

Risk Factors of Severe Disease and Methods for Clinical Outcome Prediction in Patients with COVID-19 (Review)

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Факторы риска и методы прогнозирования клинического исхода COVID-19 (обзор)

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Summary

Large population studies using statistical analysis and mathematical computer modeling could be an effective tool in studying COVID-19. The use of prognostic scales developed using correlation of changes in clinical and laboratory parameters and morphological data, can help in early prediction of disease progression and identification of patients with high risk of unfavorable outcome.

Aim of the review. To assess the risk factors for severe course and unfavorable outcome of COVID-19 and to evaluate the existing tools for predicting the course and outcome of the novel coronavirus infection.

PubMed, Medline, and Google Scholar were searched for the relevant sources.

This review contains information on existing tools for assessing the prognosis and outcome of the disease, along with the brief data on the etiology, pathogenesis of the novel coronavirus infection and the known epidemiological, clinical and laboratory factors affecting its course.

Conclusion. It is essential to develop predictive models tailored to specific settings and capable of continuous monitoring of the situation and making the necessary adjustments. The discovery of new and more sensitive early markers and developing marker-based predictive assessment tools could significantly impact improving the outcomes of COVID-19.

Keywords: COVID-19; risk factors; prognostic tools

Conflict of interest. The authors declare no conflict of interest.

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Introduction

The COVID-19 pandemic is a global problem affecting many aspects of social life. It has already caused enormous social and economic damage, and according to WHO, several waves of increasing morbidity worldwide are predicted [1]. Studying the clinical and epidemiological features of the disease and its pathogenesis could help better predict the outcomes of the infection and develop effective measures for its prevention and treatment.

The causative agent of infection is SARS-CoV-2 RNA virus of the Betacoronavirus genus. SARS-CoV-2

has multiple target cells in the human body and there are several clinical phenotypes of the disease. In most cases, the disease presents as an acute respiratory infection and/or mild to moderate pneumonia, but in some patients the virus infection leads to the development of ARDS, disseminated intravascular coagulation syndrome, and multiple organ failure. The reason for various clinical variants of disease lies in the genetic variability of SARS-CoV-2, individual characteristics of the patient's response to the infection, initial patient's status and many other factors affecting the pathological process.

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The use of prognostic scales based on correlation between changes in clinical and laboratory parameters and morphology can help in timely prediction of disease severity and selection of patients at high risk of unfavorable outcome.

The aim of this review was to assess risk factors for severe disease and adverse outcome of COVID-19, as well as current tools for predicting severity and outcome of novel coronavirus infection.

Sources were searched in PubMed, Medline, and Google Scholar databases. Key words searched were: «COVID-19», «SARS-CoV-2», «Betacoronavirus», «COVID-19 risk factors», «COVID-19 comorbidities», «COVID-19 prognosis», «COVID-19 outcome prognosis», «COVID-19 ICU», «mortality», «death». Of the more than 300 initially selected literature sources, 80 were included in the review, of them 78 sources were published within the last two years (2020–2021).

Targets and Manifestations of Viral Damage

The key factors influencing the severity of COVID-19 are the viral load and the characteristics of the patient's immune response [2]. Systemic inflammatory response of the body leading to organ damage plays the main role in the pathogenesis. Myocarditis [3–5], disorders of lungs [6], liver [7–9], kidneys [10, 11], nervous system [12, 13], skin [14–16] and other organs resulting from viral and/or autoimmune damage have been described in literature. Severe coronavirus infection is associated with the development of DIC with generalized endotheliitis [2] and multiple organ failure.

Lung damage manifested as pneumonia (in some cases associated with ARDS) is most common in COVID-19. In SARS-CoV-2 ARDS, as in ARDS of other etiologies [17, 18], several subtypes, hypo- and hyperinflammatory, were identified [19]. In a prospective observational study by Sinha P. et al. [20], the hyperinflammatory subtype was characterized by higher values of ferritin, lactate dehydrogenase (LDH), and mortality, although the differences in these parameters were not significant due to the small sample size (only 39 patients).

Pathological examination of pulmonary tissue of patients who died from COVID-19 revealed diffuse alveolar damage, microcirculatory disturbances, thrombosis of pulmonary artery branches [21]. High cytokine blood concentration during disease correlated with elevated levels of pyroptosis and apoptosis on post-mortem microscopic examination [22].

Risk Factors

This review outlines the risk factors studied in patient populations only with a confirmed diagnosis of COVID-19 by detecting RNA or viral proteins

in patient tissues *in vivo* or during pathological examination.

Given the possible heterogeneity of patient populations and different predominant factors in each of them, there are studies investigating both the general patient population [23] and separately populations of patients treated in the intensive care unit [24], patients with cancer [25], asthma [26], diabetes mellitus [27], obesity [28], and elderly [29] and pediatric patients [30]. In most studies, the groups consisted of non-survivors. The factors influencing admission to hospital [31] or ICU [32], as well as the need for mechanical lung ventilation [33] were also evaluated.

The main factors increasing the risk of mortality in the general population were various comorbidities, such as diabetes mellitus, obesity, hypertension, chronic heart, lung, liver, kidney diseases, and dementia. These factors have been identified from several meta-analyses and retrospective studies, the largest sample being 20,133 patients [34–37]. Several retrospective studies had shown that Charlson comorbidity index, which correlated well with mortality in the general population of patients with COVID-19, could be an integral tool for assessing comorbidities and their severity [38–40]. Male gender was associated with an increased risk of death in most studies [41]. Although an older age has been considered a risk factor for complicated COVID-19 in numerous studies [42–44], in a meta-analysis Starke K. et al. [45] have reported that age is a confounder but not an independent mortality risk factor. With advancing age the comorbidities are naturally increasing that contribute to the development of severe disease.

Among the parameters assessed in patients with confirmed novel coronavirus infection on hospital admission, mortality was significantly affected by the following (based on several retrospective cohort studies and meta-analyses, involving from 63 to 16100 patients): extent of lung involvement on CT [46, 47], elevated D-dimer [48] level, leukocytosis, leukopenia [49], low platelet count [50], high C-reactive protein (CRP) [51], LDH [52], ferritin [53], low CD4 and CD8 cell counts [49].

Treatment and observation in the ICU were required in 6–32.3% of cases [44, 41, 54, 55]. Patients treated in the intensive care unit are a special population that should be examined separately. The patients in the ICU are closely and regularly monitored, and the range of parameters measured is often much broader.

As in the general population, various chronic comorbidities in the ICU patients significantly influenced mortality. Male gender and older age were also associated with increased mortality in COVID-19 [24].

Lung injury with the development of ARDS-like syndrome was the main reason for ICU admission for respiratory support. An extremely low oxygenation index ($\text{PaO}_2/\text{FiO}_2$) on admission to ICU, mostly less than 100, as well as high alveolar-arterial difference were significant factors increasing mortality [24, 54, 55]. Mechanical lung ventilation per se was not a factor associated with mortality [56]. There are studies describing phenotypes of lung injury in patients with COVID-19 on mechanical ventilation [57, 58]. The presence of atelectasis, low pulmonary compliance and reduced alveolar recruitment are attributed to advanced lung damage, and this phenotype is considered to be more severe. Elevation of PEEP necessary to increase gas exchange area leads to the elevated risk of barotrauma [59, 60]. Grasselli G. et al. [61] demonstrated association between high PEEP and increased mortality.

Plasma levels of interleukin-6 (IL-6), IL-1, IL-8, tumor necrosis factor- α , interferon- γ , and α 1-antitrypsin were elevated in ICU patients who developed organ dysfunction [62]. High IL-6 and low α 1-antitrypsin were related to an increased risk of death [62].

The hypothesis of SARS CoV 2-associated endotheliitis development was confirmed by a significant increase in endothelial damage markers in patients with severe disease. Goshua G. et al. [63] showed a significant difference in plasma levels of von Willebrand factor, P-selectin and thrombomodulin in ICU patients compared to non-ICU patients. High levels of the above markers were associated with increased mortality.

Prognostic tools. The need to rapidly and accurately assess the patient's condition and predict the outcome of the disease prompted researchers to create prognostic tools. In the early period of the epidemic, patients were assessed using the existing qSOFA, APACHE II, PSI, SMART-COP, CURB-65, MuLBSTA, NEWS scales [64]. A study by Garcia-Clemente M. [65] showed that PSI and CURB-65 scales were the most accurate in predicting death in patients with SARS-CoV-2-induced pneumonia. Other researchers [66] showed the applicability of previously developed Clinical Frailty Scale (CFS) to assess the risk of fatal outcome and mechanical ventilation. Jang J. et al. [67] demonstrated the advantage of NEWS scale over qSOFA and SIRS scales to assess risk of ICU hospitalization and 28-day mortality. Kostakis I. et al. [68] recommend using the NEWS and NEWS2 scales to assess the risk of clinical deterioration in patients with COVID-19.

Later on, the growing body of evidence has led to creation of specific scales. In the largest study by Knight S. et al. [69], which included 35,463 patients from the general population, 8 variables (age, sex, number of comorbidities, respiratory rate, SpO_2 , level of consciousness, levels of urea, C-reactive

protein) affecting mortality were identified ($\text{AUC}=0.79$ with 95%CI, 0.78–0.79).

Another study [70] included 1590 patients from the general population who had severe disease, i.e., hospitalization in ICU, the need for mechanical ventilation or fatal outcome. The created scale included 10 parameters (chest radiographic abnormality, age, history of lung bleeding, dyspnea, level of consciousness, number of comorbidities, presence of cancer, neutrophil-to-lymphocyte ratio, LDH, direct bilirubin) with $\text{AUC}=0.88$, CI: 0.85–0.91. Covino M. et al. [71], comparing various predicting tools, reported the above-mentioned scales [69, 70] as the most accurate.

Yuan Y. et al. [72] evaluated several dozens of risk factors of poor prognosis and selected three most significant ones including LDH level, CRP concentration, and lymphocyte percentage. These parameters were included in a validated prognostic scale that allows to stratify all the admitted patients into three risk groups. A total of 1,479 patients from the general population participated in the study. The authors report sensitivity of over 90% with $\text{AUC}=0.96$.

In a similar study [73] based on the data of 2529 patients, the authors proposed a prognostic scale allowing to classify the admitted patients into high and low risk groups. The scale included such parameters as age, history of chronic coronary heart disease, D-dimer, procalcitonin and percentage of lymphocytes (AUC 0.92; $P=0.26$).

A. Vaid et al. [74] used machine learning to develop a model predicting the probability of fatal outcome or a critical event (tracheal intubation, ICU admission, transfer to hospice) on days 3, 5, 7, 10. Clinical and laboratory data from 3715 patients obtained within the first 36 hours of hospitalization were used for training, and the model was validated on 383 patients. The most significant drivers for critical event prediction were acute kidney injury, LDH level, respiratory rate, glucose level (both high and low), systolic and diastolic blood pressure, blood pH value, total protein, CRP, and D-dimer level. Age, anion gap, CRP, LDH, SpO_2 , urea, ferritin, lactate, red blood cell distribution width, and diastolic pressure were important for prediction of mortality.

G. Wu et al. [75] used data from 725 patients to develop a model predicting the risk of extremely severe course of COVID-19 for groups of symptomatic and asymptomatic patients, both with positive PCR test. If laboratory results and a lung CT scan were available, these data were also added. Parameters used in the model included age, hospital employment (working with COVID-19 patients), body temperature, time of onset to admission, chest CT lesion range, percentage of lymphocytes, and blood levels of CRP, LDH, urea, creatine kinase, and total calcium. The AUC increased from 0.74 to 0.86 since more patient data became available).

In a study [76], the authors developed a mortality risk assessment scale on days 7 and 14. The study used data from 931 patients. Statistical analysis was used to select 4 most significant clinical and laboratory parameters such as age, mean blood pressure, kidney injury (stage 2 or higher according to KDIGO AKI), and severe hypoxia (SpO₂ below 90%, respiratory support more than 4 liters of oxygen per minute, noninvasive/invasive lung ventilation). The AUC was 0.86 for 7-day mortality and 0.83 for 14-day mortality. When validated using data from 265 patients, the AUC for 7- and 14-day mortality assessments was 0.85 and 0.83, respectively.

Jiao G. et al. [77] proposed a nomogram determining the risk of extremely severe disease based on 7 parameters: age, LDH, CRP, direct bilirubin, albumin, urea levels, and RBC distribution width. The study involved 372 patients, sensitivity of the nomogram was 85.7%, specificity was 87.6%.

Haimovich A. et al. [78] developed a simple scale to assess the probability of respiratory failure in the next 24 hours. The study involved 1,172 patients. The scale included only three parameters: respiratory rate, SpO₂ and inhaled oxygen flow with AUC=0.81, CI: 0.73–0.89.

The team of Zhang C. et al. [79], using the parameters of 80 patients, developed a prognostic scale to assess the risk of invasive ventilation and death. The scale included patient age, white blood cell count, neutrophil count, glomerular filtration rate, and myoglobin level. The researchers reported 70.8% sensitivity and 89.3% specificity of prognosis made using this scale.

References

1. WHO 2021.02. COVID-19 strategic preparedness and response plan. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/strategies-and-plans>.
2. Maggi E., Canonica G.W., Moretta L. COVID-19: Unanswered questions on immune response and pathogenesis. *J Allergy Clin Immunol.* 2020; 146 (1): 18–22. DOI: 10.1016/j.jaci.2020.05.001. PMID: 32389590.
3. Siripanthong B., Nazarian S., Muser D., Deo R., Santangeli P., Khanji M.Y., Cooper L.T. Jr, Chahal C.A.A. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm.* 2020; 17 (9): 1463–1471. DOI: 10.1016/j.hrthm.2020.05.001. PMID: 32387246.
4. Bearse M., Hung Y.P., Krauson A.J., Bonanno L., Boyraz B., Harris C.K., Helland T.L., Hilburn C.E., Hutchison B., Jobbagy S., Marshall M.S., Shepherd D.J., Villalba J.A., Delfino I., Mendez-Pena J., Chebib I., Newton-Cheh C., Stone J.R. Factors associated with myocardial SARS-CoV-2 infection, myocarditis, and cardiac inflammation in patients with COVID-19. *Mod Pathol.* 2021; 34 (7): 1345–1357. DOI: 10.1038/s41379-021-00790-1. PMID: 33727695.
5. Sala S., Peretto G., Gramegna M., Palmisano A., Villatore A., Vignale D., De Cobelli F., Tresoldi M., Cappelletti A.M., Basso C., Godino C., Esposito A. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J.* 2020; 41 (19): 1861–1862. DOI: 10.1093/eurheartj/ehaa286. PMID: 32267502; PMCID: PMC7184339.
6. Torres Acosta M.A., Singer B.D. Pathogenesis of COVID-19-induced ARDS: implications for an ageing population. *Eur*

Prognostic tools are a good aid to the attending physician in making care decisions. Currently, based on statistical analysis and machine learning, a large number of prognostic scales, nomograms, and computer models have been developed around the world that allow predicting the outcome with varying accuracy. However, it is unclear whether these models are universal. Futoma J. and Simons M. believe that prognostic tools should be used in specific places, at specific times, and in specific patient populations, giving the ever-changing treatment guidelines, differences in resources between health care systems, demographic, phenotypic, genetic characteristics of patient populations, etc. as a rationale [80]. This suggests the need to develop prognostic models tailored to specific circumstances, with continuous monitoring of the situation and necessary adjustments.

Unfortunately, many factors that significantly correlate with an adverse outcome are markers of both existing organ damage and organ failure.

Conclusion

There is a need to develop prognostic models tailored to specific circumstances with continuous monitoring of the situation and the possibility of making adjustments if necessary. The discovery of new markers that are more sensitive in the early stages of the disease and developing biomarker-based prognostic tools could significantly improve the outcomes of COVID-19.

- Respir J.* 2020; 56 (3): 2002049. DOI: 10.1183/13993003.02049-2020. PMID: 32747391.
7. Cichoż-Lach H., Michalak A. Liver injury in the era of COVID-19. *World J Gastroenterol.* 2021; 27 (5): 377–390. DOI: 10.3748/wjg.v27.i5.377. PMID: 33584070.
8. Alqahtani S.A., Schattenberg J.M. Liver injury in COVID-19: The current evidence. *United European Gastroenterol J.* 2020; 8 (5): 509–519. DOI: 10.1177/2050640620924157. PMID: 32450787.
9. Lizardo-Thiebaud M.J., Cervantes-Alvarez E., Limon-de la Rosa N., Tejeda-Dominguez E., Palacios-Jimenez M., Méndez-Guerrero O., Delaey-Martinez M., Rodriguez-Alvarez E., Romero-Morales B., Liu W.H., Huang C.A., Kershenovich D., Navarro-Alvarez N. Direct or Collateral Liver Damage in SARS-CoV-2-Infected Patients. *Semin Liver Dis.* 2020; 40 (3): 321–330. DOI: 10.1055/s-0040-1715108. Epub 2020 Sep 4. PMID: 32886936.
10. Gagliardi I., Patella G., Michael A., Serra R., Provenzano M., Andreucci M. COVID-19 and the Kidney: From Epidemiology to Clinical Practice. *J Clin Med.* 2020; 9 (8): 2506. DOI: 10.3390/jcm9082506. PMID: 32759645.
11. Ng J.H., Bijol V., Sparks M.A., Sise M.E., Izzedine H., Jhaveri K.D. Pathophysiology and Pathology of Acute Kidney Injury in Patients With COVID-19. *Adv Chronic Kidney Dis.* 2020; 27 (5): 365–376. DOI: 10.1053/j.ackd.2020.09.003. Epub 2020 Oct 20. PMID: 33308501.
12. Iadecola C., Anrather J., Kamel H. Effects of COVID-19 on the Nervous System. *Cell.* 2020; 183 (1): 16–27.e1. DOI: 10.1016/j.cell.2020.08.028. Epub 2020 Aug 19. PMID: 32882182.
13. Sharifian-Dorche M., Huot P., Osheroov M., Wen D., Saveriano A., Giacomini P.S., Antel J.P., Mowla A. Neurological complications of coronavirus infection; a comparative review and

- lessons learned during the COVID-19 pandemic. *J Neurol Sci*. 2020 Oct 15; 417: 117085. DOI: 10.1016/j.jns.2020.117085. Epub 2020 Aug 7. PMID: 32871412.
14. Catalá Gonzalo A., Galván Casas C. COVID-19 and the Skin. *Actas Dermosifiliogr*. 2020; 111 (6): 447–449. DOI: 10.1016/j.ad.2020.04.007. Epub 2020 May 13. PMID: 32401723.
 15. Novak N., Peng W., Naegeli M.C., Galvan C., Kolm-Djamei I., Brügggen C., Cabanillas B., Schmid-Grendelmeier P., Catala A. SARS-CoV-2, COVID-19, skin and immunology — What do we know so far? *Allergy*. 2021; 76 (3): 698–713. DOI: 10.1111/all.14498. Epub 2020 Aug 12. PMID: 32658359.
 16. Gisondi P., Plaserico S., Bordin C., Alaibac M., Girolomoni G., Naldi L. Cutaneous manifestations of SARS-CoV-2 infection: a clinical update. *J Eur Acad Dermatol Venereol*. 2020; 34 (11): 2499–2504. DOI: 10.1111/jdv.16774. Epub 2020 Jul 20. PMID: 32585074.
 17. Shankar-Hari M., Fan E., Ferguson N.D. Acute respiratory distress syndrome (ARDS) phenotyping. *Intensive Care Med*. 2019; 45 (4): 516–519. DOI: 10.1007/s00134-018-5480-6. Epub 2018 Dec 5. PMID: 30519902.
 18. Calfee C.S., Delucchi K.L., Sinha P., Matthay M.A., Hackett J., Shankar-Hari M., McDowell C., Laffey J.G., O'Kane C.M., McAuley D.E.; Irish Critical Care Trials Group. Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. *Lancet Respir Med*. 2018; 6 (9): 691–698. DOI: 10.1016/S2213-2600(18)30177-2. Epub 2018 Aug 2. PMID: 30078618.
 19. Lin S.H., Zhao Y.S., Zhou D.X., Zhou F.C., Xu F. Coronavirus disease 2019 (COVID-19): cytokine storms, hyper-inflammatory phenotypes, and acute respiratory distress syndrome. *Genes Dis*. 2020; 7 (4): 520–527. DOI: 10.1016/j.gendis.2020.06.009. Epub 2020 Jun 29. PMID: 32837983.
 20. Sinha P., Calfee C.S., Cherian S., Brealey D., Cutler S., King C., Killick C., Richards O., Cheema Y., Bailey C., Reddy K., Delucchi K.L., Shankar-Hari M., Gordon A.C., Shyamsundar M., O'Kane C.M., McAuley D.E., Szakmany T. Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: a prospective observational study. *Lancet Respir Med*. 2020; 8 (12): 1209–1218. DOI: 10.1016/S2213-2600(20)30366-0. Epub 2020 Aug 27. PMID: 32861275.
 21. Calabrese E., Pezzuto F., Fortarezza F., Hofman P., Kern I., Panizo A., von der Thüsen J., Timofeev S., Gorkiewicz G., Lunardi F. Pulmonary pathology and COVID-19: lessons from autopsy. The experience of European Pulmonary Pathologists. *Virchows Arch*. 2020; 477 (3): 359–372. DOI: 10.1007/s00428-020-02886-6. Epub 2020 Jul 9. PMID: 32642842.
 22. Li S., Jiang L., Li X., Lin F., Wang Y., Li B., Jiang T., An W., Liu S., Liu H., Xu P., Zhao L., Zhang L., Mu J., Wang H., Kang J., Li Y., Huang L., Zhu C., Zhao S., Lu J., Ji J., Zhao J. Clinical and pathological investigation of patients with severe COVID-19. *JCI Insight*. 2020; 5 (12): e138070. DOI: 10.1172/jci.insight.138070. PMID: 32427582.
 23. Zhou F., Yu T., Du R., Fan G., Liu Y., Liu Z., Xiang J., Wang Y., Song B., Gu X., Guan L., Wei Y., Li H., Wu X., Xu J., Tu S., Zhang Y., Chen H., Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020; 395 (10229): 1054–1062. DOI: 10.1016/S0140-6736(20)30566-3. Epub 2020 Mar 11. Erratum in: *Lancet*. 2020; 395 (10229): 1038. Erratum in: *Lancet*. 2020 Mar 28; 395 (10229): 1038. PMID: 32171076.
 24. Grasselli G., Greco M., Zanella A., Albano G., Antonelli M., Bellani G., Bonanomi E., Cabrini L., Carlesso E., Castelli G., Cattaneo S., Cereda D., Colombo S., Coluccello A., Crescini G., Forastieri Molinari A., Foti G., Fumagalli R., Iotti G.A., Langer T., Latronico N., Lorini F.L., Mojoli F., Natalini G., Pessina C.M., Ranieri V.M., Rech R., Scudeller L., Rosano A., Storti E., Thompson B.T., Tirani M., Villani P.G., Pesenti A., Cecconi M.; COVID-19 Lombardy ICU Network. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA Intern Med*. 2020; 180 (10): 1345–1355. DOI: 10.1001/jamainternmed.2020.3539. PMID: 32667669.
 25. Giannakoulis V.G., Papoutsis E., Siempos I.I. Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data. *JCO Glob Oncol*. 2020; 6: 799–808. DOI: 10.1200/GO.20.00225. PMID: 32511066.
 26. Beaney T., Salman D., Samee T., Mak V. Assessment and management of adults with asthma during the COVID-19 pandemic. *BMJ*. 2020; 369: m2092. DOI: 10.1136/bmj.m2092. PMID: 32513811.
 27. Huang I., Lim M.A., Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia — A systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr*. 2020; 14 (4): 395–403. DOI: 10.1016/j.dsx.2020.04.018. Epub 2020 Apr 17. PMID: 32334395.
 28. Hussain A., Mahawar K., Xia Z., Yang W., El-Hasani S. Obesity and mortality of COVID-19. Meta-analysis. *Obes Res Clin Pract*. 2020; 14 (4): 295–300. DOI: 10.1016/j.orcp.2020.07.002. Epub 2020 Jul 9. Retraction in: *Obes Res Clin Pract*. 2021 Jan-Feb; 15 (1): 100. PMID: 32660813.
 29. Lee J.Y., Kim H.A., Huh K., Hyun M., Rhee J.Y., Jang S., Kim J.Y., Peck K.R., Chang H.H. Risk Factors for Mortality and Respiratory Support in Elderly Patients Hospitalized with COVID-19 in Korea. *J Korean Med Sci*. 2020; 35 (23): e223. DOI: 10.3346/jkms.2020.35.e223. PMID: 32537957.
 30. Shekerdemian L.S., Mahmood N.R., Wolfe K.K., Riggs B.J., Ross C.E., McKiernan C.A., Heidemann S.M., Kleinman L.C., Sen A.I., Hall M.W., Priestley M.A., McGuire J.K., Boukas K., Sharron M.P., Burns J.P.; International COVID-19 PICU Collaborative. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. *JAMA Pediatr*. 2020; 174 (9): 868–873. DOI: 10.1001/jamapediatrics.2020.1948. PMID: 32392288.
 31. Petrilli C.M., Jones S.A., Yang J., Rajagopalan H., O'Donnell L., Chernyak Y., Tobin K.A., Cerfolio R.J., Francois F., Horwitz L.I. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020; 369: m1966. DOI: 10.1136/bmj.m1966. PMID: 32444366.
 32. Zhao Z., Chen A., Hou W., Graham J.M., Li H., Richman P.S., Thode H.C., Singer A.J., Duong T.Q. Prediction model and risk scores of ICU admission and mortality in COVID-19. *PLoS One*. 2020; 15 (7): e0236618. DOI: 10.1371/journal.pone.0236618. PMID: 32730358.
 33. Patel U., Malik P., Usman M.S., Mehta D., Sharma A., Malik F.A., Khan N., Siddiqi T.J., Ahmed J., Patel A., Sacks H. Age-Adjusted Risk Factors Associated with Mortality and Mechanical Ventilation Utilization Amongst COVID-19 Hospitalizations—a Systematic Review and Meta-Analysis. *SN Compr Clin Med*. 2020; 29: 1–10. DOI: 10.1007/s42399-020-00476-w. Epub ahead of print. PMID: 32904541.
 34. Gao Y.D., Ding M., Dong X., Zhang J.J., Kursat Azkur A., Azkur D., Gan H., Sun Y.L., Fu W., Li W., Liang H.L., Cao Y.Y., Yan Q., Cao C., Gao H.Y., Brügggen M.C., van de Veen W., Sokolowska M., Akdis M., Akdis C.A. Risk factors for severe and critically ill COVID-19 patients: A review. *Allergy*. 2021; 76 (2): 428–455. DOI: 10.1111/all.14657. Epub 2020 Dec 4. PMID: 33185910.
 35. Jordan R.E., Adab P., Cheng K.K. Covid-19: risk factors for severe disease and death. *BMJ*. 2020; 368: m1198. DOI: 10.1136/bmj.m1198. PMID: 32217618.
 36. Parohan M., Yaghoubi S., Seraji A., Javanbakht M.H., Sarraf P., Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. *Aging Male*. 2020; 23 (5): 1416–1424. DOI: 10.1080/13685538.2020.1774748. Epub 2020 Jun 8. PMID: 32508193.
 37. Indini A., Rijavec E., Ghidini M., Cattaneo M., Grossi F. Developing a risk assessment score for patients with cancer during the coronavirus disease 2019 pandemic. *Eur J Cancer*.

- 2020; 135: 47–50. DOI: 10.1016/j.ejca.2020.05.017. Epub 2020 May 31. PMID: 32534244; PMCID: PMC7261437.
38. Price-Haywood E.G., Burton J., Fort D., Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. *N Engl J Med.* 2020; 382 (26): 2534–2543. DOI: 10.1056/NEJMsa2011686. Epub 2020 May 27. PMID: 32459916.
39. Imam Z., Odish F., Gill L., O'Connor D., Armstrong J., Vanood A., Iboronke O., Hanna A., Ranski A., Halalau A. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. *J Intern Med.* 2020; 288 (4): 469–476. DOI: 10.1111/joim.13119. Epub 2020 Jun 22. PMID: 32498135.
40. Varol Y., Hakoglu B., Kadri Cirak A., Polat G., Komurcuoglu B., Akkol B., Atasoy C., Bayramic E., Balci G., Ataman S., Ermin S., Yalniz E.; COVID Study Group. The impact of charlson comorbidity index on mortality from SARS-CoV-2 virus infection and A novel COVID-19 mortality index: CoLACD. *Int J Clin Pract.* 2021; 75 (4): e13858. DOI: 10.1111/ijcp.13858. Epub 2020 Dec 7. PMID: 33237615.
41. Docherty A.B., Harrison E.M., Green C.A., Hardwick H.E., Pius R., Norman L., Holden K.A., Read J.M., Dondelinger F., Carson G., Merson L., Lee J., Plotkin D., Sigfrid L., Halpin S., Jackson C., Gamble C., Horby P.W., Nguyen-Van-Tam J.S., Ho A., Russell C.D., Dunning J., Openshaw P.J., Baillie J.K., Sempile M.G.; ISARIC4C investigators. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ.* 2020; 369: m1985. DOI: 10.1136/bmj.m1985. PMID: 32444460.
42. Chen L., Yu J., He W., Chen L., Yuan G., Dong F., Chen W., Cao Y., Yang J., Cai L., Wu D., Ran Q., Li L., Liu Q., Ren W., Gao F., Wang H., Chen Z., Gale R.P., Li Q., Hu Y. Risk factors for death in 1859 subjects with COVID-19. *Leukemia.* 2020; 34 (8): 2173–2183. DOI: 10.1038/s41375-020-0911-0. Epub 2020 Jun 16. PMID: 32546725.
43. Sousa G.J.B., Garces T.S., Cestari V.R.F., Florêncio R.S., Moreira T.M.M., Pereira M.L.D. Mortality and survival of COVID-19. *Epidemiol Infect.* 2020; 148: e123. DOI: 10.1017/S0950268820001405. PMID: 32580809.
44. Munblit D., Nekliudov N.A., Bugaeva P., Blyuss O., Kislova M., Listovskaya E., Gamirova A., Shikhaleva A., Belyaev V., Timashev P., Warner J.O., Comberlati P., Apfelbacher C., Bezrukov E., Politov M.E., Yavorovskiy A., Bulanova E., Tsareva N., Avdeev S., Kapustina V.A., Pigolkin Y.I., Dankwa E.A., Kartsonaki C., Pritchard M.G., Victor F., Svistunov A.A., Butnaru D., Glybochko P. *StopCOVID cohort*. An observational study of 3,480 patients admitted to the Sechenov University hospital network in Moscow city for suspected COVID-19 infection. *Clin Infect Dis.* 2021; 73 (1): 1–11. PMID: 33035307 PMCID: PMC7665333 DOI: 10.1093/cid/ciaa1535.
45. Romero Starke K., Petereit-Haack G., Schubert M., Kämpf D., Schliebner A., Hegewald J., Seidler A. The Age-Related Risk of Severe Outcomes Due to COVID-19 Infection: A Rapid Review, Meta-Analysis, and Meta-Regression. *Int J Environ Res Public Health.* 2020; 17 (16): 5974. DOI: 10.3390/ijerph17165974. PMID: 32824596.
46. Büttner L., Aigner A., Fleckenstein E.N., Hamper C.M., Jonczyk M., Hamm B., Scholz O., Böning G. Diagnostic Value of Initial Chest CT Findings for the Need of ICU Treatment/Intubation in Patients with COVID-19. *Diagnostics (Basel).* 2020; 10 (11): 929. DOI: 10.3390/diagnostics10110929. PMID: 33182695.
47. Sabri A., Davarpanah A.H., Mahdavi A., Abrishami A., Khazaei M., Heydari S., Asgari R., Nekooghadam S.M., Dobrowski J., Taheri M.S. Novel coronavirus disease 2019: predicting prognosis with a computed tomography-based disease severity score and clinical laboratory data. *Pol Arch Intern Med.* 2020; 130 (7–8): 629–634. DOI: 10.20452/pamw.15422. Epub 2020 Jun 5. PMID: 32500700.
48. Zhou Y., Yang Q., Chi J., Dong B., Lv W., Shen L., Wang Y. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. *Int J Infect Dis.* 2020; 99: 47–56. DOI: 10.1016/j.ijid.2020.07.029. Epub 2020 Jul 25. PMID: 32721533.
49. Elshazli R.M., Toraih E.A., Elgaml A., El-Mowafy M., El-Mesery M., Amin M.N., Hussein M.H., Killackey M.T., Fawzy M.S., Kandil E. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: A meta-analysis of 6320 patients. *PLoS One.* 2020; 15 (8): e0238160. DOI: 10.1371/journal.pone.0238160. PMID: 32822430.
50. Wool G.D., Miller J.L. The Impact of COVID-19 Disease on Platelets and Coagulation. *Pathobiology.* 2021; 88 (1): 15–27. DOI: 10.1159/000512007. Epub 2020 Oct 13. PMID: 33049751.
51. Tan C., Huang Y., Shi F., Tan K., Ma Q., Chen Y., Jiang X., Li X. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. *J Med Virol.* 2020; 92 (7): 856–862. DOI: 10.1002/jmv.25871. Epub 2020 Apr 25. PMID: 32281668.
52. Zhang J.J.Y., Lee K.S., Ang L.W., Leo Y.S., Young B.E. Risk Factors for Severe Disease and Efficacy of Treatment in Patients Infected With COVID-19: A Systematic Review, Meta-Analysis, and Meta-Regression Analysis. *Clin Infect Dis.* 2020; 71 (16): 2199–2206. DOI: 10.1093/cid/ciaa576. PMID: 32407459.
53. Henry B.M., de Oliveira M.H.S., Benoit S., Plebani M., Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. *Clin Chem Lab Med.* 2020; 58 (7): 1021–1028. DOI: 10.1515/cclm-2020-0369. PMID: 32286245.
54. Petrilli C.M., Jones S.A., Yang J., Rajagopalan H., O'Donnell L., Chernyak Y., Tobin K.A., Cerfolio R.J., Francois F., Horwitz L.I. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ.* 2020; 369: m1966. DOI: 10.1136/bmj.m1966. PMID: 32444366.
55. Rodriguez-Nava G., Yanez-Bello M.A., Trelles-Garcia D.P., Chung C.W., Friedman H.J., Hines D.W. Performance of the quick COVID-19 severity index and the Brescia-COVID respiratory severity scale in hospitalized patients with COVID-19 in a community hospital setting. *Int J Infect Dis.* 2021; 102: 571–576. DOI: 10.1016/j.ijid.2020.11.003. Epub 2020 Nov 9. PMID: 33181332.
56. Hernandez-Romieu A.C., Adelman M.W., Hockstein M.A., Robichaux C.J., Edwards J.A., Fazio J.C., Blum J.M., Jabaley C.S., Caridi-Scheible M., Martin G.S., Murphy D.J., Auld S.C.; Emory COVID-19 Quality and Clinical Research Collaborative. Timing of Intubation and Mortality Among Critically Ill Coronavirus Disease 2019 Patients: A Single-Center Cohort Study. *Crit Care Med.* 2020; 48 (11): e1045–e1053. DOI: 10.1097/CCM.0000000000004600. PMID: 32804790.
57. Gattinoni L., Chiumello D., Caironi P., Busana M., Romitti F., Brazzi L., Camporota L. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med.* 2020; 46 (6): 1099–1102. DOI: 10.1007/s00134-020-06033-2. Epub 2020 Apr 14. PMID: 32291463.
58. Robba C., Battaglini D., Ball L., Patroniti N., Loconte M., Brunetti I., Vena A., Giacobbe D.R., Bassetti M., Rocco P.R.M., Pelosi P. Distinct phenotypes require distinct respiratory management strategies in severe COVID-19. *Respir Physiol Neurobiol.* 2020; 279: 103455. DOI: 10.1016/j.resp.2020.103455. Epub 2020 May 11. PMID: 32437877.
59. Walkey A.J., Del Sorbo L., Hodgson C.L., Adhikari N.K.J., Wunsch H., Meade M.O., Ulerik E., Hess D., Talmor D.S., Thompson B.T., Brower R.G., Fan E. Higher PEEP versus Lower PEEP Strategies for Patients with Acute Respiratory Distress Syndrome: A Systematic Review and Meta-Analysis. *Ann Am Thorac Soc.* 2017; 14 (Supplement 4): S297–S303. DOI: 10.1513/AnnalsATS.201704-338OT. PMID: 29043834.
60. Nieman G.F., Satalin J., Andrews P., Aiash H., Habashi N.M., Gatto L.A. Personalizing mechanical ventilation according to physiologic parameters to stabilize alveoli and minimize ventilator induced lung injury (VILI). *Intensive Care Med Exp.*

- 2017; 5 (1): 8. DOI: 10.1186/s40635-017-0121-x. Epub 2017 Feb 2. PMID: 28150228; PMCID: PMC5289131.
61. Grasselli G., Greco M., Zanella A., Albano G., Antonelli M., Bellani G., Bonanomi E., Cabrini L., Carlesso E., Castelli G., Cattaneo S., Cereda D., Colombo S., Coluccello A., Crescini G., Forastieri Molinari A., Foti G., Fumagalli R., Iotti G.A., Langer T., Latronico N., Lorini F.L., Mojoli F., Natalini G., Pessina C.M., Ranieri V.M., Rech R., Scudeller L., Rosano A., Storti E., Thompson B.T., Tirani M., Villani P.G., Pesenti A., Cecconi M.; COVID-19 Lombardy ICU Network. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA Intern Med.* 2020; 180 (10): 1345–1355. DOI: 10.1001/jamainternmed.2020.3539. PMID: 32667669.
 62. McElvaney O.J., McEvoy N.L., McElvaney O.E., Carroll T.P., Murphy M.P., Dunlea D.M., Ni Choileáin O., Clarke J., O'Connor E., Hogan G., Ryan D., Sulaiman I., Gunaratnam C., Branagan P., O'Brien M.E., Morgan R.K., Costello R.W., Hurley K., Walsh S., de Barra E., McNally C., McConkey S., Boland F., Galvin S., Kiernan E., O'Rourke J., Dwyer R., Power M., Geoghegan P., Larkin C., O'Leary R.A., Freeman J., Gaffney A., Marsh B., Curley G.F., McElvaney N.G. Characterization of the Inflammatory Response to Severe COVID-19 Illness. *Am J Respir Crit Care Med.* 2020; 202 (6): 812–821. DOI: 10.1164/rccm.202005-1583OC. PMID: 32584597.
 63. Goshua G., Pine A.B., Meizlish M.L., Chang C.H., Zhang H., Bahel P., Baluha A., Bar N., Bona R.D., Burns A.J., Dela Cruz C.S., Dumont A., Halene S., Hua J., Koff J., Menninger H., Neparidze N., Price C., Siner J.M., Tormey C., Rinder H.M., Chun H.J., Lee A.I. Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study. *Lancet Haematol.* 2020; 7 (8): e575–e582. DOI: 10.1016/S2352-3026(20)30216-7. Epub 2020 Jun 30. PMID: 32619411.
 64. Steinberg E., Balakrishna A., Habboushe J., Shaol A., Lee J. Calculated decisions: COVID-19 calculators during extreme resource-limited situations. *Emerg Med Pract.* 2020; 22 (4 Suppl): CD1-CD5. PMID: 32259419.
 65. García Clemente M.M., Herrero Huertas J., Fernández Fernández A., De La Escosura Muñoz C., Enríquez Rodríguez A.I., Pérez Martínez L., Gómez Mañas S., Iscar Urrutia M., López González F.J., Madrid Carbajal C.J., Bedate Díaz P., Arias Guillén M., Bailón Cuadrado C., Hermida Valverde T. Assessment of risk scores in COVID-19. *Int J Clin Pract.* 2021; 75 (12): e13705. DOI: 10.1111/ijcp.13705. Epub ahead of print. PMID: 32931634.
 66. Labenz C., Kremer W.M., Schattenberg J.M., Wörns M.A., Tonenges G., Weinmann A., Galle P.R., Sprinzel M.F. Clinical Frailty Scale for risk stratification in patients with SARS-CoV-2 infection. *J Invest Med.* 2020; 68 (6): 1199–1202. DOI: 10.1136/jim-2020-001410. Epub 2020 Jul 7. PMID: 32641351.
 67. Jang J.G., Hur J., Hong K.S., Lee W., Ahn J.H. Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients. *J Korean Med Sci.* 2020; 35 (25): e234. DOI: 10.3346/jkms.2020.35.e234. PMID: 32597046.
 68. Kostakis I., Smith G.B., Prytherch D., Meredith P., Price C., Chauhan A.; Portsmouth Academic Consortium For Investigating COVID-19 (PACIFIC-19). The performance of the National Early Warning Score and National Early Warning Score 2 in hospitalised patients infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Resuscitation.* 2021; 159: 150–157. DOI: 10.1016/j.resuscitation.2020.10.039. Epub 2020 Nov 8. PMID: 33176170.
 69. Knight S.R., Ho A., Pius R., Buchan I., Carson G., Drake T.M., Dunning J., Fairfield C.J., Gamble C., Green C.A., Gupta R., Halpin S., Hardwick H.E., Holden K.A., Horby P.W., Jackson C., Mclean K.A., Merson L., Nguyen-Van-Tam J.S., Norman L., Noursadeghi M., Olliaro P.L., Pritchard M.G., Russell C.D., Shaw C.A., Sheikh A., Solomon T., Sudlow C., Swann O.V., Turtle L.C., Openshaw P.J., Baillie J.K., Semple M.G., Docherty A.B., Harrison E.M.; ISARIC4C investigators. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. *BMJ.* 2020; 370: m3339. DOI: 10.1136/bmj.m3339. Erratum in: *BMJ.* 2020 Nov 13; 371: m4334. PMID: 32907855.
 70. Liang W., Liang H., Ou L., Chen B., Chen A., Li C., Li Y., Guan W., Sang L., Lu J., Xu Y., Chen G., Guo H., Guo J., Chen Z., Zhao Y., Li S., Zhang N., Zhong N., He J.; China Medical Treatment Expert Group for COVID-19. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. *JAMA Intern Med.* 2020; 180 (8): 1081–1089. DOI: 10.1001/jamainternmed.2020.2033. PMID: 32396163.
 71. Covino M., De Matteis G., Burzo M.L., Russo A., Forte E., Carnicelli A., Piccioni A., Simeoni B., Gasbarrini A., Franceschi E., Sandroni C.; GEMELLI AGAINST COVID-19 Group. Predicting In-Hospital Mortality in COVID-19 Older Patients with Specifically Developed Scores. *J Am Geriatr Soc.* 2021; 69 (1): 37–43. DOI: 10.1111/jgs.16956. Epub 2020 Nov 30. PMID: 33197278.
 72. Yuan Y., Sun C., Tang X., Cheng C., Mombaerts L., Wang M., Hu T., Sun C., Guo Y., Li X., Xu H., Ren T., Xiao Y., Xiao Y., Zhu H., Wu H., Li K., Chen C., Liu Y., Liang Z., Cao Z., Zhang H.T., Ch Paschalis I., Liu Q., Goncalves J., Zhong Q., Yan L. Development and Validation of a Prognostic Risk Score System for COVID-19 Inpatients: A Multi-Center Retrospective Study in China. *Engineering (Beijing).* 2020 Nov 28. DOI: 10.1016/j.eng.2020.10.013. Epub ahead of print. PMID: 33282444.
 73. Shang Y., Liu T., Wei Y., Li J., Shao L., Liu M., Zhang Y., Zhao Z., Xu H., Peng Z., Zhou F., Wang X. Scoring systems for predicting mortality for severe patients with COVID-19. *EclinicalMedicine.* 2020; 24: 100426. DOI: 10.1016/j.eclinm.2020.100426. PMID: 32766541.
 74. Vaid A., Somani S., Russak A.J., De Freitas J.K., Chaudhry F.F., Paranjpe I., Johnson K.W., Lee S.J., Miotto R., Richter F., Zhao S., Beckmann N.D., Naik N., Kia A., Timsina P., Lala A., Paranjpe M., Golden E., Danieletto M., Singh M., Meyer D., O'Reilly P.F., Huckins L., Kovatch P., Finkelstein J., Freeman R.M., Argulian E., Kasarskis A., Percha B., Aberg J.A., Bagiella E., Horowitz C.R., Murphy B., Nestler E.J., Schadt E.E., Cho J.H., Cordon-Cardo C., Fuster V., Charney D.S., Reich D.L., Bottinger E.P., Levin M.A., Narula J., Fayad Z.A., Just A.C., Charney A.W., Nadkarni G.N., Glicksberg B.S. Machine Learning to Predict Mortality and Critical Events in a Cohort of Patients With COVID-19 in New York City: Model Development and Validation. *J Med Internet Res.* 2020; 22 (11): e24018. DOI: 10.2196/24018. PMID: 33027032.
 75. Wu G., Yang P., Xie Y., Woodruff H.C., Rao X., Guiot J., Frix A.N., Louis R., Moutschen M., Li J., Li J., Yan C., Du D., Zhao S., Ding Y., Liu B., Sun W., Albarello F., D'Abramo A., Schininà V., Nicastrì E., Occhipinti M., Barisione G., Barisione E., Halilaj I., Lovinasse P., Wang X., Wu J., Lambin P. Development of a clinical decision support system for severity risk prediction and triage of COVID-19 patients at hospital admission: an international multicentre study. *Eur Respir J.* 2020; 56 (2): 2001104. DOI: 10.1183/13993003.01104-2020. PMID: 32616597.
 76. Hajifathalian K., Sharaiha R.Z., Kumar S., Krisko T., Skaf D., Ang B., Redd W.D., Zhou J.C., Hathorn K.E., McCarty T.R., Bazarbashi A.N., Njie C., Wong D., Shen L., Sholle E., Cohen D.E., Brown R.S. Jr, Chan W.W., Fortune B.E. Development and external validation of a prediction risk model for short-term mortality among hospitalized U.S. COVID-19 patients: A proposal for the COVID-AID risk tool. *PLoS One.* 2020; 15 (9): e0239536. DOI: 10.1371/journal.pone.0239536. PMID: 32997700.
 77. Gong J., Ou J., Qiu X., Jie Y., Chen Y., Yuan L., Cao J., Tan M., Xu W., Zheng F., Shi Y., Hu B. A Tool for Early Prediction of Severe Coronavirus Disease 2019 (COVID-19): A Multicenter Study Using the Risk Nomogram in Wuhan and Guangdong, China. *Clin Infect Dis.* 2020; 71 (15): 833–840. DOI: 10.1093/cid/ciaa443. PMID: 32296824.

78. Haimovich A.D., Ravindra N.G., Stoytchev S., Young H.P., Wilson F.P., van Dijk D., Schulz W.L., Taylor R.A. Development and Validation of the Quick COVID-19 Severity Index: A Prognostic Tool for Early Clinical Decompensation. *Ann Emerg Med.* 2020; 76 (4): 442–453. DOI: 10.1016/j.annemergmed.2020.07.022. Epub 2020 Jul 21. PMID: 33012378.
79. Zhang C., Qin L., Li K., Wang Q., Zhao Y., Xu B., Liang L., Dai Y., Feng Y., Sun J., Li X., Hu Z., Xiang H., Dong T., Jin R., Zhang Y. A Novel Scoring System for Prediction of Disease Severity in COVID-19. *Front Cell Infect Microbiol.* 2020; 10: 318. DOI: 10.3389/fcimb.2020.00318. PMID: 32582575.
80. Futoma J., Simons M., Panch T., Doshi-Velez F., Celi L.A. The myth of generalisability in clinical research and machine learning in health care. *Lancet Digit Health.* 2020; 2 (9): e489–e492. DOI: 10.1016/S2589-7500 (20)30186-2. Epub 2020 Aug 24. PMID: 32864600.

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