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Review Article

CHRONIC OBSTRUCTIVE LUNG DISEASES AS A RISK FACTOR FOR SEVERE COVID-19 (REVIEW)

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The review presents meta-analyses and original studies data of severe outcomes of COVID-19 infection in patients with chronic obstructive pulmonary disease.

The main risk factors for the severe course of COVID-19 in many studies have been identified as follows: age over 65 years, chronic lung diseases, systemic arterial hypertension, cardiovascular diseases, diabetes mellitus, immunosuppression, chronic kidney and liver diseases. It was shown that patients with concomitant respiratory diseases were 4.2 times more likely to have a severe course of COVID-19 (OR 4.21; 95% CI 2.9–6.0), especially in patients with chronic obstructive pulmonary disease (OR 5.8, 95% CI 3.9–8.5). Patients with bronchial asthma also more often received mechanical ventilation (OR 1.58; 95% CI 1.02–2.44; $p = 0.04$), treatment in intensive care units (OR 1.58; 95% CI 1.09–2.29; $p = 0.02$), had longer hospital stays (OR 1.30; 95% CI 1.09–1.55; $p < 0.003$) and higher mortality (OR 1.53; 95 % CI 1.01–2.33; $p = 0.04$) compared with COVID-19 patients without asthma or other chronic obstructive pulmonary diseases. Another factor contributing to severe outcomes of COVID-19 is tobacco use, which increases the risk of severe disease, hospitalization and poor outcomes.

Patients with chronic obstructive pulmonary diseases, especially smokers, were more likely to have a severe COVID-19 and adverse outcomes of this disease, which must be taken into account when prescribing treatment for coronavirus infection.

Keywords: COVID-19; chronic obstructive pulmonary disease; tobacco smoking; severe course of COVID-19.

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Обзорная статья

ХРОНИЧЕСКИЕ ОБСТРУКТИВНЫЕ ЗАБОЛЕВАНИЯ ЛЕГКИХ КАК ФАКТОР РИСКА ТЯЖЕЛОГО ТЕЧЕНИЯ COVID-19 (ОБЗОР)

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В обзоре представлены данные метаанализов и оригинальных исследований тяжелых исходов конавирусной инфекции COVID-19 у больных хроническими обструктивными заболеваниями легких.

Основными факторами риска тяжелого течения COVID-19 во многих работах определены следующие: возраст старше 65 лет, наличие хронических заболеваний легких, системной артериальной гипертензии, сердечно-сосудистых заболеваний, сахарного диабета, иммуносупрессии, хронических заболеваний почек и печени. У пациентов с сопутствующими респираторными заболеваниями в 4,2 раза чаще отмечалось тяжелое течение COVID-19 [отношение шансов (ОШ) 4,21; 95 % доверительный интервал (ДИ), 2,9–6,0], особенно у пациентов с хронической обструктивной болезнью легких (ОШ 5,8; 95 % ДИ 3,9–8,5). Больные бронхиальной астмой также чаще получали искусственную вентиляцию легких (ОШ 1,58; 95 % ДИ 1,02–2,44; $p = 0,04$) и лечение в реанимационных отделениях (ОШ 1,58; 95 % ДИ 1,09–2,29; $p = 0,02$) имели более длительное пребывание в стационаре (ОШ 1,30; 95 % ДИ 1,09–1,55; $p < 0,003$) и более высокую смертность (ОШ 1,53; 95 % ДИ 1,01–2,33; $p = 0,04$) по сравнению с больными COVID-19 без астмы и других хронических обструктивных заболеваний легких. Еще один фактор, приводящий к тяжелым исходам заболевания COVID-19, — потребление табака, которое увеличивает риски тяжелого течения, госпитализации и неблагоприятных исходов.

У больных хроническими обструктивными заболеваниями легких, особенно у курящих, чаще отмечалось тяжелое течение COVID-19 и неблагоприятные исходы этого заболевания, что необходимо учитывать при назначении лечения коронавирусной инфекции.

Ключевые слова: COVID-19; хронические обструктивные заболевания легких; табакокурение; тяжелое течение COVID-19.

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Coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first registered in December 2019 in China and has spread rapidly worldwide. By April 2020, more than 3 million cases and 208,516 lethal outcomes were registered [4, 21].

Globally, scientists and doctors were searching for methods of diagnosing and treating this disease and factors leading to an adverse outcome. By September 2022, 301,485 articles were yielded when using the keyword "COVID-19" in PubMed, including 2640 meta-analyses, and there were 30,747 articles in the Russian Science Citation Index.

Concomitant diseases represent one of the factors of severe clinical course and its adverse outcomes in patients with COVID-19. For example, in a study conducted in Mexico, patients with COVID-19 with three or more comorbidities had a higher risk of hospitalization [odds ratio (OR) = 3.1; 95% confidence interval (CI) 2.7–3.7], pneumonia (OR = 3.02; 95% CI 2.6–3.5), hospitalisations in intensive care units (OR = 2; 95% CI 1.5–2.7), and mortality (OR = 3.5; 95% CI 2.9–4.2) than patients with one or two comorbidities and patients without them [22].

Age over 65 years, chronic lung diseases, systemic arterial hypertension, cardiovascular diseases, diabetes mellitus, immunosuppression, and chronic kidney and liver diseases are risk factors for severe COVID-19 [8, 22]. Patients with obesity more often have adverse outcomes and severe disease course [22]. A study reported that patients with a body mass index of >30 kg/m^2 had the highest levels of C-reactive protein and humoral endotoxin-binding factors [12] because excess body weight leads to an increase in the endotoxin translocation from the intestine to the lymphatic system and into the blood and to the maintenance of systemic inflammation in patients with COVID-19 [12].

In other clinical studies, increased risks of a more severe course of COVID-19 are noted in men, older people and senile age, and individuals with cardiovascular diseases [15, 18, 29, 31, 33].

A meta-analysis conducted in 2020 [25] presented the first data (22 studies) on 13,184 patients with COVID-19, most of whom lived in China. Patients with COVID-19 were included in the severe outcome group if their clinical symptoms worsened, they required intensive care, or they died. Compared with the non-severe outcome group, the severe group was older with male predominance (63% versus 51%) [25] and had a higher prevalence of chronic obstructive pulmonary disease (COPD; 12% versus 4%) [25]. The meta-analysis results showed that the probability of severe COVID-19 outcomes was significantly higher in patients with respiratory comorbidities (OR 4.21; 95% CI 2.9–6.0). No significant heterogeneity was found in the study. The risks of a severe course were the highest in patients with COPD (OR 5.8; 95% CI 3.9–8.5) [25].

The high contagiousness of SARS-CoV-2, localisation of the virus in the lower respiratory tract, identical clinical presentation of COVID-19, exacerbations of COPD, and the lack of pathogenetic therapy make it difficult to provide medical care to patients with COPD during a pandemic at all its stages. In addition, patients with COPD are usually diagnosed with diseases of the heart and blood vessels, which are also risk factors for the severe course of any acute respiratory infection, including COVID-19 [9]. However, COVID-19 is characterized by the influence of the virus not only on the respiratory system but also on blood vessels with the formation of microthrombi, which contribute to increased respiratory dysfunction; patients with COVID-19 had nine times more microthrombi in alveolar capillaries than patients with influenza [1, 10]. When SARS-CoV-2 enters the body, endothelial cells are activated, which induces systemic inflammation, thrombosis, and microvascular dysfunction [16]. These pathophysiological changes are hazardous for patients with cardiovascular diseases and may represent one of the causes of high mortality from COVID-19.

Another factor that contributes to the severe disease course in patients with COPD is tobacco smoking. Tobacco smoking, including passive smoking, remains the main preventable cause of premature death worldwide and the main risk factor for the occurrence of COPD, which can affect 15%–30% of smokers [7, 17]. Epidemiological studies have shown that in Russia, COPD occurs in 21.8% of patients with respiratory symptoms and15.3% of the general population [6, 14]. Moreover, 65% of smokers have pathological changes in the lungs that can cause COPD [13]. Even in those long-term smokers who consider themselves healthy, pronounced impairment of bronchial patency was registered in 15% of cases [5]. Tobacco cessation slows the deterioration of external respiration, stabilizes the clinical COPD status, and contributes to an increase in life expectancy and quality [27].

Many studies have reported that smokers had more severe COVID-19 than non-smokers, and they required intensive care and mechanical lung ventilation 2.4 times more often [11, 20, 28].

According to the World Health Organization, 1.4%–18.5% of adult patients hospitalized for COVID-19 were smokers [30]. Although several studies have demonstrated a lower percentage of

smokers among patients hospitalized for COVID-19 than the general population, possible errors in these studies should be considered, which could be associated with a stringent epidemiological situation and smoking status is not always documented, especially in the absence of a pronounced nicotine withdrawal syndrome [11].

The pathogenesis of COVID-19 and its severe course are largely associated with angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) [19]. The ACE2 receptor level is increased in older individuals, male patients, and smokers [19]. Since smoking increases ACE2 expression, patients with COPD are prone to COVID-19 and are at higher risk of severe COVID-19 [20]. A dose-dependent increase in ACE2 expression depending on smoke exposure was revealed in the lungs of rodents and humans [26].

The expressions of ACE2 and TMPRSS2 in patients with asthma is comparable (or less common) to that in healthy people [19]. This may explain the lower incidence of COVID-19 (at least in 2020–2021) in patients with asthma than in patients with COPD. Moreover, data have been obtained not only on the lower incidence of COVID-19 in bronchial asthma (BA) but also on a decrease in the number of patients hospitalized for asthma exacerbation (data from a study in Japan) [19]. Therefore, clinical recommendations for the treatment of BA during a pandemic have remained the same in many countries.

Later, these results were called into question, and in 2022, a study in the USA analysed the clinical course of COVID-19 in patients with BA. During the initial data processing, indeed, no differences were detected in the severity of COVID-19 in patients with and without BA [23]. However, in the adjusted analysis (the analysis was adjusted for demographics, comorbidities, smoking status, and time of illness during the pandemic), patients with more often BA received mechanical lung ventilation (OR1.58; 95% CI 1.02–2.44; $p = 0.04$) and hospitalized in the intensive care unit (OR1.58; 95% CI 1.09–2.29; $p = 0.02$), had longer hospital stay (OR1.30; 95% CI 1.09–1.55; $p < 0.003$), and had higher mortality (OR1.53; 95% CI 1.01–2.33; $p = 0.04$) than the non-asthma cohort [23]. Inhaled corticosteroid use and eosinophilic phenotype were not found to be associated with significant differences in severe COVID-19 outcomes, although conflicting data demonstrate the suppression of coronavirus replication and cytokine production *in vitro* models using bronchodilators and inhaled corticosteroids [24, 32]. Comparison of the clinical course and severity of BA showed that in patients with moderate BA, the outcomes were worse than in those with severe BA [23], which requires further research to understand the role of various drugs and characteristics of the geno- and phenotypes of the disease for the prevention of severe COVID-19.

In the Russian Federation, among patients with cystic fibrosis (CF), the incidence of COVID-19 as of 1 August 2020, was 3.8 (0.38%) per 1,000 patients (2.1:1000 for children and 8.8:1000 for adults) [2]. Although patients with CF are at risk for severe COVID-19, the infection did not induce a significant deterioration in the underlying disease. No lethal outcomes from COVID-19 have been reported in Russian patients with CF [2]. Among adult patients with CF living in St. Petersburg and the Leningrad region, the incidence of COVID-19 was 17.85%, which was lower than that in the general population. In rare cases, the disease proceeded with a severe course. The efficiency of outpatient treatment and the absence of lethal outcomes from COVID-19 were also noted [3]. The risk factors for severe COVID-19 in patients with CF do not include advanced age, tobacco consumption, and active smoking [2, 25]. The role of self-isolation in serious illnesses such as CF should not be ruled out.

COPD and tobacco smoking increase the risk of severe disease and adverse outcomes of COVID-19. This is important for the development of preventive measures that will help improve the management of patient risk factors in clinical practise.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENCES

1. Ivanov DO, Chernova TM, Pavlova EB, et al. Coronaviral infection. *Pediatrician (St. Petersburg)*. 2020;11(3): 109–117. (In Russ.) DOI: 10.17816/PED113109-117
2. Kondratyeva EI, Krasovsky SA, Kashirskaya NYu, et al. COVID-19 in cystic fibrosis patients. *Pulmonologiya*. 2020;30(5):544–552. (In Russ.) DOI: 10.18093/0869-0189-2020-30-5-544-552
3. Makhmutova VR, Gembitskaya TE, Chermenskiy AG, Titova ON. Analysis of COVID-19 cases in adult cystic fibrosis patients in Saint Petersburg and the Leningrad Region. *Pulmonologiya*. 2021;31(2):189–196. (In Russ.) DOI: 10.18093/0869-0189-2021-31-2-189-196
4. Sukhovskaya OA. Coronavirus 2019-nCoV (short message). *Medical alliance*. 2019;7(4):106–108. (In Russ.) DOI: 10.36422/23076348201974106108
5. Sukhovskaya OA, Kozyrev AG, Kiseleva EA, et al. Vyyavlenie rannikh stadii zabolevanii organov dykhaniya, assotsiirovannykh s tabakokureniem. *Tyumen medical journal*. 2008;(2):3–6. (In Russ.)
6. Titova ON, Kulikov VD. Morbidity and mortality from respiratory diseases adult population of St. Petersburg. *Medical alliance*. 2019;7(3):42–48. (In Russ.) DOI: 10.36422/2307-6348-2019-7-3-42-48
7. Titova ON, Sukhovskaya OA, Kulikov VD, Kolpinskaya ND. Passive smoking in patients with chronic obstructive pulmonary diseases. *Medical alliance*. 2022;10(1):41–46. (In Russ.) DOI: 10.36422/23076348-2022-10-1-41-46
8. Khoroshinina LP, Lopatieva SO, Lazareva AA. Peculiarities of the course of coronavirus infection and some aspects of treatment of geriatric patients with SARS-CoV-2-induced lung damage. *University therapeutic journal*. 2021;3(4):103–114. (In Russ.)
9. Chaulin AM, Duplyakov DV. Comorbidity in chronic obstructive pulmonary disease and cardiovascular disease. *Cardiovascular Therapy and Prevention*. 2021;20(3): 2539. (In Russ.) DOI: 10.15829/1728-8800-2021-2539
10. Shcherbak SG, Kamilova TA, Golota AS, et al. Pathogenesis of pulmonary complications COVID-19. *Medical alliance*. 2021;9(4):6–25. (In Russ.) DOI: 10.36422/23076348-2021-9-4-6-25
11. Yablonskiy PK, Sukhovskaya OA, Smirnova MA. Influence of tobacco smoking on COVID-19 incidence and outcome. *Medical alliance*. 2020;8(2):93–97. (In Russ.) DOI: 10.36422/23076348-2020-8-2-93-97
12. Yatskov IA, Beloglazov VA, Klimchuk AV, et al. Effects of excess body weight and obesity on endotoxinemia and systemic inflammation in acute SARS-CoV-2-associated lung injury. *Medical alliance*. 2021;9(4):54–61. (In Russ.) DOI: 10.36422/23076348-2021-9-4-54-61
13. Bazzan E, Semenzato U, Turato G, et al. Symptomatic smokers without COPD have physiological changes heralding the development of COPD. *ERJ Open Res*. 2022;8(2):00202–2022. DOI: 10.1183/23120541.00202-2022
14. Chuchalin AG, Khaltaev N, Antonov NS, et al. Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation. *Int J COPD*. 2014;9(1): 963–974. DOI: 10.2147/COPD.S67283
15. Javanmardi F, Keshavarzi A, Akbari A, et al. Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. *Arch Acad Emerg Med*. 2020;8(1): e35. DOI: 10.1371/journal.pone.0241265
16. Gencer S, Lacy M, Atzler D, et al. Immunoinflammatory, thrombohaemostatic, and cardiovascular mechanisms in COVID-19. *Thromb Haemost*. 2020;20(12): 1629–1641. DOI: 10.1055/s-0040-1718735
17. Global Initiative for Chronic Obstructive Lung Disease (GOLD) [Internet]. *2022 GOLD Reports. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2022 Reports*. Available from: https://goldcopd.org/2022-gold-reports-2/
18. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–1720. DOI: 10.1056/NEJMoa2002032
19. Hojo M, Terada-Hirashima J, Sugiyama H. COVID-19 and bronchial asthma: current perspectives. *Glob Health Med*. 2021;3(2):67–72. DOI: 10.35772/ghm.2020.01117
20. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506. DOI: 10.1016/S0140-6736(20)30183-5
21. Johns Hopkins University of Medicine. Coronavirus Resource Center [Internet]. *Jill Rosen. COVID-19 data dashboard creator Lauren gardner wins lasker award* [accessed 25.08.2022]. Available from: https://coronavirus.jhu.edu/
22. Kammar-García A, Vidal-Mayo JJ, Vera-Zertuche JM, et al. Impact of comorbidities in Mexican SARS-CoV-2-positive patients: a retrospective analysis in a national cohort. *Rev Invest Clin*. 2020;72(3):151–158. DOI: 10.24875/RIC.20000207
23. Ludwig A, Brehm CE, Fung C, et al. Asthma and coronavirus disease 2019-related outcomes in hospitalized patients: A single-center experience. *Ann Allergy Asthma Immunol*. 2022;129(1):79–87.e6. DOI: 10.1016/j.anai.2022.03.017
24. Matsuyama S, Kawase M, Nao N, et al. The inhaled corticosteroid ciclesonide blocks coronavirus RNA replication by targeting viral NSP15. *J Virol*. 2020;95(1): e01648–20. DOI: 10.1128/JVI.01648-20
25. Sanchez-Ramirez DC, Mackey D. Underlying respiratory diseases, specifically COPD, and smoking are associated with severe COVID-19 outcomes: A systematic review and meta-analysis. *Respir Med*. 2020;171:106096. DOI: 10.1016/j.rmed.2020.106096

26. Smith JC, Sausville EL, Girish V, et al. Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract. *Dev Cell*. 2020;53(5):514–529.e3. DOI: 10.1016/j.devcel.2020.05.012
27. Tønnesen P. Smoking cessation and COPD. *Eur Respir Rev*. 2013;22(127):37–43. DOI: 10.1183/09059180.00007212
28. Vardavas CI, Nikitara K. COVID-19 and smoking: a systematic review of the evidence. *Tob Induc Dis*. 2020;18:20. DOI: 10.18332/tid/119324
29. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020; 323(11): 1061–1069. DOI: 10.1001/jama.2020.1585
30. Xie J, Zhong R, Wang W, et al. COVID-19 and Smoking: What Evidence Needs Our Attention? *Front Physiol*. 2021;12:603850. DOI: 10.3389/fphys.2021.603850
31. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis*. 2020;94:91–95. DOI: 10.1016/j.ijid.2020.03.017
32. Yamaya M, Nishimura H, Deng X. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells. *Respir Investig*. 2020;58(3):155–168. DOI: 10.1016/j.resinv.2019.12.005
33. Zhu J, Ji P, Pang J, et al. Clinical characteristics of 3,062 COVID-19 patients: a meta-analysis. *J Med Virol*. 2020;92(10):1902–1914. DOI: 10.1002/jmv.25884

СПИСОК ЛИТЕРАТУРЫ

1. Иванов Д.О., Чернова Т.М., Павлова Е.Б., и др. Коронавирусная инфекция // Педиатр. 2020. Т. 11, № 3. С. 109–117. DOI: 10.17816/PED113109-117
2. Кондратьева Е.И., Красовский С.А., Каширская Н.Ю., и др. COVID-19 у больных муковисцидозом // Пульмонология. 2020. Т. 30, № 5. С. 544–552. DOI: 10.18093/0869-0189-2020-30-5-544-552
3. Махмутова В.Р., Гембицкая Т.Е., Черменский А.Г., Титова О.Н. Анализ случаев COVID-19 у взрослых больных муковисцидозом в Санкт-Петербурге и Ленинградской области // Пульмонология. 2021. Т. 31, № 2. С. 189–196. DOI: 10.18093/0869-0189-2021-31-2-189-196
4. Суховская О.А. Коронавирус 2019-nCoV (краткое сообщение) // Медицинский альянс. 2019. Т. 7, № 4. С. 106–108. DOI: 10.36422/23076348201974106108
5. Суховская О.А., Козырев А.Г., Киселева Е.А., и др. Выявление ранних стадий заболеваний органов дыхания, ассоциированных с табакокурением // Тюменский медицинский журнал. 2008. № 2. С. 3–6.
6. Титова О.Н., Куликов В.Д. Заболеваемость и смертность от болезней органов дыхания взрослого населения Санкт-Петербурга // Медицинский альянс. 2019. Т. 7, № 3. С. 42–48. DOI: 10.36422/2307-6348-2019-7-3-42-48
7. Титова О.Н., Суховская О.А., Куликов В.Д., Колпинская Н.Д. Пассивное табакокурение больных хроническими обструктивными заболеваниями легких // Медицинский альянс. 2022. Т. 10, № 1. С. 41–46. DOI: 10.36422/23076348-2022-10-1-41-46
8. Хорошинина Л.П., Лопатиева С.О., Лазарева А.А. Особенности течения коронавирусной инфекции и некоторые аспекты лечения гериатрических пациентов с поражением легких, вызванным SARS-CoV-2 // Университетский терапевтический вестник. 2021. Т. 3, № 4. С. 103–114.
9. Чаулин А.М., Дупляков Д.В. Коморбидность хронической обструктивной болезни легких и сердечно-сосудистых заболеваний // Кардиоваскулярная терапия и профилактика. 2021. № 3. С. 25–39. DOI: 10.15829/1728-8800-2021-2539
10. Щербак С.Г., Камилова Т.А., Голота А.С., и др. Патогенез легочных осложнений COVID-19 // Медицинский альянс. 2021. Т. 9, № 4. С. 6–25. DOI: 10.36422/23076348-2021-9-4-6-25
11. Яблонский П.К., Суховская О.А., Смирнова М.А. Влияние табакокурения на заболеваемость и исходы COVID-19 // Медицинский альянс. 2020. Т. 8, № 2. С. 93–97. DOI: 10.36422/23076348-2020-8-2-93-97
12. Яцков И.А., Белоглазов В.А., Климчук А.В., и др. Влияние избыточной массы тела и ожирения на показатели эндотоксинемии и системного воспаления при остром SARS-CoV-2-поражении легких // Медицинский альянс. 2021. Т. 9, № 4. С. 54–61. DOI: 10.36422/23076348-2021-9-4-54-61
13. Bazzan E., Semenzato U., Turato G., et al. Symptomatic smokers without COPD have physiological changes heralding the development of COPD // ERJ Open Res. 2022. Vol. 8, No. 2. P. 00202–2022. DOI: 10.1183/23120541.00202-2022
14. Chuchalin A.G., Khaltaev N., Antonov N.S., et al. Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation // Int J COPD. 2014. Vol. 9, No. 1. P. 963–974. DOI: 10.2147/COPD.S67283
15. Javanmardi F., Keshavarzi A., Akbari A., et al. Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis // Arch Acad Emerg Med. 2020. Vol. 8, No. 1. P. e35. DOI: 10.1371/journal.pone.0241265
16. Gencer S., Lacy M., Atzler D., et al. Immunoinflammatory, thrombohaemostatic, and cardiovascular mechanisms in COVID-19 // Thromb Haemost. 2020. Vol. 120, No. 12. P. 1629–1641. DOI: 10.1055/s-0040-1718735

17. Global Initiative for Chronic Obstructive Lung Disease (GOLD) [Электронный ресурс]. 2022 GOLD Reports. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2022 Reports. Доступ по ссылке: https://goldcopd.org/2022-gold-reports-2/
18. Guan W.-J., Ni Z.-Y., Hu Y., et al. Clinical characteristics of coronavirus disease 2019 in China // N Engl J Med. 2020. Vol. 382. P. 1708–1720. DOI: 10.1056/NEJMoa2002032
19. Hojo M., Terada-Hirashima J., Sugiyama H. COVID-19 and bronchial asthma: current perspectives // Glob Health Med. 2021. Vol. 3, No. 2. P. 67–72. DOI: 10.35772/ghm.2020.01117
20. Huang C., Wang Y., Li X., et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China // Lancet. 2020. Vol. 395, No. 10223. P. 497–506. DOI: 10.1016/S0140-6736(20)30183-5
21. Jhons Hopkins University of Medicine. Coronavirus Resource Center [Электронный ресурс]. J. Rosen. COVID-19 data dashboard creator Lauren gardner wins lasker award [дата обращения: 25.08.2022]. Доступ по ссылке: https://coronavirus.jhu.edu/
22. Kammar-García A., Vidal-Mayo J.J., Vera-Zertuche J.M., et al. Impact of comorbidities in Mexican SARS-COV-2-positive patients: a retrospective analysis in a national cohort // Rev Invest Clin. 2020. Vol. 72, No. 3. P. 151–158. DOI: 10.24875/RIC.20000207
23. Ludwig A., Brehm C.E., Fung C., et al. Asthma and coronavirus disease 2019-related outcomes in hospitalized patients: A single-center experience // Ann Allergy Asthma Immunol. 2022. Vol. 129, No. 1. P. 79–87.e6. DOI: 10.1016/j.anai.2022.03.017
24. Matsuyama S., Kawase M., Nao N., et al. The inhaled corticosteroid ciclesonide blocks coronavirus RNA replication by targeting viral NSP15 // J Virol. 2020. Vol. 95, No. 1. ID e01648–20. DOI: 10.1128/JVI.01648-20
25. Sanchez-Ramirez D.C., Mackey D. Underlying respiratory diseases, specifically COPD, and smoking are associated with severe COVID-19 outcomes: A systematic review and meta-analysis // Respir Med. 2020. Vol. 171. ID 106096. DOI: 10.1016/j.rmed.2020.106096
26. Smith J.C., Sausville E.L., Girish V., et al. Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract // Dev Cell. 2020. Vol. 53, No. 5. P. 514–529.e3. DOI: 10.1016/j.devcel.2020.05.012
27. Tønnesen P. Smoking cessation and COPD // Eur Respir Rev. 2013. Vol. 22, No. 127. P. 37–43. DOI: 10.1183/09059180.00007212
28. Vardavas C.I., Nikitara K. COVID-19 and smoking: a systematic review of the evidence // Tob Induc Dis. 2020. Vol. 18. ID20. DOI: 10.18332/tid/119324
29. Wang D., Hu B., Hu C., et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China // JAMA. 2020. Vol. 323, No. 11. P. 1061–1069. DOI: 10.1001/jama.2020.1585
30. Xie J., Zhong R., Wang W., et al. COVID-19 and smoking: what evidence needs our attention? // Front Physiol. 2021. Vol. 12. ID 603850. DOI: 10.3389/fphys.2021.603850
31. Yang J., Zheng Y., Gou X., et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis // Int J Infect Dis. 2020. Vol. 94. P. 91–95. DOI: 10.1016/j.ijid.2020.03.017
32. Yamaya M., Nishimura H., Deng X. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells // Respir Investig. 2020. Vol. 58, No. 3. P. 155–168. DOI: 10.1016/j.resinv.2019.12.005
33. Zhu J., Ji P., Pang J., et al. Clinical characteristics of 3,062 COVID-19 patients: a meta-analysis // J Med Virol. 2020. Vol. 92, No. 10. P. 1902–1914. DOI: 10.1002/jmv.25884

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