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The deletion variant of the *CCR5* gene (rs333) but not the *ACE* gene (rs4340) is associated with long-term respiratory support in patients with COVID-19 pneumonia

The aim was to analyze the effect of the ACE gene (c.2306-117_404I/D, rs4340) and the CCR5 gene (del32, rs333) variants on the course of severe COVID-19 pneumonia in patients treated at the intensive care unit. Materials and methods. The study group included 31 patients (16 men and 15 women) with diagnosis «viral COVID-19 pneumonia». All patients underwent standard daily repeated clinical, instrumental and laboratory examinations. Determination of the ACE and CCR5 gene variants was carried out by a molecular method using allele-specific polymerase chain reaction. Results. The results of our retrospective study did not confirm the association of investigated genes variants with lethal outcomes. Clinical predictors of lethal outcomes were: low of SpO_2/FiO_2 ratio, tachypnea, tachycardia, low systolic blood pressure, anemia, leukocytosis during the first days of hospitalization and need of mechanical lung ventilation. Patients with heterozygous W/del32 genotype of the CCR5 gene in comparison with patients with genotype W/W had significantly longer respiratory support, namely a significantly increased duration of oxygen therapy using an oxygen mask (4.50±3.70 vs. 2.19±1.28 days, respectively), significantly longer mechanical lung ventilation (15.00±4.24 vs. 4.40±4.98 days, respectively) and the significantly greater total duration of oxygen therapy (9.60±5.68 vs. 4.19±3.84 days, respectively). Patients with the W/del32 genotype of the CCR5 gene had significantly increased white blood cell counts as compared to patients with the W/W genotype (13.64±10.66 vs. 8.38±2.85, respectively). Conclusions. Significant clinical predictors of lethal outcomes in patients with severe COVID-19 pneumonia were found on admission: lower SpO_2/FiO_2 ratios, tachypnea, tachycardia, anemia, leukocytosis during the first days of hospitalization, and need of mechanical lung ventilation. The variant of the CCR5 gene was the genetic predictor of severe course of COVID-19 pneumonia with increased need for respiratory support. The variant of the CCR5 gene was associated with elevated white blood cell count in the complete blood test. The obtained results indicate the need for further multifaceted research in this direction to determine the leading genetically mediated pathogenetic mechanisms of severe viral COVID-19 pneumonia.

Key words: *COVID-19, pneumonia, genes, ACE, CCR5.*

Introduction

At the end of 2019, an outbreak of COVID-19 caused by the coronavirus SARS-CoV-2 was observed for the first time in Wuhan, China. The disease began as an outbreak and later developed into a worldwide pandemic. COVID-19 causes a rather complex clinical presentation, which varies from mild illness to death from sepsis or acute respiratory distress syndrome, multiorgan failure, disseminated intravascular coagulation syndrome (Gabutti G. et al., 2020). Analyzing the epidemiology data on COVID-19 one can observe differences in susceptibility to infection, and mortality rates among the population of different countries (WHO, 2020). This difference may be related to the characteristics of environmental factors in different countries, such as access to health care and age, population structure, as well as the differences in the frequency of genetic variants in subpopulations, and features of the premorbid background of patients (Russo R. et al., 2020).

To date, many articles have been published analyzing the effects of polymorphic gene variants on morbidity and mortality from COVID-19. For example, a comparison of the prevalence of deletion polymorphism frequencies of *ACE* and *CCR5* genes and epidemiological data on COVID-19 concluded that these polymorphic gene variants have an impact on morbidity and mortality among the population (Panda A.K. et al., 2020; Yamamoto N. et al., 2020). In contrast, other results have already been published, not from theoretical research, but from already conducted molecular genetic studies, which do not confirm the abovementioned theoretical calculations (Annunziata A. et al., 2020; Gómez J. et al., 2020).

Due to the fact that the pandemic is still ongoing, it is not appropriate to conduct case-control research. This study design will be possible after the end of the pandemic. On the other hand, the disease of COVID-19 is accompanied by the development of viral pneumonia with severe respiratory failure. 20–25% of patients require hospitalization with high-cost medical care, including respiratory support (Karagiannidis C. et al., 2020). Therefore, the prediction of severe forms of the COVID-19 disease is relevant even in the direction of justifying the costs for the organization of intensive care units. Another aspect will be the post-COVID syndrome and the need to maintain the quality of life, which will encourage clinical trials in this context to overcome the effects of the disease.

The aim of our study was to analyze the effect of the *ACE* gene (c.2306-117_404I/D, rs4340) and the *CCR5* gene (del32, rs333) variants on the course of severe COVID-19 pneumonia in patients treated at the intensive care unit.

Materials and methods

The study group included 31 patients (16 men and 15 women) who were treated at the Department of Anesthesiology with Intensive Care Beds at Communal Enterprise «Poltava Regional Clinical Infectious

Diseases Hospital of Poltava Regional Council» in April — June 2020. According to the standards of the Ministry of Health of Ukraine (2020*a*), patients underwent clinical, laboratory and instrumental studies to diagnose «viral COVID-19 pneumonia». Patients were examined by PCR (SARS-COV-2 RNA) and ELISA (IgG and IgM) methods. 10 patients had laboratory-confirmed viral COVID-19 pneumonia.

The study was approved by the ethics committee, and informed patient consent forms were obtained.

All patients underwent standard daily repeated clinical, instrumental and laboratory examinations. The Glasgow coma scale and the number of points on the SOFA scale were evaluated. The SpO_2/FiO_2 ratio was analyzed to assess the severity of respiratory disorders due to the inability to perform the PaO_2 study. According to the recommendations of the Ministry of Health of Ukraine (2020*b*), if the SpO_2/FiO_2 index is less than 315 — it is regarded as acute respiratory distress syndrome (ARDS). Instrumental screening methods were used for all patients to confirm the diagnosis of viral pneumonia: computed tomography of the lungs and X-ray examination. In all patients, computed tomography of the lungs revealed bilateral infiltrates in the form of «ground-glass opacity», mainly in the lower and middle zones, while chest X-ray in 19 patients revealed bilateral infiltrates, and in 4 patients — the presence of pleural effusion.

The average age of patients was 58.90±18.98 years (men — 55.00±21.57, women — 63.07±15.40 years), the average Body mass index — 28.74±6.55 kg/m^2 (men — 25.05±4.89, women — 32.67±5.84 kg/m^2). 74.2% of patients had a history of comorbidities: cardiovascular, oncological diseases, tuberculosis, type II diabetes. 19 (61.3%) patients on admission to the hospital have already received oxygen therapy (using an oxygen mask), 2 of them later (due to deterioration) were intubated and transferred to mechanical lung ventilation (MVL). 5 (16.1%) patients were hospitalized immediately for MVL due to the severity of the condition and respiratory failure. Out of 7 patients on MVL, 6 patients died of complications caused by COVID-19, and according to the study design, they were included to the Group 1. The Group 2 consisted of 25 patients, who were subsequently transferred from the intensive care unit to the somatic departments, depending on the need for further treatment.

Determination of the *ACE* and *CCR5* gene variants was performed using the allele-specific PCR method as previously published (Sivak L.A. et al., 2017; Gorovenko N.G. et al., 2011). For molecular genetic testing, DNA was isolated from peripheral blood using the commercial kit «Quick-DNA Miniprep Plus Kit» («Zymo Research») according to the manufacturer's instructions. The studied gene regions were amplified using the commercial kit «Dream Taq Green PCR Master Mix» («ThermoScientific») and specific oligonucleotide primers («Metabion»).

Statistical data processing was performed using Microsoft Excel Pro Plus 2016 and SPSSv.27 software. In the analysis of the basic clinical characteristics, the mean value±mean-square deviation was calculated. The studied parameters were checked for the normality of the distribution using the Kolmogorov — Smirnov test. In the case of a normal distribution, the probability of differences in quantitative results was determined using Student's t-test, and in a distribution that differed from the normal one, the Mann — Whitney U-test was used. To compare the frequency distribution of genotypes in groups and subgroups, the study used descriptive statistics and calculation of Pearson's χ^2 criteria (Pearson's χ^2 with Yates correction). A correlation analysis was also performed between the studied indicators. Differences were considered significant for all types of analysis at a level of $p<0.05$.

Results and discussion

We investigated the effect of gene variants on the development of lethal outcomes in patients with severe viral COVID-19 pneumonia. We did not find significant differences in the distribution of genotypes by *ACE* (I/D polymorphism) and *CCR5* (del32) genes in the comparison groups. The frequency of detection of the W/del32 genotype was 16.7% in Group 1 and did not differ significantly not only from Group 2, but also from the frequency given for healthy individuals — 16.9% in the previously published data (Dovzhenko S.P. et al., 2010). The *ACE* genotype II was detected in only 16% of patients in Group 1, which did not differ significantly from the frequency of spread of this genotype in Group 2–36% of patients and from the frequency of detection of this genotype in healthy individuals — 30.4% (Fishchuk L.E., Gorovenko N.G., 2013). Given the number of people involved in the study and increasing the size of the examined group, one can detect a protective effect of genotype II of the *ACE* gene on the development of lethal outcomes of the disease.

Thus, variants of the *ACE* and *CCR5* genes were not associated with the development of lethal outcomes in the examined patients. When assessing respiratory support, it was found that the frequency of intubation/stay on MVL was significantly higher in Group 1 as compared to Group 2. In Group 1, there was a higher frequency of systemic inflammatory response syndrome (SIRS), as well as oxygen therapy through facial oxygen mask in the form of non-invasive ventilation, but these differences are beyond reliability (Table 1).

Table 1. Basic clinical and genetic characteristics of the examined patients, depending on lethal outcomes

Characteristic		Group 1 (n=6)	Group 2 (n=25)	Statistical differences
CCR5 (del32)	W/W	5 (83.3%)	21 (84.0%)	p>0.05
	W/del32	1 (16.7%)	4 (16.0%)	p>0.05
	del32/del32	0 (0.0%)	0 (0.0%)	p>0.05
	allele W	0.92	0.92	p>0.05
	allele del32	0.08	0.08	p>0.05
ACE (I/D polymorphism)	II	1 (16.7%)	9 (36.0%)	p>0.05
	ID	3 (50.0%)	7 (28.0%)	p>0.05
	DD	2 (33.3%)	9 (36.0%)	p>0.05
	allele I	0.42	0.5	p>0.05
	allele D	0.58	0.5	p>0.05
SIRS	+	5 (83.3%)	8 (32.0%)	p>0.05
	–	1 (16.7%)	17 (68.0%)	
MVL	+	6 (100.0%)	1 (4.0%)	χ^2=20.31, p<0.0001
	–	–	24 (96.0%)	
Oxygen mask	+	4 (66.7%)	8 (32.0%)	p>0.05
	–	2 (33.3%)	17 (68.0%)	

In patients of both groups, the dynamic characteristics of 43 indicators were analyzed. Hence, the results of clinical, laboratory and instrumental examinations and their impact on lethal outcomes were assessed. Significant differences obtained in the comparison are shown in Table 2.

Table 2. Significant results of comparative analysis of clinical, laboratory and instrumental indicators depending on lethal outcomes

Indicator (day)	Group 1 (n=6)	Group 2 (n=25)
Respiratory rate, per minute (day 1)	30.33±14.61	23.25±3.61
SpO_2/FiO_2, % (day 1)	85.41±44.01	102.60±66.01
SpO_2/FiO_2, % (day 2)	209.04±91.44	281.36±135.20
Heart rate, per minute (day 3)	100.00±20.31	81.79±15.78
Systolic blood pressure, mm Hg (day 1)	120.33±29.13	145.25±24.54
SOFA scale score, balls (day 1)	2.83±0.41	2.25±0.53
Glasgow coma scale score, balls (day 1)	5.50±1.23	8.05±1.46
Hemoglobin, g/l (day 1)	100.17±18.78	122.46±24.08
White blood cells, · 10^9/l (day 1)	14.63±7.30	8.80±3.57

As can be seen from Table 2, patients in Group 1 as compared to patients in Group 2 had a significantly increased respiratory rate, heart rate, white blood cell count in the complete blood test, significantly lower systolic blood pressure, hemoglobin in the complete blood test. The results of the assessment on the Glasgow scale were significantly lower in patients of Group 1 in contrast to group 2, which is associated with the development of multiple organ dysfunction syndrome. In patients of Groups 1 and 2, the SpO_2/FiO_2 ratio indicated severe respiratory disorders and ARDS, but in Group 1, the rate was critically low. It should be noted that on the 2nd day, the SpO_2/FiO_2 indicator improved in both groups, but did not exceed 315.

The mortality of critically ill patients with COVID-19, according to the literature, is very different — from 11 to 61% (Liu S. et al., 2020) and it depends on the timely initiation of medical interventions based on clinical assessment of patients using the SOFA scale. To assess the risk of death and multiple organ dysfunction syndrome, we also used the SOFA scale in our study. Its initial values in patients from Group 1 were significantly higher than in patients from Group 2. The results suggest the use of the SOFA scale to predict adverse or lethal outcomes in patients with viral COVID-19 pneumonia. The conducted comparisons allowed us to establish clinical predictors of lethal outcomes, which were tachypnea, tachycardia, low systolic pressure, high white blood cell count and low hemoglobin on admission (Table 2).

We have evaluated the relationship between the studied variants of *ACE* and *CCR5* genes in the dynamics of clinical, laboratory and

instrumental studies. In the analysis of clinical, laboratory and instrumental indicators of patients depending on the genotypes of the *ACE* gene, no significant differences were found.

Patients with heterozygous W/del32 genotype of the *CCR5* gene as compared to patients with W/W genotype showed a significantly increased need for respiratory support, namely a significantly increased duration of stay on oxygen therapy using an oxygen mask (4.50±3.70 *vs*. 2.19±1.28 days, respectively), significantly longer stay on MVL (15.00±4.24 *vs.* 4.40±4.98 days, respectively) and the significantly greater total duration of oxygen therapy (9.60±5.68 *vs*. 4.19±3.84 days, respectively) (Fig. 1).

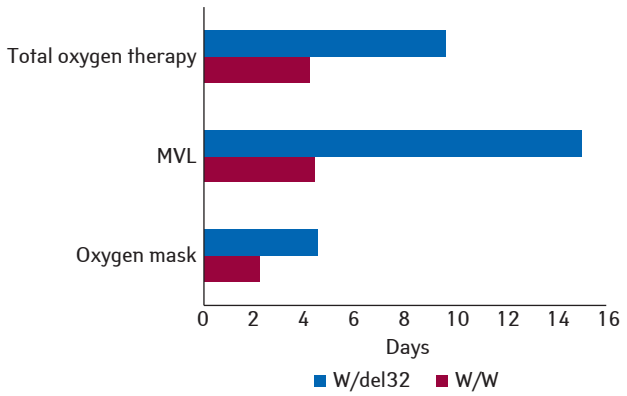

Figure 1. The average duration of different types of oxygen therapy depending on the W/del32 and W/W genotypes of the *CCR5* gene

Of all analyzed laboratory parameters depending on *CCR5* gene variants, only one significant difference was found — for the level of leukocytes in the complete blood count on the 2nd day of treatment at the intensive care unit. Patients with the W/del32 genotype of the *CCR5* gene had significantly increased white blood cell counts as compared to patients with the W/W genotype (13.64±10.66 *vs*. 8.38±2.85, respectively, Fig. 2).

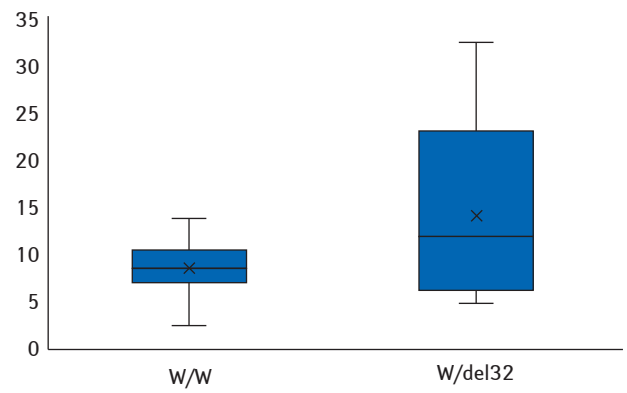

Figure 2. The level of leukocytes in the complete blood count on day 2 of treatment depending on W/del32 and W/W genotypes of the *CCR5* gene

The admitted patients belonged to the senior age group (almost elderly). They were overweight and had comorbidities, which coincides with previously published data that patients of the older age group (especially those with comorbidities) belong to the group of high risk of developing a complicated course of COVID-19 (Garg S. et al., 2019; O'Driscoll M. et al., 2020).

We found no effect of the *ACE* (I/D) and *CCR5* (del32) genes variants on lethal outcomes in the treatment of severe COVID-19 pneumonia. Contrary to our results, some researchers have found that such associations exist (Panda A.K. et al., 2020; Yamamoto N. et al., 2020). A possible explanation for this discrepancy is either the size of our study group, or the study design — our observation group included individuals with pneumonia and did not include individuals with uncomplicated COVID-19. Our retrospective study did not confirm the association of genetic polymorphism with lethal outcomes, but revealed their clinical predictors: low SpO_2/FiO_2 ratio, tachypnea, tachycardia, low systolic blood pressure, anemia, leukocytosis during the first days of hospitalization. These clinical features in the prognosis of lethal outcomes have been reported by other authors (Grasselli G. et al., 2020; Zhou F. et al., 2020). In particular, it was shown that high levels of leukocytes are associated with mortality in patients with COVID-19, and severe leukocytosis was more common in severe respiratory distress syndrome (Chen C.Y. et al., 2005; Feng X. et al., 2020; Zhao K. et al., 2020).

A. Annunziata et al. (2020) showed that the presence of the D allele of the *ACE* gene correlated with the level of respiratory failure. In our study, we found no association between the *ACE* (I/D) gene variants and viral pneumonia. From our results, the association of the heterozygous variant of the *CCR5* gene (W/del32) with the need for respiratory support and its duration is obvious. Patients with the heterozygous W/del32 variant had a significantly elevated white blood cell count in the complete blood count, which was a clinical predictor of lethal outcome in the examined patients. That is, patients with the heterozygous W/del32 variant are at risk of adverse effects and require early and long-term medical interventions, namely, long-term respiratory support. Contrary to our results, J. Gómez et al. (2020) indicate the protective effect of the del32 allele on the development of a complicated course of the COVID-19 disease. These differences in results can be explained by different research designs. In addition, we did not find a significant difference when comparing the frequencies of genotypes of the *CCR5* gene obtained for patients with COVID-19 in our study and in the study conducted by J. Gómez et al. (2020). It should be noted that the concept of the control group in the study of COVID-19 today is somewhat conditional because the pandemic has not ended yet, and patients in the study by J. Gómez et al. (2020) still have a chance to fall ill.

It is well known that the *CCR5* (del32) genetic variant is protective against HIV-infection — carriers of the heterozygous W/del32 variant have a lower risk, and carriers of the homozygous del32/del32 variant are not infected at all. It should be noted that recently the perspective of research of *CCR5* has changed, because *CCR5* is a component of the chemokine system. The *CCR5* receptor is expressed by monocytes, macrophages, neutrophils, dendritic cells, T lymphocytes (Th1, Treg, T_{17}-cells, memory T-cells — CD4rm), natural killers and basophils. Normally, the *CCR5* receptor binds to chemokine ligands of macrophage inflammatory proteins (MIP-1α, MIP-1β), monocyte chemotactic protein 2–4, RANTES and thus participates in the activation of immunocompetent cells and their migration into the inflammatory focus (Cherkashina I.I. et al., 2010). From the results of our study, we can assume that the receptor is involved in the development of a cytokine storm, which was found for carriers of the heterozygous W/del32 variant in which leukocytosis at the beginning of hospitalization and resulted in the increased need for respiratory support.

In this research, we expected that no W/del32 and del32/del32 variants of the *CCR5* gene would be detected in patients with severe viral COVID-19 pneumonia based on the analyzed studies. However, the frequency of distribution of these gene variants in the examined patients, which does not differ from that published in our previous studies (Dovzhenko S.P. et al., 2010), indicates that the *CCR5* (W/del32) variant affects not the risk of severe COVID-19 pneumonia, but its course with long-term respiratory support. This *CCR5* gene related mechanism in long-term respiratory support is likely to be neither unique nor leading, but will enable us to offer personal therapeutic strategies to a proportion of individuals with viral COVID-19 pneumonia and infected subjects. The obtained results indicate the need for further multifaceted research in this direction to determine the leading genetically mediated pathogenetic mechanisms of severe viral COVID-19 pneumonia.

Conclusions

1. Significant clinical predictors of lethal outcomes in patients with severe COVID-19 pneumonia were found on admission: lower SpO_2/FiO_2 ratios, tachypnea, tachycardia, anemia, leukocytosis during the first days of hospitalization, and need of mechanical lung ventilation.

2. The use of SOFA and Glasgow coma scales is promising for assessing the condition of a patient with severe COVID-19 pneumonia on admission and for predicting lethal outcomes during treatment.

3. The *CCR5* gene variant predisposed to long-term respiratory support in patients with severe COVID-19 pneumonia course. The overall duration of non-invasive and invasive respiratory support was significantly longer in patients with W/del32 genotype of the *CCR5* gene.

4. Patients with the W/del32 genotype of the *CCR5* gene had a significantly elevated white blood cell count in the complete blood test, and significantly increased leukocytes level was a clinical predictor of lethal outcomes in the examined patients.

5. The further search for predictors of severity in patients with COVID-19 pneumonia and the post-COVID syndrome development require urgent analysis based on a multidisciplinary approach for the development of personalized programs for the rehabilitation of patients and improving their quality of life.

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Делеційний варіант гена *CCR5* (rs333), а не варіант гена *ACE* (rs4340), пов'язаний із тривалою респіраторною підтримкою у пацієнтів із COVID-19-асоційованою пневмонією

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Резюме. *Мета — проаналізувати вплив варіантів генів ACE (c.2306-117_404I/D, rs4340) і CCR5 (del32, rs333) на перебіг тяжкої COVID-19-асоційованої пневмонії у пацієнтів, яким проводили лікування у відділенні інтенсивної терапії. Об'єкт і методи дослідження. У дослідження включений 31 пацієнт (16 чоловіків і 15 жінок) з діагнозом «вірусна COVID-19-асоційована пневмонія». Усім учасникам щодня проводили стандартні клінічні, інструментальні та лабораторні обстеження. Визначення варіантів генів ACE і CCR5 проводили молекулярно-генетичним методом із застосуванням алельспецифічної полімеразної ланцюгової реакції. Результати. Значущими клінічними предикторами летального кінця у пацієнтів із тяжкою COVID-19-асоційованою пневмонією були низький показник співвідношення SpO_2/FiO_2, тахіпное, тахікардія, знижений систолічний артеріальний тиск, анемія, лейкоцитоз при госпіталізації, а також потреба у тривалій штучній вентиляції легень. Пацієнти з гетерозиготним генотипом W/del32 за геном CCR5 порівняно із пацієнтами з генотипом W/W мали значуще тривалішу респіраторну підтримку, а саме — значуще більшу тривалість кисневої терапії з використанням кисневої маски (4,50±3,70 та 2,19±1,28 дня відповідно), значуще тривалішу штучну вентиляцію легень (15,00±4,24 та 4,40±4,98 дня відповідно) та значуще більшу загальну тривалість оксигенотерапії (9,60±5,68 та 4,19±3,84 дня відповідно). У пацієнтів із генотипом W/del32 за геном CCR5 був значуще підвищеним рівень лейкоцитів порівняно з пацієнтами із генотипом W/W (13,64±10,66 та 8,38±2,85 відповідно). Висновки. Значущими клінічними предикторами летального кінця у пацієнтів із тяжкою COVID-19-асоційованою пневмонією були низькі показники співвідношення SpO_2/FiO_2, тахіпное, тахікардія, анемія, лейкоцитоз при госпіталізації, а також потреба у штучній вентиляції легень. Генетичним предиктором перебігу тяжкої COVID-19-асоційованої пневмонії з підвищеною потребою у респіраторній підтримці був варіант гена CCR5. Варіант гена CCR5 асоційований із підвищеним рівнем лейкоцитів при госпіталізації. Отримані результати свідчать про необхідність подальших багатопланових досліджень у цьому напрямі з метою визначення провідних генетично опосередкованих патогенетичних механізмів розвитку тяжкої вірусної COVID-19-асоційованої пневмонії.*

Ключові слова: *COVID-19, пневмонія, гени, ACE, CCR5.*

Делеционный вариант гена *CCR5* (rs333), а не вариант гена *ACE* (rs4340), связан с длительной респираторной поддержкой у пациентов с COVID-19-ассоциированной пневмонией

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Резюме. *Цель — проанализировать влияние вариантов генов ACE (c.2306-117_404I/D, rs4340) и CCR5 (del32, rs333) на течение тяжелой COVID-19-ассоциированной пневмонии у пациентов, которым проводили лечение в отделении интенсивной терапии. Объект и методы исследования. В исследование включен 31 пациент (16 мужчин и 15 женщин) с диагнозом «вирусная COVID-19-ассоциированная пневмония». Все участники проходили ежедневно стандартные по-*

вторные клинические, инструментальные и лабораторные обследования. Определение вариантов генов ACE и CCR5 проводили молекулярно-генетическим методом с применением аллельспецифической полимеразной цепной реакции. Результаты. Значимыми клиническими предикторами летального исхода у пациентов с тяжелой COVID-19-ассоциированной пневмонией были низкий показатель соотношения SpO_2/FiO_2, тахипноэ, тахикардия, сниженное систолическое артериальное давление, анемия, лейкоцитоз при госпитализации, а также потребность в длительной искусственной вентиляции легких. Пациенты с гетерозиготным генотипом W/del32 по гену CCR5 в сравнении с пациентами с генотипом W/W имели достоверно более длительную респираторную поддержку, а именно — значимо большую продолжительность кислородной терапии с использованием кислородной маски (4,50±3,70 и 2,19±1,28 дня соответственно), значимо большую продолжительность искусственной вентиляции легких (15,00±4,24 и 4,40±4,98 дня соответственно) и значимо более длительную общую продолжительность оксигенотерапии (9,60±5,68 и 4,19±3,84 дня соответственно). У пациентов с генотипом W/del32 по гену CCR5 был значимо повышен уровень лейкоцитов по сравнению с пациентами с генотипом W/W (13,64±10,66 и 8,38±2,85 соответственно). Выводы. Значимыми клиническими предикторами летального исхода у пациентов с тяжелой COVID-19-ассоциированной пневмонией были низкие показатели соотношения SpO_2/FiO_2, тахипноэ, тахикардия, анемия, лейкоцитоз при госпитализации, а также потребность в искусственной вентиляции легких. Генетическим предиктором течения тяжелой COVID-19-ассоциированной пневмонии с повышенной потребностью в респираторной поддержке был вариант гена CCR5. Вариант гена CCR5 ассоциирован с повышенным уровнем лейкоцитов при госпитализации. Полученные результаты свидетельствуют о необходимости дальнейших многоплановых исследований в этом направлении с целью определения ведущих генетически опосредованных патогенетических механизмов развития тяжелой вирусной COVID-19-ассоциированной пневмонии.

Ключевые слова: *COVID-19, пневмония, гены, ACE, CCR5.*

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