thrombotic events [75].

Conclusion:

To intubate is known to be a critical decision. However, a delayed decision to intubate mainly in COVID-19 patients, may worsen the clinical outcomes of the disease, hence leading to death. In this review paper, we confirmed all clinical, laboratory and demographical parameters as predictors for intubation in COVID-19 patients.

References:

1. Varun Arvind, Samuel K. Cho. (2020). "Development of a machine learning algorithm to predict intubation among hospitalized patients with COVID-19," Journal of Critical Care.
2. Balazs Banfai, Solveig Badillo. (2020). "An Introduction to Machine Learning," Clin Pharmacol Ther.
3. Luis F García. (2020). "Immune Response, Inflammation, and the Clinical Spectrum of COVID-19," Front Immunol.
4. Aylin Çalıca Utku , Gökçen Budak .(2022). "Main symptoms in patients presenting in the COVID-19 period ," Scott Med J. 127-132.
5. Caroline P E Price , Kevin Hur . (2020). "Factors Associated With Intubation and Prolonged Intubation in Hospitalized Patients With COVID-19," Otolaryngol Head Neck Surg. 170-178.
6. Mirza Kovačević , Nermina Rizvanović. (2021). "Predictive factors for noninvasive mechanical ventilation failure among COVID-19 critically ill patients - a retrospective cohort study ," Med Glas (Zenica). 362-369
7. Koichi Yuki, Miho Fujiogi. (2020). "COVID-19 pathophysiology: A review ," Clin Immunol.
8. Maurizio Vanelli , Domenico Cucinotta. (2020). "WHO Declares COVID-19 a Pandemic ," Acta Biomed. 157-160
9. Behnaz Bakhshandeh, Zohreh Jahanafrooz. (2021). "Mutations in SARS-CoV-2; Consequences in structure, function, and pathogenicity of the virus ," Microb Pathog.
10. Kenji Nakamichi, Jolie Z Shen. (2021). "Hospitalization and mortality associated with SARS-CoV-2 viral clades in COVID-19".
11. Nicholas Zareifopoulos, Maria Lagadinou. "Intubation and mechanical ventilation of patients with COVID-19: what should we tell them? ," Monaldi Arch Chest Dis.
12. Ankur Khandelwal, Arvind Chaturvedi. (2020). "The “COVID-19 Score” can predict the need for tracheal intubation in critically ill COVID-19 patients – A hypothesis ," Med Hypotheses.
13. Haijun Li, Baoguo Pang. (2021). "Machine learning models for predicting critical illness risk in hospitalized patients with COVID-19 pneumonia ," J Thorac Dis. 1215-1229
14. Abdul Mannan Baig. (2020). "Computing the Effects of SARS-CoV-2 on Respiration Regulatory Mechanisms in COVID-19," ACS Chem Neurosci. 2416-2421
15. Shari B. Brosnahan, Annemijn H. Jonkman. (2020). "COVID-19 and Respiratory System Disorders ," Arterioscler Thromb Vasc Biol. 2586-2597
16. Eric Arnaud Diendéré, Kongnimissom Apoline Sondo. (2021). "Predictors of severe hypoxemia among COVID-19 patients in Burkina Faso (West Africa): Findings from hospital based cross-sectional study," Int J Infect Dis, vol. 108: 289-295
17. B. Jiang, H. Wei. (2020). "Oxygen therapy strategies and techniques to treat hypoxia in COVID-19 patients ," Eur Rev Med Pharmacol Sci. 10239-10246.
18. Ahsab Rahman, Tahani Tabassum. (2021). "Silent hypoxia in COVID-19: pathomechanism and possible management strategy," Mol Biol Rep. 3863-3869.
19. Ruff Joseph Macale Cajanding. (2022). "Silent Hypoxia in COVID-19 Pneumonia: State of Knowledge, Pathophysiology,

Mechanisms, and Management ," AACN Advanced Critical Care. 1-11.
20. Ali Lari, Mohammad Alherz. (2020). "Caution against precaution: A case report on silent hypoxia in COVID-19", Ann Med Surg (Lond) . 301-303.
21. Fernando Mejía, Carlos Medina. (2020) "Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru ," PLoS One.
22. Martin J Tobin, Franco Laghi. (2020). "Why COVID-19 silent hypoxemia is baffling to physicians," American journal of respiratory and critical care medicine.
23. Tatum S Simonson, Tracy L Baker. (2021)." Silent hypoxaemia in COVID-19 patients," J Physiol. 1057-1065
24. Atanu Chandra , Uddalak Chakraborty .(2020). "Silent hypoxia: a frequently overlooked clinical entity in patients with COVID-19," BMJ Case Rep.
25. Nicholas R Evans, Jasmine Wall. (2020) "Clinical frailty independently predicts early mortality after ischaemic stroke," Age Ageing. 588-591.
26. Shibani S. Mukerji , Sudeshna Das. (2021). "Prolonged Intubation in Patients With Prior Cerebrovascular Disease and COVID-19," Frontiers in Neurology.
27. Lucas M. Fleuren, Tariq A. Dam. (2021) "Predictors for extubation failure in COVID-19 patients using a machine learning approach ," Critical Care.
28. Dina Ragab, Haitham Salah Eldin. (2020). "The COVID-19 Cytokine Storm; What We Know So Far," Front. Immunol.
29. Anny Rouvel-Tallec, Geoffroy Vellieux. (2020). "COVID-19 associated encephalopathy: Is there a specific EEG pattern? ," Clinical Neurophysiology. 1928-1930
30. Jie Mu, Weixi Xiong. (2020). "New onset neurologic events in people with COVID-19 in 3 regions in China," Neurology. 1479-1487
31. Jose R. Navas-Blanco, Roman Dudaryk . (2020). "Management of Respiratory Distress Syndrome due to COVID-19 infection," BMC Anesthesiol.
32. Andrey I. Yaroshetskiy , Sergey N. Avdeev. (2020) "Acute Respiratory Distress Syndrome in COVID-19: Do All These Patients Definitely Require Intubation and Mechanical Ventilation? ," American Journal of Respiratory and Critical Care Medicine.
33. Alisa A. Mueller, Tomoyoshi Tamura. (2020). "Inflammatory Biomarker Trends Predict Respiratory Decline in COVID-19 Patients," Cell Rep Med.
34. Kun Yang, Qiurong Ruan. (2020). "Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China ," Intensive Care Med. 846-848.
35. Nathaniel R Smilowitz, Dennis Kunichoff. (2021). "C-reactive protein and clinical outcomes in patients with COVID-19," Eur Heart J.
36. Maryame Ahnach, Saad Zbiri. (2020). "C-reactive protein as an early predictor of COVID-19 severity ," J Med Biochem. 500-507
37. Ilias Giannakodimos, Georgia-Vasiliki Gkountana. (2021). "The Role of Interleukin-6 in the Pathogenesis, Prognosis and Treatment of Severe COVID-19 ," Curr Med Chem. 5328-5338
38. P Sabaka , A Koščálová . (2021). "Role of interleukin 6 as a predictive factor for a severe course of Covid-19: retrospective data analysis of patients from a long-term care facility during Covid-19 outbreak ," BMC Infect Dis.
39. Mitra Abbasifard, Hossein Khorramdelazad. (2020). "The bio-mission of interleukin-6 in the pathogenesis of COVID-19: A brief look at potential therapeutic tactics ," Life Sci.
40. Boran Hao, Shahabeddin Sotudian. (2020) "Early prediction of level-of-care requirements in patients with COVID-19 ," eLife.
41. Yihui Huang, Liang Guo. (2021) "Serum Lactate Dehydrogenase Level as a Prognostic Factor for COVID-19: A Retrospective Study Based on a Large Sample Size ," Front Med (Lausanne).
42. Yong-Ping Zhu, Xiao-Ting Lv. (2020). "High serum lactate dehydrogenase and dyspnea: Positive predictors of adverse outcome in critical COVID-19 patients in Yichang ," World J Clin Cases. 5535-5546
43. Xiaokai Feng , Bin Zhu. (2021). "Correlation between white blood cell count at admission and mortality in COVID-19 patients: a retrospective study," BMC Infect Dis.
44. Ping Yang, Ye Tu. (2021) "Risk factors for mortality of critically ill patients with COVID-19 receiving invasive ventilation," International Journal of Medical Sciences. 1198-1206
45. J L Vincent, R Moreno. (1996). "The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine ," Intensive Care Med. 707-710
46. Stephen Trzeciak, Alan E. Jones. (2009). "The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation," Crit Care Med.1649-1654
47. Hassan Mansouritorghabeh, Mehrdad Rostami. (2020). "D-dimer level in COVID-19 infection: a systematic review," Expert Rev Hematol. 1265-1275.
48. Ayusha Poudel, Yashasa Poudel. (2021). "D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19," PLoS One.
49. Shailesh Advani, Ita Daryanti Saragih. (2021). "Frailty as a mortality predictor in older adults with COVID-19: A systematic review and meta-analysis of cohort studies ," Geriatr Nurs. 983-992
50. Alessandra Marengoni, Alberto Zucchelli. (2021). "Beyond Chronological Age: Frailty and Multimorbidity Predict In-Hospital Mortality in Patients With Coronavirus Disease," J Gerontol A Biol Sci Med Sci.38-45
51. Goyal P, Choi JJ. (2020). "Clinical Characteristics of Covid-19 in New York City ," N Engl J Med. 2372-2374
52. Matt Arentz, Eric Yim. (2020). "Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State ," Jama. 1612-1614.
53. Pavan K Bhatraju, Bijan J Ghassemieh. (2020). "Covid-19 in critically ill patients in the Seattle region—case series," New England Journal of Medicine. 2012-2022
54. Leonidas Palaiodimos, Damianos G. Kokkinidis. (2020). " Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York," Metabolism.
55. Gabrielle C Douglas, , Moira K O'Bryan. (2004). "The novel angiotensin-converting enzyme (ACE) homolog, ACE2, is selectively expressed by adult Leydig cells of the testis ," Endocrinology. 4703-4711
56. Jaillon S, Berthenet K. (2019). "Sexual dimorphism in innate immunity," Clin Rev Allergy Immunol. 308-321
57. Nanshan Chen, Min Zhou. (2020). "Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study". 507-513

58. Cynthia L Ogden, Tala H Fakhouri. (2017). "Prevalence of obesity among adults, by household income and education—United States," Morbidity and mortality weekly report.
59. Carlos Santos-Burgoa, William Dietz. (2020). "Obesity and its implications for COVID-19 mortality ," Obesity.
60. Jennifer Lighter, Sarah Hochman. (2020). "Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission ," Clinical Infectious Diseases. 896-897
61. Kevin Hur, Elizabeth L. Gray. (2020). "Factors Associated With Intubation and Prolonged Intubation in Hospitalized Patients With COVID-19," Otolaryngology– Head and Neck Surgery. 170-178
62. Welaia A. Alsaffar, Albatool A. (2022) Alwesaibi. "The Effectiveness of COVID-19 Vaccines in Improving the Outcomes of Hospitalized COVID-19 Patients".
63. J.Muthukrishnan, VasuVardhan. (2021) "Vaccination status and COVID-19 related mortality: A hospital based cross sectional study ," Medical Journal Armed Forces India. 278-282
64. Daniel E Speiser, Martin F Bachmann. (2020). "COVID-19: Mechanisms of Vaccination and Immunity ," Vaccines (Basel).
65. Jinyong Zhang , Hao Zeng. (2020). " Progress and Prospects on Vaccine Development against SARS-CoV-2 ," Vaccines (Basel).
66. Janaka Karalliedde, Antonella Corcillo. (2021). "Diabetic retinopathy is independently associated with increased risk of intubation: A single centre cohort study of patients with diabetes hospitalised with COVID-19 ," Diabetes Research and Clinical Practice.
67. Stephen Milne, Firoozeh V. Gerayeli. (2021). "COPD and the risk of poor outcomes in COVID-19: A systematic review and meta-analysis ," EClinicalMedicine.
68. Ebru Çakır Edis. (2020). "Chronic Pulmonary Diseases and COVID-19 ," Turk Thorac J. 345-349
69. Thales de Almeida Pinheiro, Antônio Sérgio Barcala-Jorge. (2017). "Obesity and malnutrition similarly alter the renin-angiotensin system and inflammation in mice and human adipose ," J Nutr Biochem. 74-82
70. Caroline Richard , Michael Wadowski. (2017). "Individuals with obesity and type 2 diabetes have additional immune dysfunction compared with obese individuals who are metabolically healthy," BMJ Open Diabetes Res Care.
71. Ahmed Abdalazim Dafallah Albashir. (2020). "The potential impacts of obesity on COVID-19 ," Clin Med (Lond). 109-113
72. George E Zakynthinos, Vasiliki Tsolaki. (2020). "Increased mortality among hypertensive COVID-19 patients: Pay a closer look on diuretics in mechanically ventilated patients ," Heart Lung. 894-895.
73. Jinjun Ran, Ying Song. (2020). "Blood pressure control and adverse outcomes of COVID-19 infection in patients with concomitant hypertension in Wuhan, China ," Hypertens Res. 1267-1276
74. Sahrai Saeed, Marijana Tadic. (2020). "Coronavirus disease 2019 and cardiovascular complications: focused clinical review," J Hypertens. 1282-1292
75. Fabio Angeli, Paolo Verdecchia. (2021). "Pharmacotherapy for hypertensive urgency and emergency in COVID-19 patients," Expert Opin Pharmacother, 1-8.

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