Research Article
https://doi.org/10.23934/2223-9022-2021-10-4-636-641

COVID-19 Course in Vaccinated Patients

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AIM OF STUDY To conduct a retrospective analysis of treatment outcomes for COVID-19 in unvaccinated and vaccinated patients.
MATERIAL AND METHODS The present retrospective single-center study included 209 patients who were vaccinated in history and hospitalized at the City Aleksandrovskaya Hospital for infection with COVID-19 in the period from April 5, 2020 to July 9, 2021. The average period between vaccine administration and hospitalization was 18.0 ± 11.0 days. In all cases, a positive result of the polymerase chain reaction (PCR) for the presence of SARS-CoV-2 was obtained. These patients were included in Group 1. The comparison group included 475 unvaccinated patients with comparable lung tissue damage according to multispiral computed tomography of the chest (MSCT) and a positive PCR result for the presence of SARS-CoV-2, selected randomly over the same observation period.
RESULTS The lesions of the lung tissue according to the results of chest MSCT upon admission of the group were comparable (p=0.55). All deaths were observed in the group of unvaccinated patients (n=46; 9.7%; p<0.0001). In all cases, the cause was an increase in multiple organ failure. In the same cohort of patients, there was a statistically significantly greater number of deep vein thrombosis of the upper and lower extremities (p=0.02). In the group of vaccinated patients (1st), arterial thrombosis of various location was not diagnosed, while in the 2nd group (comparison), this pathology was detected in every 10th patient. At the same time, thrombosis of the arteries of the lower extremities developed statistically more often (n=52; 10.9%; p<0.0001). This condition was accompanied by an increase in laboratory parameters of the inflammatory reaction and coagulopathy with the progression of lung tissue damage to the 3–4th degree according to the results of MSCT. However, in 37 (7.8%) cases, open thrombectomy was not possible, and on the first day after the operation, repeated thrombosis developed, followed by amputation of the limb. In 23 (4.8%) cases, a fatal outcome was observed.
CONCLUSION Vaccination prevents the severe course of covid-19: the progression of pneumonia, coagulopathy, and inflammatory syndrome. In vaccinated patients, no deaths, pulmonary embolism were observed, which demonstrates the absence of a severe course of the disease. All arterial thrombosis associated with covid-19 develops in unvaccinated patients and is accompanied by a high incidence of repeated thrombosis, requiring subsequent amputation of the limb. The widespread introduction of vaccination will help reduce the severity of the course and prevent complications of the new coronavirus infection.
Key words: COVID-19, novel coronavirus infection, thrombosis, SARS-CoV-2, vaccine
For citation Linets YuP, Artyukhov SV, Kazantsev AN, Zaitseva TY, Roshkovskaya LV, Sokolova SV, et al. COVID-19 Course In Vaccinated Patients. *Russian Sklifosovsky Journal of Emergency Medical Care*. 2021;10(4):636–641. https://doi.org/10.23934/2223-9022-2021-10-4-636-641 (in Russ.)
Conflict of interest Authors declare lack of the conflicts of interests
Acknowledgments, sponsorship The study had no sponsorship
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APTT - activated partial thromboplastin time
CI - confidence interval
ALV - artificial lung ventilation
CEE - carotid endarterectomy
CABG - coronary artery bypass grafting
INR - international normalized ratio
MSCT - multislice computed tomography
ChO - organs of the chest
ACVA - acute cerebrovascular accident
ICU - intensive care unit
OR - odds ratio
PT - prothrombin time
PCR - polymerase chain reaction
DM - diabetes mellitus
*C*RP - *C*-reactive protein
TIA — transient ischemic attack
COPD - chronic obstructive pulmonary disease
CRF - chronic renal failure
PCI - percutaneous coronary intervention

INTRODUCTION

In the process of studying the incidence of a new coronavirus infection (*COVID*-19) it was confirmed that the virus affects all segments of the population, regardless of gender and age [1–3]. At the same time, the only way to prevent the severe course of the pathology become vaccination with the formation of herd immunity. The first vaccine in the world that showed its effectiveness and safety was Sputnik V (Gam-*COVID*-Vac - a combined vector vaccine), developed by the National Research Center for Epidemiology and Microbiology named after N.F. Gamaleya [4]. Mass voluntary vaccination on the territory of the Russian Federation began in the fall of 2020 and continues to the present. However, the use of the vaccine cannot completely prevent infection *COVID*-19 [4–7]. At the same time, vaccinated patients can carry a new coronavirus infection in a mild form and without severe complications (thrombosis, etc.) [4–7]. To date, there are not enough studies demonstrating the results of the course of *COVID*-19 in this cohort of patients. There is also no data on the incidence of arterial and venous thrombosis of various localization in vaccinated patients infected with *COVID*-19.

Goal and objectives of the study: to conduct a retrospective analysis of *COVID*-19 treatment outcomes in unvaccinated and vaccinated patients.

MATERIAL AND METHODS

St. Petersburg GBUZ "City Alexander Hospital" is a multidisciplinary hospital that provides care to 95,000 or more patients a year. After reprofiling in April 2020, the hospital, while maintaining its profile, began accepting patients with *COVID*-19.

This retrospective single-center study included 209 patients vaccinated with both full and incomplete cycle vaccines available in the country and hospitalized in St. Petersburg State Budgetary Institution of Health "City Alexander Hospital" due to infection with *COVID*-19 in the period from April 5, 2021 to July 9, 2021. The mean period between vaccine administration and hospitalization was 18.0±11.0 days. In all cases, a positive polymerase chain reaction (PCR) result was obtained for the presence of *SARS*-CoV-2. These patients were included in the 1st (main) group.

The comparison group (Group 2) included 475 unvaccinated patients with comparable lesions of the lung tissue according to multislice computed tomography of the chest (MSCT of the chest) and a positive PCR result for the presence of *SARS-CoV*-2, randomly selected over the same follow-up period.

Inclusion Criteria:

1. Positive PCR result for the presence *SARS-CoV*-2;
2. The presence of community-acquired viral polysegmental pneumonia according to MSCT of the OGK.

Exclusion criterion: the presence of a decompensated comorbid pathology (myocardial infarction, acute cerebrovascular accident, end-stage cancer, etc.), which determines the severity of the condition and requires treatment in the intensive care unit with a negative prognosis for the course of the disease.

Assistance to patients with a new coronavirus infection was provided in accordance with the current version of the Interim Guidelines for the Prevention, Diagnosis and Treatment of a New Coronavirus Infection (*COVID*-19) Ministry of Health of the Russian Federation and in accordance with the standards and Procedures for the provision of assistance for each profile, as in the pre-Covid period.

The end points studied in this work were: death, venous and arterial thrombosis of various localization, limb amputation.

STATISTICAL ANALYSIS

The type of distribution was determined using the Kolmogorov–Smirnov test. Groups were compared using the Mann-Whitney test and Pearson's Groups were compared using the Mann-Whitney test and Pearson's χ-square with Yates correction. Differences were rated as significant at $p<0{,}05$. The research results were processed using a package of applied programs *Graph Pad Prism (www.graphpad.com)*.

RESULTS

The groups were comparable in all respects. Most of the patients were elderly and of male gender. One in five patients had type II diabetes. In isolated cases, patients had a history of revascularization of the brain (carotid endarterectomy) or myocardium (percutaneous coronary intervention, coronary bypass grafting). One patient in 10 had chronic obstructive pulmonary disease. Damage to the lung tissue according to MSCT of the ChO most often corresponded to the 2nd degree. Oxygen support for breathing through nasal cannulas (oxygen insufflation at a rate of 5 to 10 l/min) was required in 28 patients (13.4%) in the 1st group, 54 patients (11.4%) in the 2nd group (Table 1).).

Table 1

Clinical and anamnestic characteristics

Indicator	Group 1 Vaccinated patients	Group 2 Unvaccinated patients	*p*	Odds ratio	95% confidence interval
	n=209	*n*=475			
Age, *M*±*m*, years	66,4±5,7	65,2±4,9	0,43		
Male gender, *n* (%)	135 (64,6)	297 (62,5)	0,66	1,09	0,77–1,53
Diabetes, *n* (%)	41 (19,6)	96 (20,2)	0,94	0,96	0,64–1,44
COPD, *n* (%)	22 (10,5)	54 (11,4)	0,84	0,91	0,54–1,55
CRF, *n* (%)	28 (13,4)	56 (11,8)	0,64	1,15	0,71–1,88
History of PCI, *n* (%)	7 (3,3)	18 (3,8)	0,95	0,87	0,36–2,14
CSh in history, *n* (%)	2 (0,9)	6 (1,2)	0,96	0,75	0,15–3,77
History of stroke/TIA, *n* (%)	8 (3,8)	21 (4,4)	0,88	0,86	0,37–1,97
CEE in history, *n* (%)	3 (1,4)	5 (1,05)	0,96	1,36	0,32–5,78
Oncological disease, *n* (%)	12 (5,7)	34 (7,1)	0,60	0,79	0,4–1,55
Damage to lung tissue, *M*±*m*, %	31,7±12,5	34,1±11,6	0,55		
SpO_2, *M*±*m*, %	94,5±2,0	95,0±3,0	0,27		

Notes: MLV — mechanical lung ventilation, CABG — coronary artery bypass grafting, CEE — carotid endarterectomy, ACVA — acute cerebrovascular accident, DM — diabetes mellitus, TIA — transient ischemic attack, COPD — chronic obstructive pulmonary disease, CRF — chronic renal failure, PCI — percutaneous coronary intervention, SpO_2 — oxygen saturation

According to the dynamics of laboratory parameters, in both groups at the time of admission, coagulopathy was noted with an increase in the level of *D*-dimer. At the same time, this indicator had statistically significantly higher values among unvaccinated patients. (p=0.01). The same trend was revealed by the concentration of ferritin (p=0.01), interleukin-6 (p=0.02) and *C*-reactive protein (*C*RP) (p=0.04). On the 3rd day after admission, despite ongoing anticoagulant therapy, a statistically significant decrease in activated partial thromboplastin time (APTT) was recorded in the group of unvaccinated patients.) (p=0.001) and prothrombin time (PT) (p=0,04). Also, in both groups, there was an increase in the values of other indicators of inflammation/coagulation with a statistically significant predominance in the cohort of unvaccinated patients: *D*-dimer, p=0,001; ferritin, p=0,001; *C*RP, p=0.001; interleukin-6, p=0.01. At the time of discharge from the hospital/death, APTT and PT in the group of unvaccinated patients continued to decrease with a critical increase in other indicators. At the same time, the levels of *D*-dimer and ferritin in the cohort of those vaccinated corresponded to the norm (Table 2).

Table 2

Dynamics of the patient's laboratory parameters

Indicator	Norm	On admission		p	3rd day after admission		p	At the time of release/ fatality		p
		Group 1	Group 2		Group 1	Group 2		Group 1	Group 2	
APTT, *M*±*m*, сек	25–35	28,3±2,9	25,3±1,2	0,74	37,1±2,4	20,2±0,1	0,001	37,5±1,3	18,1±0,5	0,001
Prothrombin time, *M*±*m*, sec	11,5–16,0	12,8±1,2	12,2±0,5	0,89	16,5±1,3	9,7±0,2	0,04	16,8±0,3	9,4±0,3	0,04
INR, *M*±*m*	0,8–1,2	1,02±0,1	1,03±0,2	0,10	1,02±0,1	1,00±0,3	0,09	1,04±0,2	1,00±0,1	0,09
D- dimer, *M*±*m*, ng/ml	<230	382,5±111,6	534,1±182,7	0,01	399,8±103,5	964,7±148,3	0,001	215,3±36,1	1143,4±363,1	0,0001
Ferritin, *M*±*m*	21,81–274,66	231,7±89,4	446,5±116,1	0,01	236,4±64,3	782,6±103,4	0,001	128,1±53,2	831,5±64,2	0,0001
*C*RP, *M*±*m*, mg/l	0–5,0	125,8±41,2	321,5±82,3	0,04	133,1±51,0	527,5±91,9	0,001	64,6±22,8	672,3±73,1	0,0001
Interleukin -6, *M*±*m*, pg/ml	<7	114,2±70,7	189,6±90,5	0,02	118,1±64,5	195,1±76,3	0,01	23,0±6,2	362,3±36,1	0,001

Notes: APTT — activated partial thromboplastin time, INR — International Normalized Ratio, *C*RP — *C*-reactive protein

Hospital complications

Speaking about the results of hospitalization, it should be noted that all deaths were recorded in the group of unvaccinated patients (n=46; 9.7%; p<0.0001). In all cases, the cause was an increase in multiple organ failure. In the same cohort of patients, there was a statistically significantly greater number of deep vein thrombosis of the upper and lower extremities (p=0.02). In the group of vaccinated patients, arterial thrombosis of different localization was not diagnosed, while in the 2nd group this lesion was detected in every 10th patient. At the same time, thrombosis of the arteries of the lower extremities developed statistically significantly more often (n=52; 10.9%; p<0.0001). This complication was accompanied by an increase in laboratory parameters of the inflammatory response and coagulopathy with progression of lung tissue damage to grade 3-4 according to the results of MSCT. In 37 cases (7.8%), open thrombectomy was impossible, and on the first day after the operation, repeated thrombosis developed, which required subsequent amputation of the limb. Of these, in 23 cases (4.8%) a fatal outcome was recorded (Table 3).

Table 3

Hospital acquired complications

Indicator	Group 1 Вакцинированные	Group 2 Невакцинированные	p	Odds ratio	95% DI
	n=209	n=475			
Fatal outcome, n (%)	0	46 (9,7)	<0,0001	0,02	0,001–0,35
Thrombosis of the superficial veins of the upper extremities, n (%)	0	1 (0,2)	0,67	0,75	0,03–18,62
Deep vein thrombosis of the upper extremities, n (%)	2 (0,9)	23 (4,8)	0,02	0,18	0,04–0,81
Deep vein thrombosis of the lower extremities, n (%)	7 (3,3)	39 (8,2)	0,02	0,38	0,17–0,88
Ascending thrombophlebitis of the great saphenous vein, n (%)	0	2 (0,4)	0,86	0,45	0,02–9,46
Pulmonary embolism, n (%)	0	4 (0,8)	0,43	0,25	0,01–4,66
Thrombosis of the internal carotid artery followed by carotid endarterectomy, n (%)	0	4 (0,8)	0,43	0,25	0,01–4,66
Thrombosis of lower extremity arteries followed by thrombectomy, n (%)	0	52 (10,9)	<0,0001	0,01	0,001–0,31
Thrombosis of the arteries of the upper limbs followed by thrombectomy, n (%)	0	2 (0,4)	0,86	0,45	0,02–9,46
Retrombosis of arteries of the lower extremities after thrombectomy, n (%)	–	37 (7,8)	–	–	–
Amputation of the lower limb, n (%)	–	37 (7,8)	–	–	–

It should be noted that due to the increase in the severity of the condition, 7 vaccinated patients were transferred to the intensive care unit (ICU) in 4.5 ± 1.5 days after hospitalization. (3,3%). After compensation for the state and regression of the intoxication syndrome, after 2.5±1.0 days, all these patients were transferred to the infectious departments. Also, 69 unvaccinated patients were transferred to the ICU 2.5±1.0 days after hospitalization (14.5%). Of these, compensation of the condition with subsequent transfer to the infectious diseases department was achieved only in 17 cases (3.6%) after 4.0±1.0 days, and in 46 cases (9.7%) a fatal outcome developed after 2.5±1.5 days.

DISCUSSION

Despite the fact that initially all patients were comparable in terms of the severity of lung tissue damage and clinical and anamnestic characteristics, a negative trend in the course of the disease was revealed among unvaccinated patients. In particular, in this cohort of patients, already during hospitalization, a statistically significantly higher level of the concentration of *D*-dimer and the inflammatory marker ferritin was noted (see Table 2). In the future, with a progressive increase in all laboratory parameters of coagulopathy and inflammation, an increase in the volume of lung tissue damage was noted according to MSCT of the ChO (45,5±15,5%). Arterial thrombosis of various localization became a complication of the infectious process. In the vast majority of cases, thrombectomy from the arteries of the lower extremities was ineffective, followed by repeated thrombosis and amputation.

Unvaccinated patients were transferred to the ICU in a shorter time after hospitalization. They needed much more time to stabilize their condition than patients of the 1st group. At the same time, in contrast to the vaccinated, all deaths (n=46) were recorded in the 2nd group.

Thus, the analysis of the material clearly demonstrates that vaccination prevents the negative course of *COVID*-19: coagulopathy, inflammatory syndrome and the development of thrombotic complications. At the same time, an important observation was that the development of thrombosis of the arteries of the lower extremities in the vast majority of cases became a precursor to subsequent death. This relationship demonstrates the presence of severe microcirculatory disorders in the body, followed by decompensation and the development of multiple organ failure. The absence of arterial thrombosis in the group of vaccinated patients shows the possibility of preventing the development of endothelitis with subsequent occlusion of the lumen of the vessel against the background of a viral infection.

On October 12, 2021, President of the Russian Federation Vladimir Vladimirovich Putin, at a meeting with deputies of the State Duma of the VIII convocation, said that vaccination can save people from infection, a severe course of the disease [8]. Thus, the widespread introduction of vaccination will help reduce the severity of the course and complications of a new coronavirus infection.

CONCLUSIONS

1. Vaccination, even incomplete cycle, prevents severe *COVID*-19 associated with the progression of coagulopathy and inflammatory syndrome.

2. In vaccinated patients, there are no deaths, pulmonary embolism, which demonstrates the absence of a severe course of the disease.

3. Arterial thrombosis associated with *COVID*-19 develops in unvaccinated patients and is accompanied by a high frequency of recurrent thrombosis requiring subsequent limb amputation. REFERENCES

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Received on 17.07.2021

Review completed on 01.09.2021

Accepted on 28.09.2021