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Transplantation of solid organs during the pandemic of new coronavirus infection

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Abstract

The end-stage stage of chronic diseases of solid organs is rather significant in the structure of morbidity and mortality among patients worldwide. To date, there are more than six million patients in this status worldwide. Heart, liver and kidney transplantation is the gold standard of treatment for these patients. The number of transplants is growing every year.

At the end of 2019, the world faced a new type of viral infection - SARS-CoV-2 − a highly contagious systemic respiratory disease transmitted by airborne droplets, which in three months led to a pandemic and killed hundreds of thousands of people. The pandemic has made adjustments to the structure of planned medical care. The number of planned operations has decreased significantly, and the number of the infection-associated complications has increased.

Patients with end-stage chronic diseases initially have weakened immunity and represent the category most susceptible to the infection. At

the moment, the question of patient management tactics remains open. There is no consensus on the patient management tactics before surgery and in the posttransplantation period for patients at the end-stage chronic disease of different organs. This topic requires further study and the development of treatment algorithms for such patients.

Keywords: heart transplantation, kidney transplantation, liver transplantation, viral infection, new coronavirus infection

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AT2, alveolar type II cells

ACE, angiotensin converting enzyme

CKD, chronic kidney disease

COPD, chronic obstructive pulmonary disease

DM, diabetes mellitus

HT, heart transplantation

KT, kidney transplantation

MLV, mechanical lung ventilation

RAAS, renin-angiotensin-aldosterone system

WHO, World Health Organization

Introduction

End-stage chronic diseases of solid organs play a definite role in the structure of morbidity and mortality among patients worldwide. To date, there are more than 6 million patients in this status in the world.

Annually, more than 150,000 kidney, heart, liver, and lung transplants are performed worldwide, which largely does not correspond to the number of recipients on the waiting list. For example, in the United States, the number of organ transplants performed makes about 40,000 operations, while the waiting list includes about 120,000 people, and 77,000 of them die while waiting for a donor organ. According to the World Health Organization (WHO), more than 1.5 million people with transplanted organs are registered in the world [1].

According to the Registry of the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA Registry), the overall incidence of chronic kidney disease (CKD) is 129 per million of the population, with diabetes mellitus (DM) being the cause of this disease in 20%. To date, the rate of kidney transplantation (KT) in the world corresponds to 35 operations per million population, 30% of them are related donor transplants. The 5-year survival rates for patients with a transplanted kidney from a cadaveric donor and a related donor differ and in 2018 were 86.6% and 93.9%, respectively [2]. In the Russian Federation (RF), about 50,000 people are monitored and treated with hemodialysis, of whom 13.7% are on the KT waiting list. In 2019, 1473 KTs were performed, which corresponded to 10 operations per million of population [3].

According to the Registries of the International Society for Heart and Lung Transplantation (ISHLT Registries), more than 147,000 heart transplants (HTs) have been performed worldwide, a significant number of them having been performed since 1992. The mean life expectancy of recipients is 12.5 years [4].

There are more than 700 potential recipients on the HT waiting list in the Russian Federation, and this list is growing every year. In 2019, the previously noted positive dynamics in reducing mortality on the waiting

list continued and made 6.7%. At the same time, the number of HTs exceeded 300 operations per year.

Orthotopic liver transplantation (OLT) has been performed in 132,000 patients; meanwhile, more than 7,000 operations are performed annually worldwide. In the Russian Federation, more than 350 operations are performed annually. According to the European Liver Transplant Registry (ELTR), five-year survival for this type of transplantation is 71%, and twenty-year survival is 41% [5].

New coronavirus infection

Novel coronavirus infection of 2019 (COVID-19) is a highly contagious, systemic, airborne respiratory disease that led to a global pandemic in 3 months and killed hundreds of thousands of people. Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) is a single-stranded positive RNA-containing virus, belongs to the Beta-CoV B lineage of the Coronaviridae family and has group II pathogenicity. It contains four major structural proteins, namely spike (S), envelope (E), membrane (M), and nucleocapsid (N). The main route of transmission of COVID -19 is airborne.

Initially, the virus enters the host by binding the S protein to *the angiotensin-converting enzyme (ACE) type II receptor* on the host cell membrane. The most accessible target for the virus is type II alveolar cells (AT2) of the lungs, which determines the development of pneumonia.

The SARS-CoV-2 pandemic made significant adjustments to the tactics of examination and treatment of patients with chronic diseases and transplanted organs.

The manifestations of the disease are extremely variable, from asymptomatic carriage to multiple organ dysfunction. The most common symptoms of COVID-19 are fever, cough, and shortness of breath [6].

The systemic inflammatory response induced by SARS-CoV-2 leads to a cytokine storm and organ dysfunction [7]. Patients with obesity, diabetes mellitus (DM), people of the older age group and patients with chronic kidney disease, immunocompromised patients are at the group of risk of a new coronavirus infection. Among patients with identified COVID-19 and CKD, in contrast to patients with COVID-19, the severe course of the disease is much more common than in the rest patient cohort, even in those with extrarenal chronic diseases [3]. Organ transplant recipients stand out separately in the high-risk patients due to the use of immunosuppressive therapy. The effect of immunosuppressants on the course of COVID-19 has not yet been sufficiently studied, however, patients taking appropriate therapy have a high risk of developing hypertension, DM. In patients with CKD, SARS-CoV-2 affects the renin-angiotensin-aldosterone system (RAAS), overactivating it, especially in patients with concomitant DM. Moreover, the use of ACE inhibitors in such cases often has no effect on the RAAS activity [5]. Despite optimizing the treatment of patients with COVID-19, the development of acute kidney injury is common. The totality of these data makes us to be more wary of the course of the disease, to develop relevant methods of the prevention and treatment for these patients.

The spread of SARS-CoV-2 acute respiratory infection carries risks not only for patients with chronic diseases. According to V.G. Puelles et al., the virus of a new coronavirus infection is characterized by a high tropism for kidney tissues, which in 77% of cases leads to the renal structure abnormalities [8], which consist of microvascular occlusion, endothelial injury, indicating the damage caused by SARS CoV-2 [9].

The pathophysiology of acute kidney injury in COVID-19 is characterized by the effect of the virus on ACE2. Thus, SARS-CoV-2 directly affects the tubular epithelium and podocytes, causing significant damage to them. Clinically, about 20% of patients in an intensive care unit have acute kidney injury characterized by proteinuria and hematuria and requiring the use of extracorporeal hemofiltration methods. However, all these abnormalities tend to regress, and when patients are discharged, their kidney function is fully restored [10, 11].

To date, the number of detected SARS-CoV-2 infection cases is approaching 300 million in the world and has already exceeded 10 million in Russia. The number of patients who has died makes more than 5 million in the world, more than 300,000 in Russia since the start of the pandemic. The number of people infected is growing daily; the virus mutation and the fragility of immunity to it expose people to the risk of reinfection and the involvement of an increasing number of previously immune populations.

In the Chinese patient cohort, the majority of hospitalized patients in 2020 were men over 56 years of age, 26% needed treatment in an intensive care unit, and the mortality rate was 28%. More than half of the patients had comorbid diseases. The most common risk factors for developing a severe course of the disease were hypertension, DM, and coronary heart disease.

Clinically, COVID-19 presents with fever and cough accompanied by fatigue. In clinical analyzes, 40% of patients had lymphocytopenia [12].

A large study by S. Richardson et al. based on the data from 5700 hospitalized patients demonstrated that the most common comorbidities were hypertension (56.6%), obesity (41.7%), and DM (33.8%). The most common manifestations of the disease were fever and shortness of breath. Mortality was 21%, and all patients under 20 years of age remained alive,

but the older was the age, the higher became mortality. In the group of patients over 65 years of age who required the use of mechanical lung ventilation (MLV), the mortality rate was 97.2%. Among patients who received treatment without mechanical ventilation in the same age range, this figure was 26.6% [13].

There have been studies evaluating the survival of organ transplant patients with COVID-19.

Organ transplantation in conditions of pandemic

Since the beginning of the SARS-CoV-2 pandemic, the structure of medical care in various countries of the world has changed significantly. The number of organ transplants significantly decreased, which led to an increase in mortality rates among patients on the waiting list suffering the end-stage organ failure [14, 15].

According to the International Registry in Organ Donation and Transplantation (IRODAT), there is a decrease in the activity of organ transplantation surgery in most countries of the world; however, in some countries, transplantation activity continues to grow [16].

According to A. Loupy et al., since the onset of the COVID-19 pandemic, the number of solid organ transplants had significantly decreased, which was largely accounted to a decrease in the number of kidney transplants [17].

In a meta-analysis by M. Alfishawy et al. including the data from 46 studies, and a total of 320 recipients who had previously undergone organ transplantation, showed that only 21.7% of patients had an asymptomatic or mild course of a new coronavirus infection. Moderate and severe course of the disease occurred in comparable proportions in this patient category: 38.7% and 39.6%, respectively. The study included 220 kidney recipients, 42 liver recipients, 22 lung recipients, 19 heart

recipients, 8 recipients who underwent bone marrow or hematopoietic stem cell transplantation (HSCT), and 9 recipients of two organs [18]. Overall mortality among these patients was 20%. It is worth noting that in 58% of deaths, patients had a number of comorbidities having a negative prognostic sign in the general population. Thus, 58% of the deceased patients suffered from hypertension, 29% had DM, as well as malignant neoplasms, obesity, chronic obstructive pulmonary disease (COPD), hepatitis C or HIV. We should note that only 14% of recipients had no comorbidities. The most common cause of death was the respiratory distress syndrome [19].

In their study, M. Pereira et al. analyzed the data of 90 recipients of whom 51% were kidney recipients, 18.8% lung recipients, 14% liver recipients, 10% heart recipients, and 5% recipients of two organs. Most of the patients had a mild or moderate course of the disease. Twenty-three patients required treatment in the intensive care unit, which made 26% of the total number of infected organ transplant patients and 34% of hospitalized patients. Of these, 16 patients died, which corresponded to 52% of all recipients treated in the intensive care unit. During the study period, there were no documented cases of thromboembolic complications or rejection after making the COVID-19 diagnosis [19].

Summarizing the data, it is worth noting that older age is one of the most common predictors of adverse outcomes in organ transplant recipients with comorbidities. And lethality among recipients who underwent organ transplantation is higher than in the general population [18, 20].

According to the national multicenter observational study "ROKKOR-recipient", the risk of adverse outcomes in transplanted patients against the background of COVID-19 is higher than in the general population. Among the risk factors, there are those similar to the

world ones, such as hypertension, DM, renal failure, and concomitant cardiovascular diseases [21].

Renal transplant recipients and candidates tend to be at a high risk due to the high incidence and prevalence of hypertension, diabetes, obesity, and advanced age in this group. According to some data, 81% of kidney transplant recipients with COVID-19 have high-risk comorbidities [22].

The study by A. Imam et al. showed that in the cohort of recipients after KT, the most common complaint was fever; but unlike the general population, 15% of patients did not have this symptom. Despite this, it was shown that all other symptoms were significantly more common, and patients also had chest tightness and pain, dehydration, conjunctivitis, dizziness, and weight loss, which were not characteristic of both populations. Approximately 57% of patients had severe course of the disease, and 43% had mild to moderate disease course [22]. According to WHO, the recovery period was about 2 weeks for mild cases of the disease, and from 3 to 6 weeks for severe.

Among the deceased KT recipients, more than half were over 65 years of age; and hypertension, DM, and COPD were seen in 88.8%, 33.3% and 100%, respectively. Also in these patients, blood tests showed lymphocytopenia and high levels of *C*-reactive protein [36]. Lymphocytopenia may be a predictor of poor outcome in the general cohort of patients; however, immunosuppressive drugs given to kidney transplant recipients may cause these changes. These events occur in 66.6% of deceased patients and may be an independent predictor of mortality [23].

In kidney transplant recipients diagnosed with COVID-19, acute kidney injury occurs in 44.4% of cases, which is significantly higher than in the general cohort and is associated with a worse prognosis [24].

According to B.G. Abu Jawdeh et al., 20% of patients who underwent KT required treatment in the intensive care unit, and 24.6% of patients required the use of mechanical ventilation. Mortality in this group was significantly higher and amounted to 18.8% when compared with the total cohort of patients with a new coronavirus infection (3.4%). Meanwhile, among recipients who underwent surgical treatment more than a year ago, 16.3% died, and among those operated on less than a year ago, 11.1% died [25].

In their study, R.O. Kantaria et al. found that patients with respiratory failure requiring mechanical ventilation had a 17.2 times greater risk of death and a 21.5 times greater risk of needing hemodialysis. Meantime, the absence of sepsis in this category of patients reduced the risk of death by 2.6 times [26].

According to world literature, HT recipients have comparable results to those in the absence of the COVID-19 pandemic within 30 days after surgical treatment It was shown that in the early postoperative period in patients who underwent HT in 2020, there were no statistically significant differences in the incidence of acute rejection, the use of renal replacement therapy, and survival. However, it is noted that the strict isolation of patients is an essential link in preparing a patient for transplantation [27].

Data analysis of patients undergoing HT (A. Singhvi et al.) showed that severe and critical course of COVID-19 occurred in 23% of cases, and the most common symptoms were fever, cough, and complaints of painful manifestations in the gastrointestinal tract. The mean time after HT before getting infected with SARS-CoV-2 was 4.6 years. All patients showed increased blood levels of inflammatory biomarkers. Patients required intubation in 18% of cases, and cardiotonic support in 14%. Mortality among patients who had a positive PCR test was 23%, and not

a single patient on mechanical ventilation survived. In conclusion, it was noted that the course of the disease in patients with a transplanted heart is similar to that in the general group of patients with COVID-19 [28]. Despite the presented data, H.Aziz et al. showed that when a patient is hospitalized in the center where transplantation was performed, mortality in this cohort decreased to 12.5%. The main predictors of death were the blood level of D-dimer over 1 mg/mL and elevated troponin levels [29].

J. Vilaro et al. described a clinical case of severe disease caused by SARS-CoV-2. The recipient had a positive PCR test result for COVID-19 within 30 days after the HT. The rapid deterioration of the condition was accompanied by a newly diagnosed biventricular cardiac dysfunction, reversible acute kidney injury, and distress syndrome. During the observation period, the patient did not show an acute graft rejection; immunosuppressive therapy remained at the same level, and a decrease in myocardial contractile function was qualified as stress cardiomyopathy. For the treatment of the cardiac graft dysfunction, the tactics chosen were consistent with the treatment of acute rejection. At the same time, the developed acute respiratory failure required a prolonged mechanical ventilation. Owing to the treatment, the patient was discharged on the 12th day with complete regression of the pathological process of the lungs, kidneys, and heart. Thus, it was shown that SARS-CoV-2 can provoke a severe course of the disease in heart transplant recipients with reversible consequences [30].

The liver ranks second among the most common organ transplanted in the world [31]. Unlike the end-stage of kidney and heart diseases, in which the use of auxiliary life support techniques is possible, no effective medical technologies for protecting liver function currently exist. This makes OLT an indispensable procedure in the treatment of patients with end-stage liver diseases.

The lungs are most often affected by a new coronavirus infection, and acute kidney damage often occurs. However, there is evidence of acute liver injury characterized by an increase in the levels of alanine aminotransferase and aspartate aminotransferase in the blood serum. These changes occur in 14%-53% of cases in patients with confirmed COVID-19. In some studies, there is an increase in the level of γ-glutamyltransferase, which also indirectly indicates the involvement of hepatic structures in the pathological process [32].

There is currently no statistically significant evidence that patients with liver failure are more susceptible to novel coronavirus infection. Despite this, SARS-CoV-2 can lead to reactivation of diseases such as HBV infection [33]. And the mortality in patients with pre-existing liver diseases and COVID-19 can reach 40% [34].

Among patients who underwent OLT, the percentage of patients requiring hospitalization is comparable to the group of patients who did not undergo surgical treatment. The need for monitoring the patients in the critical and intensive care unit, as well as for assisted lung ventilation was more frequent in the group of transplanted patients (26-28%). However, mortality in these patients is lower and amounted to about 19–22% [35, 36].

An important issue in the OTP process during the pandemic is the exclusion of COVID-19-infected donors.

The American Association for the Study of the Liver (AASLD), the European Society for the Study of the Liver (EASL), and the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) recommend that the donor be screened for active infection with SARS-CoV-2 to prevent COVID-19 infection in the recipient, and if the infection is present in the donor, it is worth refusing to use the organs of this patient. The recipient infection through organ transplantation can

lead to severe disease manifestations in patients receiving immunosuppressive therapy [37, 38].

S.M. Lagana et al described a clinical case of infection in a recipient of a liver lobe from a living donor infected with COVID-19. Clinical manifestations of infection appeared in the patient in the form of developed respiratory disorders and fever on the 4^{th} day after surgical treatment. When conducting a PCR test, a positive result was obtained. Liver biopsy revealed the changes characteristic of moderate acute hepatitis, as well as the portal features typical of mild and moderate cellular rejection. Clinically the patient was in the hospital patient ward having mild respiratory symptoms that did not require the use of mechanical ventilation [39].

R. Romagnoli et al. conducted a study that included 10 liver transplant recipients from the post-mortem donors infected with COVID-19. However, the liver biopsy test for SARS-CoV-2 RNA was negative in all donors. The recipients had a history of previous COVID-19 or vaccination history. During the follow-up period, none of the recipients had a positive PCR test. Despite the small sample size of the study, the conclusion was made that it is possible to safely use organs from donors infected with COVID-19, provided that the recipient has immunity to a prior novel coronavirus infection [40].

Immunosuppressive therapy

One of the most controversial issues in the management of patients with COVID-19 after organ transplantation is the change in the immunosuppression regimen. There is currently no absolute understanding of the impact of immunosuppression on the COVID-19 progression. Immunosuppressive therapy in recipients may carry the risks of developing a more severe course of the disease and longer duration of

its active phase compared to other patients with COVID-19. However, the reduction or withdrawal of immunosuppressive therapy may lead to an acute rejection.

Immunosuppressive drugs may make patients more susceptible to SARS-CoV-2 infection. For example, mycophenolate mofetil prevents the proliferation of lymphocytes and the production of antibodies, which reduces the immune response and is associated with a higher incidence of viral infections [41]. Drugs used for immunosuppression can also activate the RAAS and, as a result, ACE2, a target for SARS-CoV-2 [28].

Patients after organ transplantation have to take immunosuppressive drugs in the postoperative period to maintain the graft function. The principal maintenance immunosuppressive drug groups are corticosteroids, calcineurin inhibitors, mycophenolates, and proliferative signal inhibitors (mTOR inhibitors) [42]. According to S.V. Gautier et al., recipients of the heart, liver, and kidney at the time of the manifestation of a new coronavirus infection received tacrolimus alone or in combination with methylprednisolone. However, some liver and kidney recipients took methylprednisolone as monotherapy or in combination with everolimus, everolimus in combination with cyclosporine or tacrolimus, or cyclosporine with methylprednisolone [21].

According to A. Imam et al., the most common immunosuppressive regimen in kidney transplant recipients included tacrolimus, mycophenolate mofetil, and prednisone (56.9%). It was noted that 13.8% of patients with COVID-19 recovered without changing immunosuppressive therapy. Among the patients who died, the following were used: tacrolimus in 50%, mycophenolate mofetil in 100%, prednisolone in 28.5%, cyclosporine in 100%, sirolimus in 100%, mizoribine in 100%. The dose of tacrolimus was reduced in 33.3% of cases, and that of prednisolone in 71.4% [22].

Currently, there are no statistically significant data on the adverse effect of immunosuppressive therapy on the severity of COVID-19, which is not a recognized risk factor for adverse events [43]. Therefore, there is no need to reduce dosage or discontinue immunosuppressive therapy in organ transplant recipients with asymptomatic or mild COVID-19 [44]. Lymphopenia, a developed bacterial or fungal infection in the cases of severe COVID-19 can be regarded as factors for making a decision to reduce the dose of immunosuppressive therapy [45]. Glucocorticoids reduce the release of inflammatory mediators and inhibit neutrophil migration, thus reducing systemic inflammation associated with COVID-19. On the other hand, in order to reduce the risk of developing adrenal insufficiency, it is worth reducing the prednisolone dosage [46]. Glucocorticoid drugs such as dexamethasone and methylprednisolone can lower blood serum tacrolimus concentrations by induction of some liver cytochromes [18]. According to M. El Cassas et al., in the presence of fever, severe polysegmental pneumonia, and lymphopenia, it is recommended to reduce the dosage of the calcineurin inhibitor, consider reducing the doses for tacrolimus/cyclosporine, withdraw mycophenolate mofetil and azathioprine [43].

In liver transplant recipients on immunosuppression therapy infected with COVID-19, the virus may retain its activity longer, which does not entail an increase in the risk of adverse events [47].

In the treatment of patients with COVID-19, it is worth considering the drug interactions of immunosuppressive drugs and drugs aimed at suppressing SARS-CoV-2. It is worth noting that hydroxychloroquine and an IL-6 inhibitor can significantly increase the metabolism of calcineurin inhibitors and mTOR inhibitors and increase their concentration. This requires increased attention and possible reduction in drug dosing [42].

A lopinavir and ritonavir combination is not recommended to use with many forms of steroids, or with simvastatin, atorvastatin, domperidone or sirolimus. There is, in addition, the risk of potential interactions with cyclosporine, mycophenolate, tacrolimus. A side effect of these regimens may be a change in the QT interval duration, which requires careful monitoring in patients with cardiovascular diseases [43]. However, there is evidence of COVID-19 successful treatment in liver transplant recipients in such cases [48].

M. Fernandez-Ruiz et al. used lopinavir and ritonavir to treat 8 kidney [44%], 6 liver [33%], and 3 heart [22%] recipients infected with SARS-CoV-2. Hydroxychloroquine was added to the therapy in 50% of cases. At the same time, immunosuppressive therapy was not canceled in any case. The mortality rate was 28% [47].

M.R. Pereira et al. used hydroxychloroquine to treat the patients, and remdesivir was added when therapy was insufficient. Additionally, azithromycin or tocilizumab was used in the development of a "cytokine storm". The approach to immunosuppressive therapy included a moderate dose reduction of drugs, especially of mycophenolate mofetil and azathioprine. Mortality was 18%. This study did not provide data on the course of the disease and the difference in treatment approaches with regard to the prior transplanted organ, although it included 46 patients: 17 patients with lung transplants, 13 with transplanted liver, 9 with transplanted heart, and 5 with two transplanted organs [19].

According to E. Montagud-Marrahi et al., lopinavir and ritonavir were administered to treat 33 kidney transplant recipients, two of whom were also pancreas recipients. As for the approach to immunosuppression, mycophenolate mofetil, calcineurin inhibitors, and mTOR inhibitors were withdrawn in all patients. It should be noted that the result of this treatment regimen was a 94% survival of recipients [49].

Mortality among organ transplant recipients with SARS-CoV-2 infection was higher compared to that among the patients with COVID-19 in general. The maximum immunosuppressive load in recipients is noted in the first 3 months after transplantation, when patients are at a maximum risk of viral infection and the severity of its manifestations during this period [50]. In organ transplant patients, the clinical presentation of COVID-19 may differ significantly from the general population, so they should be treated with more caution.

American Society of Transplantation (AST), in addition to limiting contact with infected people and the strictest self-isolation, recommends vaccinating all patients with transplanted organs [51]. To date, the following technology platforms are used to create vaccines: inactivated whole-virion vaccines, vector non-replicating vaccines, RNA vaccines, and recombinant protein vaccines [52].

The SARS-CoV-2 pandemic poses a huge threat to organ transplant patients and is associated with higher mortality risks than in the general population. Vaccination may reduce the risk of infecting with SARS-CoV-2 or the disease severity. However, immunosuppressive therapy can significantly reduce or change the efficacy of different types of vaccines [53].

Vaccination

In the 21st century, humanity is faced with diseases such as the severe acute respiratory syndrome, Middle East respiratory syndrome, and the Ebola virus. Thanks to the accumulated experience, the SARS-CoV-2 vaccine was developed in a short time and has a high efficiency.

To date, the following technology platforms are used to create vaccines: inactivated whole-virion vaccines, vector non-replicating vaccines, mRNA vaccines, and recombinant protein vaccines [54].

The effectiveness of the humoral immunity formed in recipients of solid organs is significantly lower when compared to that in the general population. Older age and concomitant DM are recognized as risk factors for a decrease in the immune response. There is also a correlation between the time elapsed since transplantation and the kidney function indicator (glomerular filtration rate). The need for high doses and triple immunosuppressive therapy reduces the seroconversion rate [55, 56].

The humoral immunity response after one dose of the mRNA vaccine was noted in fewer than 11% of patients and in 36% after the second dose. Only when vaccinated with three doses of this type of vaccine, a seropositive result was obtained in 65.6% of cases. When using a vector vaccine, the serological response reaches a level of 16.7%, but after the second and third doses it does not exceed 50% [57].

In some cases, vaccination in recipients takes place with minimal undesirable manifestations (increase in body temperature up to 37.5° C, myalgia). In the vast majority of cases, it is tolerated asymptomatically, regardless of the vaccine [58].

In their study, S.E. Voskanyan et al. demonstrated the clinical significance of vaccination in liver transplant recipients. In the group of vaccinated, who were not previously ill, a new coronavirus infection was detected in 7% of liver transplant recipients, while in 34% among those unvaccinated [59].

As with influenza vaccination, one of the options for improving the immune response may be to increase the dose of the vaccine for recipients of solid organs [60].

Conclusion

Thus, COVID-19 in patients in the end-stage of a renal, liver, or heart disease and in patients undergoing solid organ transplantation has

diverse disease course and requires different treatment options, depending on the severity of the disease, clinical and morphological characteristics of patients, as well as on the previously transplanted organ. Despite comparable results in the treatment of hospitalized patients, algorithms for the management and monitoring of patients in this group have not yet been developed, which requires further research in this field.

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