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ORIGINAL ARTICLE

The social and clinical impact of the COVID-19 epidemic on the Strasbourg lung transplant cohort: A single-center retrospective cohort study

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Abstract

The clinical and social impacts of the COVID-19 epidemic on lung transplant (LTx) recipients remain poorly known. We aimed to evaluate its social, clinical, and behavioral consequences on the LTx patients followed in Strasbourg university hospital. A questionnaire was used to collect details concerning patients' lifestyles, their protection methods used to avoid COVID-19 contamination, and clinical infection-related information for March 2020. A specific score was created to quantify patients' contacts and the associated risk of infectious contagion. Data were collected from 322 patients (91.2%). A majority reported a higher application than usual of social distancing and barrier measures. 43.8% described infectious-related symptoms and 15.8% needed an anti-infective treatment. There was no difference in symptom onset according to age, native lung disease, diabetes, or obesity. Nineteen patients were tested for COVID-19, and four were diagnosed positive, all with a favorable outcome. The infection risk contact score was higher for symptomatic patients (p: 0.007), those needing extra-medical appointments ($p < .001$), and those receiving anti-infective treatments ($p = .02$). LTx patients reported a careful lifestyle and did not seem at higher risk for COVID-19. Our score showed encouraging preliminary results and could become a useful tool for the usual infection-related follow-up of the LTx patients.

KEYWORDS
COVID-19, lifestyle factors, lung transplantation, protective measures

1 | INTRODUCTION

In late December 2019, a new virus from the coronavirus family (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) was identified as a worldwide epidemic (coronavirus disease 2019 [COVID-19]). Although the clinical impact of the disease on immunocompetent patients has been well described, its consequences on populations treated with immunosuppressive (IS) drugs remain poorly understood, especially concerning solid organ transplant (SOT) recipients.[1,2] To date, very few cases of lung transplant (LTx) patients affected by COVID-19 have been reported.[3-5] After lung transplantation, a long-term maintenance IS treatment is prescribed. This can lead to an increased risk of infections, especially viral infections, which are sometimes more severe than in the general

population.[6] It is also interesting to consider that SOT recipients' lifestyles are often different to those of the general population with a greater respect of self-protective measures, even when there is not an epidemic.

The "Grand Est" region of France was one of the most affected by the COVID-19 epidemic. Strasbourg University Hospital has one of the largest French cohorts of LTx patients, with a follow-up for more than 350 patients. With this study, we wanted to understand the social and clinical impact of the COVID-19 epidemic on the Strasbourg LTx cohort, as well as whether these patients' lifestyles and characteristics had an influence. We hypothesized that LTx patients from our cohort were not at higher risk of being infected by COVID-19 or of developing more severe forms of the infection compared to the rest of the population, partly because of their behavior with regard to the risk of infection. The first aim of this study was to describe the lifestyles of the LTx patients followed at Strasbourg University Hospital, as well as the protective measures they applied during the COVID-19 epidemic. To this end, we used a composite criterion to assess the proportion of patients that (1) complied with home confinement and social distancing, (2) continued to go outside their home, (3) used protective masks, (4) purchased basic necessities (groceries and medication) themselves, and (5) continued their professional activities.

The study's secondary objectives were (1) to assess the patients' contacts with their friends and family using a specific score developed in our department, (2) to determine whether the patients' native lung disease, age, sex, or smoking status impacted their compliance with protective measures, and (3) to assess the clinical impact of the COVID-19 epidemic on this cohort (acute symptom onset, unscheduled medical appointments needed, and number of patients screened and treated for COVID-19).

2 | MATERIAL AND METHODS

2.1 | Study population

The study recruited all LTx patients transplanted before March 2020 that were older than 18 years and followed at Strasbourg University Hospital. This study was approved by the Institutional Review Board of the French Learned Society for Respiratory Medicine (CEPRO 2020-025).

2.2 | Data collection

This was a retrospective, observational, single-center study. To achieve our aims, we used a specific questionnaire developed by staff members from the respiratory department, in order to standardize long-distance follow-up (Appendix). Usual in-hospital follow-up appointments were canceled for the patients considered as stable, due to the epidemic risk. During April 2020, this questionnaire was distributed to LTx patients followed at Strasbourg University Hospital. The information received pertained to the month of March 2020, since a period of lockdown was implemented in France thereafter due to the COVID-19 epidemic and where French government recommended to limit every non-essential activity outside the home, to respect social distancing, and encouraged teleworking. In Strasbourg, LTx patients are trained to frequently wash their hands, respect protective measures such as wearing a protection mask when going to the hospital, respecting social distancing, paying attention to unusual symptoms, and contacting their regular LTx medical manager if necessary, even during "non-pandemic" times. In addition to the official French recommendations, a letter was sent to the LTx patients with specific guidance and advises provided by our department such as avoiding public spaces and contagious people, avoiding non-necessary travels, requesting a work stoppage if impossible to work from home, and trying to live in a different place if presence of COVID-19-like symptoms in one of the family members. Wearing a protection mask when going outside was not requested except when going to the hospital. The questionnaire was directly administered to the patient by a staff member during the follow-up appointment in the clinic, if it was maintained. In case of cancelation, the patient was contacted by phone and the questionnaire was then either submitted by phone, sent by mail or e-mail according to the patient's preference.

We were able to collect the following data:

- Details about the patient's lifestyle (marital status, number of people living at home, number of children, type of home, professional status).
- Symptom onset that was suggestive of an infection.
- Any unscheduled medical appointments that were needed and led to the prescription of antibiotic and/or antiviral treatment.
- Whether a specific screening test for COVID-19 was performed.
- Whether one or more members of the patient's family and friends experienced symptom onset that was suggestive of COVID-19, including whether this required specific medical care and whether it was responsible for changes in the patient's lifestyle.
- Compliance with measures required to protect against COVID-19 (self-isolation at home, social distancing, use of personal protective equipment, frequency of hand washing).
- Continuation of out-of-home activities (grocery shopping, ongoing professional activities).
- Details of all contacts between the patient and their family, friends, others… In order to quantify the patient's social contact during the lockdown period and to estimate the potential induced risk of contagion, we established a specific score based on several criteria that we collected in our questionnaire (Table 1) and on findings from previous studies.[7,8] We assessed the type of contact (family living at home, friends, shop owners, coworkers, healthcare workers, etc), whether contact occurred once or several times during March 2020, the frequency of contact, and its duration. The attributed risk for every criterion was graded as low, middle-low, middle-high, or high.[8] For repetitive contacts, induced risk was considered as "not important" for non-medical

TABLE 1 Contact-related risk score for COVID-19 infection

CONTACT-RELATED RISK SCORE					
Risk	**0 (none)**	**2 (low)**	**4 (middle-low)**	**6 (middle-high)**	**8 (high)**
Type of contact	None	Once, short contact	• Shop owners • Neighbors • Coworkers	• Family, friends, or relatives not living at the same place • At-home medical care (nurse, doctor, etc)	• Family, friends, or relatives living at the same place • All other types of medical care (at the hospital, etc) • Contact with a **COVID**-19-diagnosed person
Repetitive contacts		No	Yes (not important risk)	Yes (important risk)	
Frequency		<1/week	1-3/week	>3/week	
Duration		<15 min	15-60 min	>60 min	

Note: Clinical score aimed at quantifying patients' social contacts during the **COVID**-19 lockdown period and at determining the associated potential risk of contagion. The criteria assessed were the type of contacts, whether they happened only once or several times, their frequency, and their duration. Based on the questionnaire, we graded all the contacts that the patient had in March 2020. For repetitive contacts, "low risk" concerned non-medical contacts, such as with family members, friends, or shop owners, while "high risk" related to contacts with healthcare workers or anyone diagnosed with **COVID**-19. Every contact was scored between 8 and 26, based on our grading system. The sum of all the scores was calculated for each patient to determine a total score.

contacts, such as with family members, friends, or shop owners, while "important" related to contacts with healthcare workers or anyone diagnosed with COVID-19. Based on the questionnaire, we graded all the patient's contacts with another person during March, with a score between 8 and 26, based on our grading system and regarding its potential degree of severity. The sum of all the scores was calculated for each patient to determine a total contact-related risk score.

The COVID-19 diagnosis was performed with a nasopharyngeal swab using a specific reverse transcription-polymerase chain reaction for SARS-CoV-2 and/or a positive chest CT scan. Patients' data were collected from the computerized medical records (using DxCare software) and laboratory results server. We recorded each patient's gender, age, native lung disease, type of LTx, time post-LTx, detailed maintenance IS treatment, and long-term azithromycin treatment. Among the data we collected, we were also interested in the presence of risk factors for severe COVID-19 infection (smoking status,[9] obesity,[10] hypertension,[11] diabetes,[11] obstructive sleep apnea [OSA],[12] chronic kidney disease,[13] stroke,[14] myocardial infarction or cardiac insufficiency,[15] chronic liver disease,[16] active cancer,[17] connective tissue disease[18]). All the data were completely anonymized for this study. Every patient received a complete explanation about the study and was informed of the entirely voluntary nature of their participation in this research.

2.3 | Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or median with interquartile range, depending on the normality of distribution. The Kolmogorov–Smirnov test was used for normality analysis. Categorical variables are presented as numbers and percentages. Comparison of proportions was made using the chi-squared test. The Mann–Whitney U test was applied for the statistical evaluation of differences between two groups. Statistical significance was defined as a two-tailed p value less than or equal to 0.05. All analyses were conducted using SPSS statistical software (version 11).

3 | RESULTS

3.1 | Study population

In total, 353 patients are followed up for their lung transplantation as part of the Strasbourg Lung Transplant Program. We contacted 348 of these patients to request they complete our questionnaire (four were hospitalized and thus not able to answer, one was unable to answer for another reason). We were able to obtain information from 322 patients (24 did not answer and two declined to participate in our study) (Figure 1). The questionnaire was directly administered during the follow-up appointment in the clinic to 67 (20.8%)

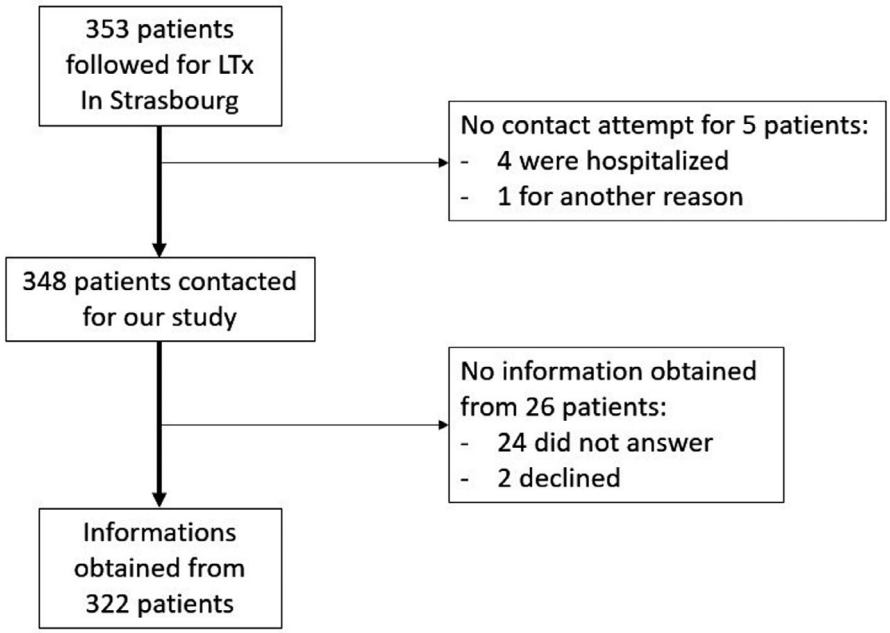

FIGURE 1 Patient inclusion flowchart

patients, submitted by phone to 83 (25.8%), sent by e-mail to 153 (47.5%), and by mail to 19 (5.9%) of them.

3.2 | General characteristics

The main patient characteristics are summarized in Table 2. Patients' native lung diseases were divided into four different groups: Group 1 patients were transplanted for chronic obstructive pulmonary disease (COPD) and alpha-1 antitrypsin deficiency (A1ATD), Group 2 for interstitial lung disease, Group 3 for cystic fibrosis, and Group 4 for all other causes. Nearly half of our patients were in Group 1 (47.8%), with a majority of patients transplanted for COPD. The most frequent maintenance IS treatment combination was an anti-calcineurin treatment (tacrolimus or cyclosporine) with an anti-metabolite (mycophenolate mofetil [MMF] or Myfortic) and steroids. The most frequent type of procedure performed was double LTx (87.9%), and time post-LTx was less than one year for 38 patients (11.8%). Most patients were former smokers (64.9%), and a small proportion presented active smoking (2.8%). The main comorbidities in our cohort were high blood pressure (52.2%), diabetes (47.5%), and chronic kidney disease (creatinine clearance ≤ 60ml/min) (40.4%). We found obesity (body mass index [BMI] ≥30kg/m^2) in 14.3% of our patients, and we confirmed OSA in 9.3%.

In terms of lifestyle, less than half of patients were married (45.7%). Only 26.7% reported living alone at home. Most of the patients reported living in a house (64.6%), mostly in the countryside (57.1%). Sixty-eight patients (21.1%) declared that they had a professional activity before the start of the COVID-19 epidemic. Among these patients, the professional activity was an office work for 38.4% of them, related to the healthcare field for 7.7%, to teaching/research for 7.7%, to computer science for 10.8%, and to delivery/professional driving for 4.6%. However, only 33 patients continued their professional activity after the lockdown began, 20 of whom had an office work or a job related to computer science.

3.3 | Presence of infectious symptoms and their consequences

We sought to assess the impact of the COVID-19 epidemic on these patients, particularly with regard to the medical care they received and their lifestyle. Patients were asked to report any acute infectious symptoms that could be consistent with COVID-19 that occurred during March 2020. Less than half of patients described symptoms that occurred during this period (43.8%). The most common symptoms reported were rhinorrhea (18.9%), diarrhea (14%), headache (11.8%), fatigue (11.5%), and nasal obstruction (10.2%). Details of other symptoms are presented in Table 3. The proportion of symptomatic patients was significantly higher in women (p = .02). There was a trend toward a higher presence of symptoms in patients diagnosed with OSA (p = .08). Interestingly, no significant difference was observed regarding patients' age, native lung disease, time post-LTx, smoking status, presence of hypertension or diabetes, long-term treatment with azithromycin, or obesity (Figure 2). Due to the onset of infectious symptoms, 24.2% of patients needed a medical appointment in addition to their usual post-LTx follow-up. An anti-infective treatment was prescribed to 15.8% of patients. For at-home patients, an empiric treatment was prescribed (amoxicillin or azithromycin), and for patients hospitalized, anti-infective treatment was adapted regarding clinical data and microbiological findings

TABLE 2 General characteristics of the patients

Population Size	322
Male (%)	145 (45%)
Age	56.1 ± 13.1
BMI (kg/m^2)	24.2 ± 5
TRANSPLANTATION CHARACTERISTICS	
Time post-LTx (days)	1960 ± 1934
Patients with time post-LTx ≤ 1 year	38 (11.8%)
Native lung disease	
Group 1 (COPD, A1ATD)	154 (47.8%)
Group 2 (interstitial lung diseases)	51 (15.9%)
Group 3 (cystic fibrosis)	56 (17.4%)
Group 4 (other)	61 (18.9%)
Type of LTx	
Single	18 (5.6%)
Double	283 (87.9%)
Heart-lung	14 (4.3%)
Liver-lung	3 (0.9%)
Islets of Langerhans-lung	4 (1.2%)
Re-transplantation	8 (2.5%)
LTx-RELATED DATA	
Tacrolimus/Cyclosporine	307 (95.3%)
Azathioprine	35 (10.9%)
MMF/Myfortic	265 (82.3%)
mTOR inhibitor	40 (12.4%)
Steroids	307 (95.3%)
Daily dose of steroids (mg)	10.1 ± 5.2
Long-term treatment with azithromycin	151 (46.9%)
Previously treated acute rejection	78 (24.2%)
Cardiovascular risk factors	
Smoking status	
Never smoker	97 (30.1%)
Current smoker	9 (2.8%)
Former smoker	209 (64.9%)
Nicotine substitute user	1 (0.3%)
Electronic cigarette user	1 (0.3%)
Cardiovascular comorbidities	
Hypertension	168 (52.2%)
Stroke	31 (9.6%)
Cardiac insufficiency	8 (2.5%)
Myocardial infarction	29 (9%)
Diabetes	153 (47.5%)
Obesity	46 (14.3%)
Other Comorbidities	
Chronic kidney disease	130 (40.4%)
Obstructive sleep apnea	30 (9.3%)
Chronic liver disease	5 (1.6%)
Connective tissue disease	7 (2.2%)
Active cancer	6 (1.9%)
Lifestyle Characteristics	
Living alone at home	86 (26.7%)
Marital status	
Single	64 (19.9%)
Married	147 (45.7%)
Divorced	49 (15.2%)
Widowed	25 (7.2%)
Other	37 (11.5%)
Number of children	1.64 ± 1.6
Actual professional activity	68 (21.1%)
Type of home	
House	208 (64.6%)
Apartment	113 (35.1%)
Other	1 (0.3%)
Living place	
City	137 (42.5%)
Countryside	184 (57.1%)

Abbrevations: A1ATD, alpha-1 antitrypsin deficit; COPD, chronic obstructive pulmonary disease; LTx, lung transplantation; MMF, mycophenolate mofetil.

from blood or bronchoalveolar lavage fluid samples. The proportion of patients that received such a treatment was significantly higher in female patients (p = .03), and those with OSA (p = .01). The rest of the patients' characteristics did not show any significant differences.

During March 2020, only 19 patients (5.9%) were tested for COVID-19 using nasopharyngeal swab. Testing was positive for three of them (0.9%). A chest CT scan was consistent with a COVID-19 infection in four patients (1.2%). These four patients were all considered as positive for COVID-19 infection, even if the nasopharyngeal swab testing was lacking for one of them; 2 of these patients reported COVID-19 cases in their entourage. Hospitalization was required for these four patients. Their clinical outcome was favorable, and none of them experienced any sequelae. Among the other patients, 16 were hospitalized in March for another reason, including bacterial pneumonia for 2 of them (1 patient tested negative for COVID-19, the second one was not tested), 1 for *Mycobacterium abscesuss*-related pneumonia, and 13 for non-infectious reasons (1 for acute cellular rejection treatment). All patients diagnosed with COVID-19 were symptomatic.

Regarding our patients' entourage, 13% of patients had a confirmed COVID-19 case among their family and friends. Nearly half of these "COVID-19 family cases" required specific medical care, including hospitalization. The high degree of contact with the COVID-19 family members, such as living in the same home, resulted in a lifestyle change for six patients (1.9%), including measures such as sleeping in an isolated room or self-containment in one room of the house (Table 3).

3.4 | Protective measures adopted against COVID-19 and their impact

We were also interested in the measures adopted by our patients to protect themselves against COVID-19 during the containment period (Table 3). A majority of patients complied with recommendations regarding social distancing and barrier measures (missing data for 2 patients). A large majority of them reportedly increased the frequency of their daily hand washing (81.4%). Most of them used both soap and hydroalcoholic solution (64.9%). More than a third of patients (34.2%) reported following strict self-confinement at home and did not leave their home during the lockdown period. Protective masks were available at home for 275 patients (85.4%); these were mostly surgical and Filtering facepiece 2 (FFP2) masks. Among patients that had masks at home, only 164 (50.9%) reported wearing a mask outside their home. It should be noted that 89 patients did not answer this last question. Among our patients, 104 patients (32.3%) self-purchased basic necessities such as groceries, while the rest received help from their family and friends. Among the 33 who continued their professional activity during the COVID-19 epidemic, working conditions were adapted for 27 of them, mainly with changes such as teleworking. When comparing patients that were younger than 50 years to older patients, we did not observe any difference for professional activity continuation. However, the younger patients more frequently benefited from adaptations to their working conditions (95% vs. 73%, $p = .023$).

Only four patients reported having no contact with their family and friends during the containment period (1.2%). For each patient, we tried to assess the quantity of social contacts with family and friends, as well as the potential infection-related risk of contamination, as described above (Table 1). The median contact score was 44 (IQR, 32–57.5) (Table 3). Values of this contact score were not normally distributed according to the Kolmogorov–Smirnov test ($p < .001$). Interestingly, we observed that the median score was significantly higher in symptomatic patients [48 (IQR, 38–60)] than in asymptomatic patients [40 (IQR, 29–53); p:.007], also in those who needed an extra-medical appointment [51 (IQR, 41–64) vs 41 (IQR, 27–54); $p < .001$] and those who received an anti-infectious treatment [52 (IQR, 37–61) vs 42 (IQR, 32–56); p:.02] (Figure 3). There were no significant differences in score values according to the patients' age, native lung disease, sex, or smoking status.

In terms of respecting and using protection measures, we did not observe any difference according to the patients' age, time post-LTx, native lung disease, or smoking status. None of these protective measures showed significant efficiency in decreasing the risk of developing infection-like symptoms. The continuation of professional activities after the COVID-19 epidemic's onset was related to a significantly increased risk ($p = .006$). There was a trend toward a higher presence of symptoms in patients that purchased basic necessities themselves ($p = .07$).

4 | DISCUSSION

The department of Respiratory Diseases of Strasbourg University Hospital is in charge of one of the largest French cohorts of LTx patients. Due to the high risk associated with COVID-19, our department has had to adapt its activity, including canceling follow-up consultations with many patients, and using telemedicine instead. One of the strengths of this study is that we collected a large amount of data from almost all our patients, rather than just from COVID-19-diagnosed patients. We used the same questionnaire to collect medical and social information from all our patients, allowing us to perform similar and systematic follow-ups for all of them. Given that nearly half of the patients had risk factors for developing a severe form of COVID-19 infection, such as high blood pressure, chronic kidney failure, or diabetes, it was necessary to continue regular follow-up within the context of this epidemic. Due to the high variability of COVID-19-related symptoms, our questionnaire screened a high number of symptoms. Therefore, our results have no individual specificity for COVID-19. Although several studies have shown that older age and obesity are risk factors for severe COVID-19 infection, we could not confirm these findings in our cohort of LTx patients. These two parameters were not related to an increased risk of presenting symptoms. This lack of significance could also be a consequence of the low number of screened patients for COVID-19.

Nineteen patients were screened for COVID-19 by nasopharyngeal swab, which tested positive for three of them, and a fourth patient was considered positive for COVID-19, his chest CT scan being consistent with COVID-19 pneumonia. However, we must underline that it has been sometimes difficult to obtain diagnostic swabs at that beginning of the epidemic, because of the limited number of laboratories performing these testing. This could have been responsible for an underestimation of the exact number of COVID-19-positive cases among our patients. The evolution has been favorable for these four patients. Although these results seem reassuring, it is impossible to extrapolate them to the entire LTx patient population, due to the small number of screened patients and COVID-19-positive cases in our study.

The lifestyle of LTx patients appears to play an important preventive role. We found that a majority of patients respected and implemented the recommended containment measures, social distancing, and barrier measures but only 50.9% of the patients reported wearing a mask when going outside. In the guidance we provided to our patients, wearing a mask was not recommended, except when going to the hospital. This was in accordance with early March government recommendations that consider that available mask stocks were limited at that time in France. As a result, it was more difficult to obtain new masks, including for LTx patients. The COVID-19 outbreak encouraged a significant proportion of our patients to limit their out-of-home activities, more than usual. Indeed, one-third of patients preferred to adhere to strict self-confinement at home. In a recent monocentric study, *Bennett et al*[19]

TABLE 3 COVID-19-related data collected for the month of March 2020

Presence Of Infectious Symptoms	
All patients	141 (43.8%)
Group 1 (COPD, A1ATD)	70 (21.7%)
Group 2 (interstitial lung disease)	18 (5.6%)
Group 3 (cystic fibrosis)	21 (6.6%)
Group 4 (other)	32 (9.9%)
Acute symptoms	
Rhinorrhea	61 (18.9%)
Diarrhea	45 (14%)
Headache	38 (11.8%)
Fatigue	37 (11.5%)
Nasal obstruction	33 (10.2%)
Body aches	29 (9%)
Cough	29 (9%)
Nausea/vomiting	29 (9%)
Weight loss	28 (8.7%)
Dyspnea	28 (8.7%)
Sputum	27 (8.4%)
Sore throat	27 (8.4%)
Fever	26 (8.1%)
Anorexia	12 (3.7%)
Ageusia	7 (2.2%)
Anosmia	4 (1.2%)
Hemoptysis	2 (0.6%)
Chest pain	2 (0.6%)
Confusion	1 (0.3%)
Skin rash	3 (0.9%)
Others	5 (1.6%)
Additional Medical Care	
Unscheduled medical appointment	78 (24.2%)
Anti-infective treatment prescribed	51 (15.8%)
COVID-19 Testings	
Total number of COVID-19 cases	4 (1.2%)
Nasopharyngeal swab	19 (5.9%)
Patients tested positive	3 (0.9%)
Positive chest CT for COVID-19	4 (1.2%)
Hospitalization necessary if COVID-19	4 (1.2%)
Favorable outcome	4 (1.2%)
Acute Symptoms In Patients' Friends/Family	43 (13.4%)
COVID-19 Cases In Patients' Friends/Family	42 (13%)
Average number of COVID-19 cases	1.2 ± 0.98
Specific medical care needed	20 (6.2%)
Patient's lifestyle modification induced	6 (1.9%)
Sleeping in separate rooms	2 (0.6%)
Self-confinement in one room	2 (0.6%)
Other	2 (0.6%)
Protection measures used against COVID-19	
Compliance with confinement and social distancing recommendations	320 (99.4%)
Permanent at-home self-isolation	110 (34.2%)
Protective masks available at home	275 (85.4%)
Surgical mask	168 (52.2%)
FFP2	11 (3.4%)
Surgical and another type of mask (FFP2, tissue, etc)	37 (11.5%)
Other	12 (3.7%)
Missing data	47 (14.6%)
Wearing a mask when going outside	164 (50.9%)
Increased hand washing	262 (81.4%)
Soap	97 (30.1%)
Hydroalcoholic gel	6 (1.9%)
Both	209 (64.9%)
Other	7 (2.1%)
Self-purchase of basic necessities	104 (32.3%)
Professional activity continued during COVID-19	33 (10.2%)
Modification of working conditions	27 (8.4%)
Work interruption because of COVID-19	14 (4.3%)
No contacts with friends/family	4 (1.2%)
Contact score with friends/family, median (IQR)	44 (IQR, 32-57.5)

Abbrevations: COPD, A1ATD, alpha-1 antitrypsin deficit; chronic obstructive pulmonary disease; CT scan, computed tomography scan, FFP2, Filtering facepiece 2.

evaluated the incidence of COVID-19 in 41 LTx patients using a patient-perspective survey. Compared to our results, the authors found a higher proportion of patients with an increased use of face mask (65.8% vs 50.9%), but the proportion of patients reporting an increased handwash and an increased isolation at home were higher in our study (respectively, 81.4% vs 70.7% and 34.2% vs 21.9%). While 43.8% of our patients reported symptoms compatible with COVID-19, there were only 14.5% in the Italian study. We must consider that the number of symptoms screened was more important in our questionnaire. Only one of their patients (2.5%) was diagnosed with COVID-19.

Another aim of this study was to assess the social contacts between patients and their family and friends during the containment period. The nature and type of contact varied greatly from patient to patient, which complicated collection of this information. For this reason, we created a score to quantify these contacts and the associated risk of infectious contagion. The results we obtained with this score were encouraging with a significantly higher score in at-risk patients, who subsequently developed symptoms and needed additional medical care. We must acknowledge a lack of specificity for COVID-19 with our score, which could also be used for another

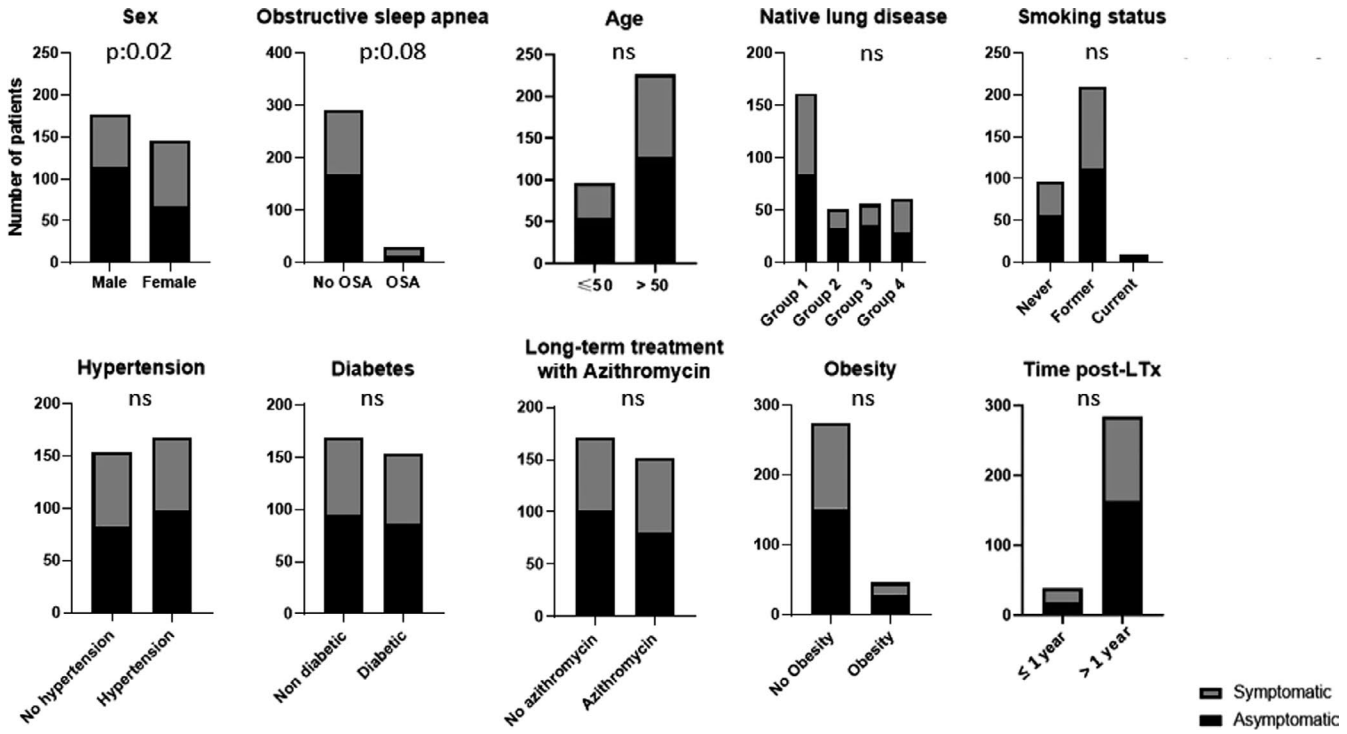

FIGURE 2 Proportion of patients that reported infectious-like symptoms during the month of March 2020, according to specific characteristics. LTx: Lung transplantation. Native lung disease: group 1 (COPD, A1ATD), group 2 (interstitial lung disease), group 3 (cystic fibrosis), group 4 (other). Statistical significance was defined as a two-tailed p value less than or equal to 0.05

seasonal infection, for example, the flu. This epidemic context was for us an interesting opportunity to improve our methods to assess the global infectious risk related to physical and social contacts within our LTx cohort. With stronger data, we envisage this score becoming a useful tool for the usual infection-related follow-up of our patients.

Otherwise, previous papers showed that COVID-19 in transplant patients can have severe outcomes and high rate of mortality.[20] Many patients told us that they were extremely worried about COVID-19 and felt more at risk of developing a severe form of the infection than the rest of the population. This may partly explain the considerable compliance with protective measures. This pandemic is likely to be long drawn, and we should keep improving our information system to our patients regarding COVID-19 and encouraging them to maintain their lifestyle which seems to be one of the most effective protection against this virus.

The current results should be interpreted in light of some limitations. First, although data collection was conducted on almost the

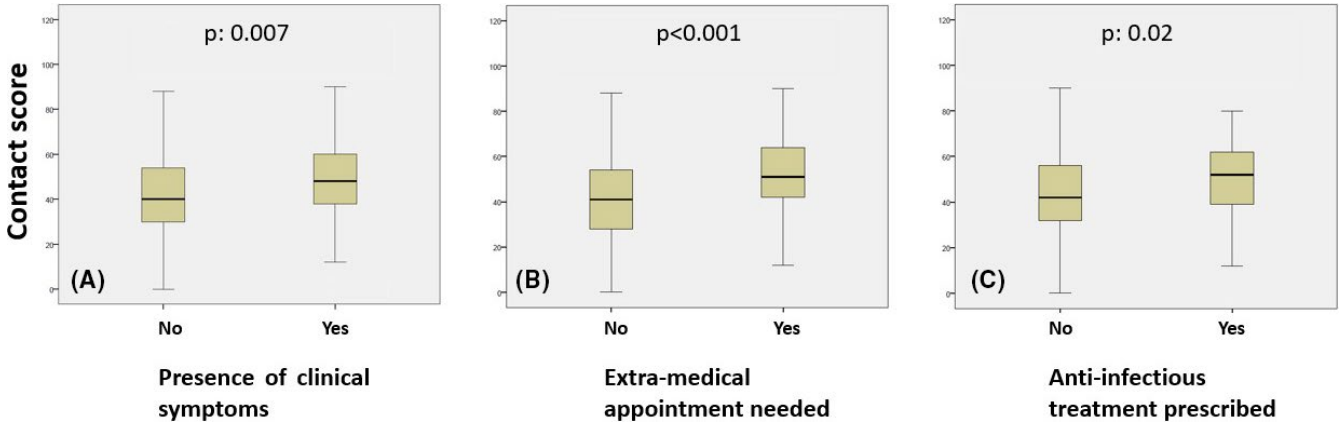

FIGURE 3 "Contact" score values of patients who developed infectious symptoms or needed additional medical care. The median score was significantly higher in symptomatic patients [48 (IQR, 38-60)] than in asymptomatic patients [40 (IQR, 29-53); p: 0.007] (A), also in those who needed an extra-medical appointment [51 (IQR, 41-64) vs 41 (IQR, 27-54); $p < .001$] (B) and those who received an anti-infectious treatment [52 (IQR, 37-61) vs 42 (IQR, 32-56); p: 0.02] (C)

entire cohort, the collection method was not the same for all patients. It is conceivable that patients answered in different ways, depending on whether they completed the questionnaire themselves or were asked the questions by a staff member from the department of respiratory diseases. This is particularly true for questions about compliance with certain rules. We did not observe a difference in response rate by patients between the different methods used to administer the questionnaire, but it seemed that having an assistance to answer to the questions was appreciated by many patients. This might be the best method to carry out such questionnaires. Another limitation is potential recall bias since the questions were asked in April about behaviors in March. Some patients did not answer all the questions (due to refusal or perhaps a lack of understanding of the question). Some items were subjective and included an element of interpretation, such as questions that relied on the patient's own estimation of their contacts with family and friends. We made every effort to clarify this data with a specific score. However, its preliminary, non-specific, and not statistically validated nature encourages us to remain cautious about the interpretation of these results, which need to be confirmed through studies that employ a blind inter-user comparison of the scores. The data we collected through our questionnaire only covered March 2020, which meant we were only able to collect data for a single point in time. Finally, as some of our results only concerned a low number of patients, we must remain careful about their interpretation.

We want to confirm our results by prospectively using an updated version of the questionnaire over the next few months, after the end of the lockdown period in France. This would occur in conjunction with the collection of blood samples that would be subject to specific serology for SARS-CoV-2. We aim to investigate a correlation between COVID-19 serologic status and the clinical characteristics of our patients, their lifestyles, and the protective methods they used against COVID-19.

In conclusion, we found a high proportion of LTx recipients applying recommended protective measures against the risk of **COVID**-19 contagion. LTx patients from our cohort did not appear to be more at risk of developing a severe form of the disease, compared to the rest of the population. These patients' usual cautious lifestyles may have played a major role in protection against contagion. In this preliminary study, the results obtained with our infection risk grading score for patients' contacts were encouraging. Given the current epidemic context and the risk of new major infections emerging, further studies are needed to develop more clinical follow-up scores and tools for at-risk populations, such as SOT patients.

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CONFLICT OF INTEREST

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Benjamin Renaud-Picard: Conceptualization; Data acquisition and interpretation; Writing – original draft; Writing – review & editing; Final approval. Floriane Gallais: Conceptualization; Data acquisition and interpretation; Writing – review & editing; Final approval. Marianne Riou: Data acquisition and interpretation; Writing – review & editing; Final approval. Eva Chatron: Data acquisition and interpretation; Writing – review & editing; Final approval. Tristan Degot: Data acquisition and interpretation; Writing – review & editing; Final approval. Sophie Freudenberger: Data acquisition and interpretation; Writing – review & editing; Final approval. Michele Porzio: Data acquisition and interpretation; Writing – review & editing; Final approval. Armelle Schuller: Data acquisition and interpretation; Writing – review & editing; Final approval. Julien Stauder: Data acquisition and interpretation; Writing – review & editing; Final approval. Sandrine Hirschi: Conceptualization; Data acquisition and interpretation; Writing – review & editing; Final approval. Romain Kessler: Conceptualization; Data acquisition and interpretation; Writing – review & editing; Final approval.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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