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COVID-19 Among Lung Transplant Recipients: A Single Center Study

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ABSTRACT

Background. When COVID-19 became a pandemic, it was difficult to predict how it would affect lung transplant recipients. The aim of this study was to assess the mortality, influence on graft function as well as attitude toward SARS-CoV-2 vaccination among lung transplant recipients from a single center.

Methods. We analyzed medical data pertaining to 124 recipients who received lung transplants between 2008-2021 from a single center and original questionnaire on the COVID-19 severity classification system and the patients' attitude toward SARS-CoV-2 vaccination. Graft function was assessed by spirometry and a 6-minute walk test (6MWT), at least at the first postCOVID-19 visit.

Results. Among 29 patients who were confirmed to have COVID-19, 6 people died during or directly after contracting this infectious disease. The significant decrease in spirometry and distance in a 6MWT has been rarely observed in COVID-19 survivors. After vaccination (n=107 patients) , most patients reported mild symptoms with slight pain and discomfort at the injection site being the most common (51.4%). 67.7% of all studiedpatients did not have any fears regarding the vaccination. Others reported being significantly worried about its effects (19.4% agreed to receive a vaccination anyway and 12.9% refused to be vaccinated).

Conclusions. COVID-19 may present significant mortality among lung transplant recipients. The short-term safety and outcomes of vaccinations among these patients seemed encouraging. We are aware of the small study group limitations and hope to research this issue further.

THE COVID-19 pandemic is a serious challenge for health care systems worldwide. More than 265 million confirmed cases and 5.2 million deaths were documented by the World Health Organization in a report released on December 5, 2021 [1]. Clinical signs and symptoms ranged from mild to severe. Most often, patients complained of fever, cough, and myalgia, which are typical responses to viral infection. Some patients also experienced sore throat, headache, chills, nausea or vomiting, diarrhea, ageusia, and conjunctival congestion [2]. However, a significant number of patients developed a critical course of an inflammatory response with dyspnea and hypoxemia all the way up to life-threatening organ disorders such as acute respiratory distress syndrome, shock, and heart failure [3]. One group of patients at high risk of severe SARS-CoV-2 infection are those receiving immunosuppressive therapy after lung transplantation (LTx). In order to prevent the critical consequences of COVID-19, vaccination was introduced to LTx recipients [4].

The aim of the study was to examine the number of COVID-19 cases among patients after LTx in a single center, as well as mortality and influence on graft function in this group of patients. Our research also included the topic of the patients' attitude toward SARS-CoV-2 vaccination.

MATERIALS AND METHODS

A retrospective analysis was performed in a single center. The medical data of 124 lung recipients who received a transplant between 2008-2021 as well as the original questionnaire, which were created by the

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authors of the article on the COVID-19 severity classification system and the patients' attitude toward SARS-CoV-2 vaccination, were analyzed. Graft function was assessed by spirometry and a 6-minute walk test (6MWT). Spirometry parameters included forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), whereas 6MWT assessment was based on obtained distance. The results were compared before COVID-19 infection at the first visit and at 6 months after illness.

Among the general group of patients, those with COVID-19 infection after LTx were distinguished. There were 23 patients in this group, and SARS-CoV-2 infection was confirmed by polymerase chain reaction-based assay. The characteristics of both groups of patients are shown in Table 1. There are no significant differences in their baseline characteristics with regard to age, sex, and underlying lung disease before LTx.

RESULTS

A total of 29 LTx recipients with confirmed SARS-CoV-2 infection were included in this analysis. Six people died during or directly after contracting this infectious disease, so the mortality rate is 20.7%. Among 23 patients who survived, the course of the infection was assessed in 3 categories: mild, moderate, and severe. Most often, the course of COVID-19 infection was moderate (n = 10; 43.5%), whereas mild was presented in 7 patients (30.4%), and severe was presented in 6 patients (26.1%). Sixteen of 23 patients did not require respiratory support during SARS-CoV-2 infection. Passive oxygen therapy was used in 4 patients (17.4%), and noninvasive ventilation was used in 3 patients (13.0%).

Spirometry and 6MWT were used to evaluate the function of transplanted lungs in patients with COVID-19. The results were compared in 2 summaries: before COVID-19 infection and at the first visit after contracting the disease, and then before SARS-CoV-2 infection and at 6 months after having the illness. The following criteria were adopted in the assessment: a significant decrease in FEV1 and FVC was defined as a decrease of more than 200 mL and in 6MWT distance there was a decrease by over 50 m. Each significant decrease in spirometry was defined as a percentage of the baseline value. Not all patients with COVID-19 met the criteria for comparison of the results because they did not come to the follow-up visit or 6 months had not passed since the onset of their infection. The results of both summaries are presented in Table 2. In follow-up 1, a significant decrease in results were compared before COVID-19 infection and at the first visit after contracting the disease whereas in follow-up 2—before COVID-19 infection and at 6 months after the aquiring this particular disease.

After COVID-19, there was no significant decrease in FEV1 in 68.4% of patients in follow-up 1 and 60.0% of patients in follow-up 2, no significant loss in FVC in 63.2% of patients in follow-up 1 and 66.7% of patients in follow-up 2, and, taking into account the distance in 6MWT, no significant decrease in 73.7% of patients in follow-up 1 and 85.7% of patients in follow-up 2.

The mean decrease in FEV1 in follow-up 1 was 640 mL while in follow-up 2 it was 733 mL. In follow-up 1, the mean loss in FVC was 559 mL and was 804 mL in follow-up 2. Regarding the distance achieved in 6MWT, its mean decrease in follow-up 1 was 116.5 m and 306.4 m in follow-up 2.

Regarding vaccination among patients after LTx, out of the general group of patients (n = 124), 86.3% were vaccinated against SARS-CoV-2. The vast majority of patients (n = 91; 85.0%) were vaccinated with Comirnaty (Pfizer Europe, Brussels, Belgium), 11 (10.3%) with Spikevax (Moderna, Cambridge, Mass, USA), and 5 (4.7%) with Vaxzevria (AstraZeneca, Cambridge, Great Britain). Of the vaccinated patients, 104 people (97.2%) received 2 doses and 3 patients (2.8%) received 1 dose.

After vaccination, 32 patients (29.9%) did not report any side effects. The most frequently mentioned symptoms were pain and discomfort at the injection site (n = 55; 51.4%). Fifteen patients (14.0%) felt pain and discomfort at the injection site and had a fever while 5 patients (4.7%) had a fever. There were no patients who required hospitalization after vaccination.

The original questionnaire created by the authors included questions about the patients' attitudes toward vaccination. Eighty-four patients (67.7%) of the general group (n = 124) did not have any fears regarding vaccination. Others reported being

Table 1. Characteristics of General Group of Patients and of Patients Testing Positive for COVID-19

	General Group; n = 124	COVID-19 Positive Patients; n = 23
Sex, n (%)	Female: 47 (37.9)	Female: 9 (39.1)
	Male: 77 (62.1)	Male: 14 (60.9)
Mean age (y)	42 ± 15	42 ± 15
Indications for LTx, n (%)	Cystic fibrosis: 54 (43.5)	Cystic fibrosis: 8 (34.8)
	COPD: 24 (19.4)	COPD: 5 (21.7)
	Pulmonary fibrosis: 16 (12.9)	Pulmonary fibrosis: 2 (8.7)
	Pulmonary hypertension: 13 (10.5)	Pulmonary hypertension: 3 (13.1)
	Others: 17 (13.7)	Others: 5 (21.7)
Tacrolimus, n (%)	89 (71.8)	16 (69.6)
BMI	22.3 ± 3.7	22.2 ± 3.6
Hemoglobin (g/dL)	Female: 12.5 ± 1.6	Female: 12.4 ± 1.6
	Male: 12.5 ± 1.7	Male: 12.5 ± 1.5
eGFR >60 mL/min/1.73 m^2, n (%)	54 (43.5)	13 (56.5)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; LTx, lung transplantation.

Table 2. Results of the Function of Transplanted Lungs in Patients With COVID-19

	Follow-Up 1*	Follow-Up 2†
FEV1 (%)	24.26 (11.83-41.15); n = 6	28.74 (11.83-42.93); n = 6
FVC (%)	17.68 (7.71-31.40); n = 7	23.85 (5.27-38.61); n = 5
Distance in 6MWT (m)	116.5 (51.1-256.8); n = 5	306.4 (249.6-363.1); n = 2

The results of spirometry are presented as mean, minimal, and maximal values of significant decreases as a percentage of the baseline value. The results of 6MWT are presented as mean, minimal, and maximal values of significant decreases expressed in meters.

6MWT, 6-minute walk test; FEV1, forced expiratory volume in first second; FVC, forced vital capacity.

*Follow-up 1 was defined as comparing the results before COVID-19 infection and at the first visit after contracting the disease.

† Follow-up 2 was defined as comparing the results before COVID-19 infection and at 6 months after contracting the disease.

significantly worried about its effects; 24 patients (19.4%) agreed to receive a vaccination anyway and 16 patients (12.9%) refused to be vaccinated. The most common concern indicated by patients was the various vaccination side effects.

The function of transplanted lungs was also assessed in the vaccinated group, excluding those who had positive test for SARS-CoV-2 (n = 91). The medical data used for comparison were obtained at least one month before and at least one month after vaccination. The results were not compared for all vaccinated patients because some people missed a follow-up visit or the last dose was too close to the last visit so the data could not be taken into account. Among 48 patients, the significant decrease in FEV1 (defined as a decrease of more than 200 mL) occurred in 6 (12.5%). Out of 50 patients whose distance was analyzed in 6MWT before and after vaccination, 1 (2.0%) had a significant shortening of the distance (defined as a decrease by >50 m).

From the beginning of the pandemic in Poland until the introduction of vaccinations for organ transplant recipients, 17 patients from our center contracted COVID-19 and 5 of them died. According to the National Immunization Program, organ transplant recipients were allowed to be vaccinate since the March 15, 2021 [5]. Since then, another 12 patients acquired SARS-CoV-2 infection. Four were not vaccinated and the remaining 8 were vaccinated. Out of the 8 vaccinated patients, 4 people contracted the disease before vaccination and 4 people after vaccination. Among the 4 who contracted it after vaccination, 2 acquired COVID-19 after receiving the first dose of vaccination, and the remaining 2 after the second dose. One of the fully vaccinated patients died of SARS-CoV-2.

DISCUSSION

This article reports the clinical courses of a group of 29 LTx recipients from the center who were diagnosed with SARS-CoV-2 infection. Six died (20.7%) as a result of COVID-19. Most often, the course of this infection among surviving LTx recipients was so mild that they did not require any respiratory support (69.6%).

The reported mortality rates from recently published works were slightly higher than those obtained at our facility. Kamp et al presented data on the outcomes of 31 LTx recipients with confirmed COVID-19 with a mortality rate of 39% [6]. Saéz-Giménez et al also reported a mortality rate of 39% among 44 LTx recipients from Spain [7], whereas Aversa et al reported 32 LTx recipients infected with SARS-CoV-2 from New York City with a mortality rate of 34% [8].

In their study, Aversa et al also classified patients based on the severity of the course of SARS-CoV-2 infection. They received the following results: 5 patients (16%) had mild COVID-19 infection, 14 patients (44%) had moderate COVID-19 infection, and 13 patients (41%) had severe COVID-19 [8]. The results obtained in our center indicate a more frequent occurrence of a mild course and a less frequent occurrence of a severe course of SARS-CoV-2 infection among LTx recipients compared to the study by Aversa et al. In the study by Magnusson et al, they reported that 22 patients (46.8%) had mild COVID-19 infection and 20 LTx recipients (42.5%) developed moderate or severe COVID-19 infection. In this study, the authors distinguished an additional group of 4 patients (8.5%) in whom the infection was critical [9].

Messika et al described 35 LTx recipients hospitalized due to COVID-19. They reported that among the 25 patients primarily hospitalized in the general hospital ward, 22 (88.0%) received low-flow oxygen therapy. Also, among the 13 patients in the ICU, 5 received noninvasive respiratory support, 7 (53.8%) received invasive mechanical ventilation, and 1 received veno-venous extracorporeal membrane oxygenation [10]. Compared to the results from the Messika et al study, not all patients from our center required hospitalization due to SARS-CoV-2 infection; 69.6% of them did not need any respiratory support. Permpalung et al also reported the necessity for oxygen therapy among patients with COVID-19 and that among the 20 hospitalized patients, 4 received high-flow oxygen, 2 required mechanical ventilation, and no patients required extracorporeal membrane oxygenation [11].

In our study, we examined a significant decrease in FEV1 and FVC (defined as a decrease of more than 200 mL) in a group of 23 surviving LTx recipients who had contracted COVID-19. In the first summary (before COVID-19 infection and at the first visit after contracting the disease), a significant loss in FEV1 occurred in 6 patients (31.6%) and a significant loss in FVC occurred in 7 patients (36.8%). In the second summary (before SARS-CoV-2 infection and at 6 months after contracting the illness) a significant decrease in FEV1 occurred in

6 patients (40.0%) and a significant decrease in FVC occurred in 5 patients (33.3%). Mahan et al also presented in their publication a persistent and significant loss of FVC or FEV1 (>10% from pre-COVID-19 baseline). They observed it among 18 patients (40.9%) [12]. The significant decrease in spirometry has been rarely observed in patients with COVID-19 from our center. This might be caused by the timing of the pandemic, which made LTx recipients more concerned about their health than before.

Magnusson et al researched contracting COVID-19 after vaccination. In their study, out of 47 patients, 9 tested positive for SARS-CoV-2 after being vaccinated [9]. In our study, out of 29 patients with COVID-19, 4 contracted SARS-CoV-2 after vaccination. Despite this, most of the patients at our center have been vaccinated against SARS-CoV-2 and either had not contracted COVID-19 or had a mild course of this disease, which demonstrated why this is an important topic, especially among the group of patients receiving immunosuppressive therapy. The decrease in FEV1 observed in some patients from our facility after vaccination may have been due to various reasons as well as a short follow-up period after taking the last dose; therefore, we plan to continue monitoring our patients and investigating this topic.

CONCLUSIONS

COVID-19 may present significant mortality among LTx recipients and may cause significant declines in spirometry and a 6MWT. Short-term safety and the outcomes of vaccinations among these patients seem encouraging. We are aware of the small study group limitations and hope to research this issue further.

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