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RESEARCH ARTICLE

The Nationwide Impact of COVID-19 on Lung Donation and Transplantation in Belgium

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ABSTRACT

SARS-CoV-2 primarily infects the respiratory tract. Consequently, lung transplantation (LTx) programs have been significantly impacted by the COVID-19 pandemic. This study aimed to summarize the impact of the pandemic on LTx in Belgium. Eurotransplant recorded lung donation and transplantation rates from January 2015 to June 2024. Recipient mortality and LTx for COVID-19 patients were reported by all Belgian LTx centers from January 2016 to June 2023. With the onset of the pandemic, lung donation rates decreased abruptly, reaching their lowest point in the 1st half of 2020 and 2nd half of 2021, with a 44% decrease. Donation rates did not recover until the 2nd half of 2023. Concurrently, annual LTx activity decreased by 20% in 2020, 19% in 2021, and 18% in 2022, subsequently recovering in 2023. Recipient mortality peaked in the 1st half of 2022, with 42% of deaths attributed to COVID-19. Three patients received LTx for COVID-19, and all survived for more than 2 years. LTx programs should prepare for future respiratory virus pandemics. The rapid implementation of evidence-based donor screening; and the reservation of intensive care and operating room capacity can safeguard LTx activity. The high risk of breakthrough infections in LTx recipients requires close follow-up and prompt treatment.

Abbreviations: ARDS, acute respiratory distress syndrome; CLAD, chronic lung allograft dysfunction; CT, computed tomography; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; ISHLT, international society for heart and lung transplantation; LTx, lung transplantation; OR, operating room; PCR, polymerase chain reaction.

1 | Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, abruptly disrupted the functioning of our healthcare system. Lung transplantation (LTx) programs have been severely impacted because the respiratory tract is the primary target of SARS-CoV-2 [1] Direct effects of the virus on lung health include viral pneumonia, which can progress to acute respiratory distress syndrome (ARDS) and irreversible lung injury, potentially requiring LTx [2, 3]. Additionally, SARS-CoV-2 affects lung donation, transplantation activity, and LTx recipient outcomes. Lung donor screening and selection became more challenging due to limited intensive care unit (ICU) capacity and the potential risk of virion transmission from donor to recipient [4–7]. Reduced operating room (OR) and ICU capacity also affected hospitals' ability to perform transplant surgery, despite the availability of suitable organs [8] Finally immunocompromised LTx recipients remained at increased risk of severe and fatal SARS-CoV-2 infection [9].

This study aimed to describe the nationwide impact of the COVID-19 pandemic on lung donation and LTx rates, LTx recipient mortality, and the use of LTx as a treatment for COVID-19 related respiratory failure in Belgium, from 2020 to 2024. In 2019, Belgium's annual LTx rate was 9.7 per million people, similar to North American rates of 8.4 in the USA and 10.8 in Canada [10]. Data from the Eurotransplant organ exchange network and each Belgian LTx program were combined to provide a comprehensive overview of the impact of COVID-19 on LTx.

2 | Materials and Methods

2.1 | Study Design

Belgium is a member of Eurotransplant, an organ exchange organization for eight European countries that provided retrospective data on lung donation and LTx activity [11]. The total number of deceased donors for any organ; donors whose lungs were reported but declined for transplantation; and donors from whom one or both lungs were procured for transplantation, was recorded per 6-month interval from January 1, 2015 to June 30, 2024. A similar approach was employed in the analysis of single- and double-LTx procedures performed in Belgium.

There are four LTx programs in Belgium: University Hospitals Leuven (UZL), Hôpital Erasme in Brussels (ULB), Centre Hospitalier Universitaire Mont-Godinne in Namur (UCL), and University Hospital Antwerp (UZA). A multicenter retrospective analysis was performed in which mortality among LTx recipients and LTx for COVID-19-related respiratory failure was documented at 6-month intervals from January 1, 2016 to June 30, 2023.

2.2 | Organ Donation and Lung Transplantation in Belgium

The median number per 6 months in the pre-pandemic interval from 2015 to 2019 was used as the denominator to calculate the observed changes in organ donation and LTx rates during the pandemic. The lung utilization rate was defined as the number of deceased donors from whom one or both lungs were transplanted, divided by the total number of deceased donors.

2.3 | Lung Transplant Recipient Mortality in Belgium

Mortality in the total cohort of recipients in follow-up was calculated by dividing the number of recipients who died during a 6-month interval by the number of recipients in follow-up at the beginning of that interval. COVID-19-related mortality was defined as death associated with a positive SARS-CoV-2 polymerase chain reaction (PCR) test result.

2.4 | Lung Transplantation for COVID-19

The disease course before LTx, surgical variables, and postoperative recovery were extracted from the electronic medical records. Based on strict selection criteria previously published [12, 13]; and confirmation of irreversible lung injury by chest computed tomography (CT), patients were referred to a single center (Leuven), where the three cases were performed. All patients were bridged to LTx with veno-venous extracorporeal membrane oxygenation (ECMO) and double-LTx was performed after the final pre-LTx workup and high-urgency listing. Further details are described in the Supporting Information.

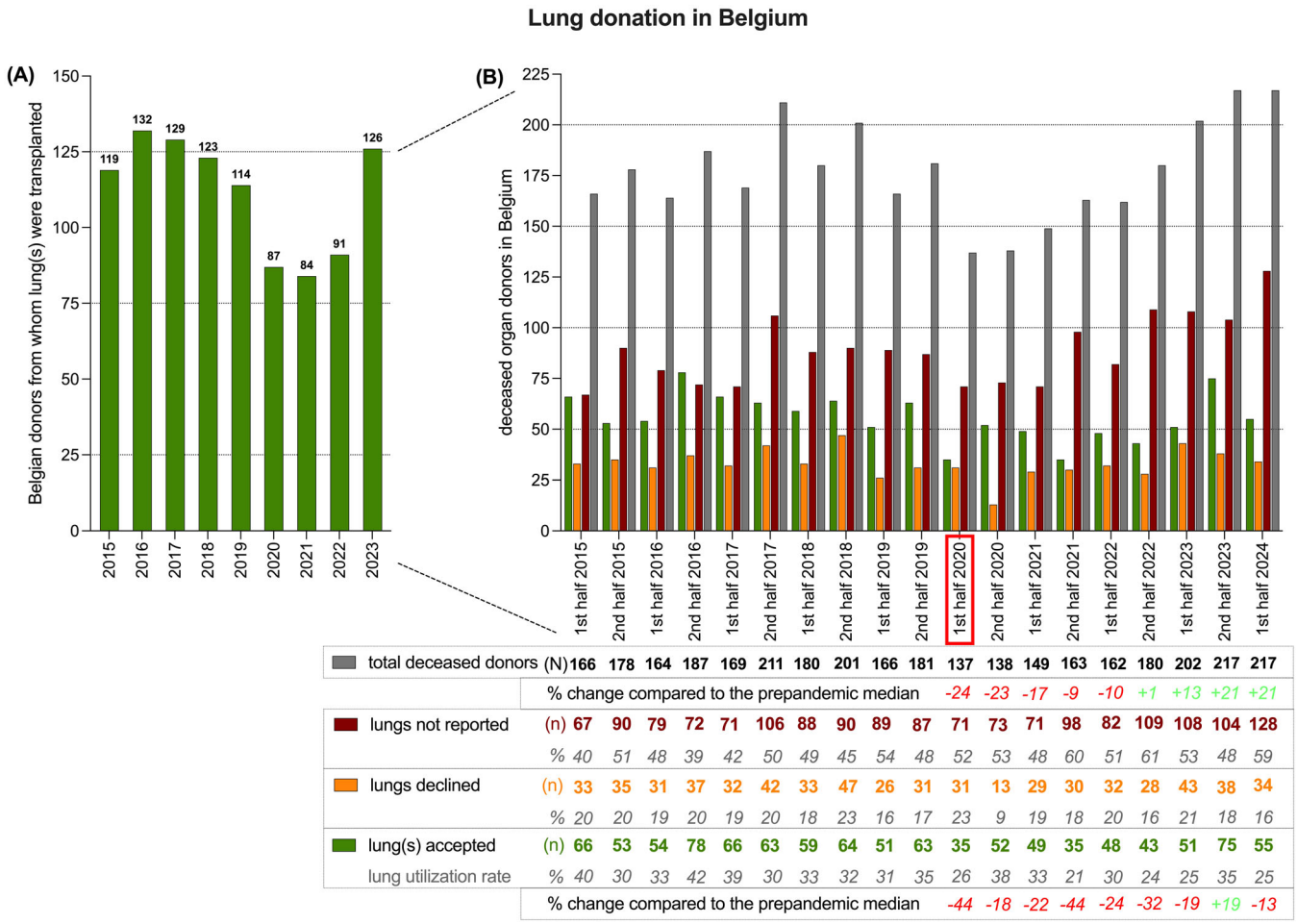
2.5 | Ethical Statement

The study was approved by the Ethics Committee UZ/KU Leuven (S67343). Eurotransplant and the transplant programs in Namur, Brussels, and Antwerp provided anonymized data.

3 | Results

3.1 | The Number of Lung Donations in Belgium Decreased due to COVID-19

Figure 1A shows the annual rate of Belgian donors from whom one or both lungs were procured for transplantation. A marked decrease was observed from 2020 to 2022 followed by a recovery in 2023. Figure 1B shows the total number of deceased donors (for any organ), donors whose lungs were reported but declined, and donors from whom one or both lungs were transplanted. In the 1st and 2nd halves of 2020, which corresponded to the 1st and 2nd waves of widespread SARS-CoV-2 infection, the total number of deceased donors decreased by 24% and 23%, respectively. The decrease in reported deceased donors continued until the 1st half of 2022. An increase of 1% was observed only in the 2nd half of 2022 compared to the pre-pandemic period. The decrease in donors from whom lungs were procured for LTx was most pronounced in the 1st half of 2020 and the 2nd half of 2021, with a 44% decrease observed in each period. The decrease in lung donation rates continued until the 1st half of 2023. It was not until the 2nd half of 2023 that lung donations increased by 19%. The lung utilization rate reached its lowest point of 21% during the pandemic in the 2nd half of 2021, while the minimum utilization rate before the pandemic was 31%.



total deceased donors (N)	166	178	164	187	169	211	180	201	166	181	137	138	149	163	162	180	202	217	217
% change compared to the prepandemic median											-24	-23	-17	-9	-10	+1	+13	+21	+21
lungs not reported (n)	67	90	79	72	71	106	88	90	89	87	71	73	71	98	82	109	108	104	128
%	40	51	48	39	42	50	49	45	54	48	52	53	48	60	51	61	53	48	59
lungs declined (n)	33	35	31	37	32	42	33	47	26	31	31	13	29	30	32	28	43	38	34
%	20	20	19	20	19	20	18	23	16	17	23	9	19	18	20	16	21	18	16
lung(s) accepted (n)	66	53	54	78	66	63	59	64	51	63	35	52	49	35	48	43	51	75	55
lung utilization rate %	40	30	33	42	39	30	33	32	31	35	26	38	33	21	30	24	25	35	25
% change compared to the prepandemic median											-44	-18	-22	-44	-24	-32	-19	+19	-13

FIGURE 1 | Annual number of donors from whom lungs were procured for transplantation (A); Belgian deceased organ donors and lung donation numbers per 6 months (B).

3.2 | The Number of Lung Transplants in Belgium Decreased due to COVID-19

Figure 2A shows the annual number of LTx procedures in Belgium. The number of LTx procedures decreased by 20%, 19%, and 18% in 2020, 2021, and 2022 respectively, compared to the pre-pandemic level. It was only in 2023 that the number of LTx procedures equaled that of pre-pandemic era. Figure 2B shows more detailed numbers per 6 months. LTx activity declined to its lowest point in the 1st half of 2020, with a 33% reduction. Decreased LTx numbers persisted until the 1st half of 2023. An upward trend was first observed in the 2nd half of 2023, with a 7% increase compared to the pre-pandemic period. The number of Belgian donors from whom lungs were procured does not exactly correspond to the number of LTx procedures performed in Belgium because organs are exchanged between Eurotransplant member countries.

3.3 | Mortality of Lung Transplant Recipients in Belgium Increased due to COVID-19

The mortality rate per 6 months from January 2016 to June 2023 among all Belgian lung transplant recipients is summarized in Figure 3. Post-LTx mortality not related to COVID-19 ranged from 2.6% to 4.6% in the pre-pandemic period and remained relatively unchanged during the pandemic, ranging from a minimum of 2.0% to a maximum of 3.9%. However, additional mortality resulting from COVID-19 ranged from 0.1% to 2.1%. The peak occurred in the 1st half of 2022, when 42% of deaths were related to SARS-CoV-2 infection.

3.4 | COVID-19 as an Indication for Lung Transplantation in Belgium

In Belgium, three patients underwent double-LTx for COVID-19 ARDS. Figure 4 illustrates the sequence of events, and a detailed case description is provided in the Supporting Information. All cases were performed in a high-urgency setting after 43, 78, and 54 days of mechanical ventilation before LTx. The bridging-to-LTx interval with ECMO was 8, 63, and 36 days. Chest CT scans before listing showed progression to irreversible lung injury. The post-LTx ICU length of stay was 18, 59, and 73 days. Each recipient developed a pulmonary embolism 38 months, 57 days and 52 days after LTx, respectively. All three patients are alive and home at 40, 40 and 28 months post-LTx without a diagnosis of chronic lung allograft dysfunction (CLAD), as shown in Figure 5. One patient was listed for post-COVID-19 fibrosis but ultimately died before undergoing LTx.

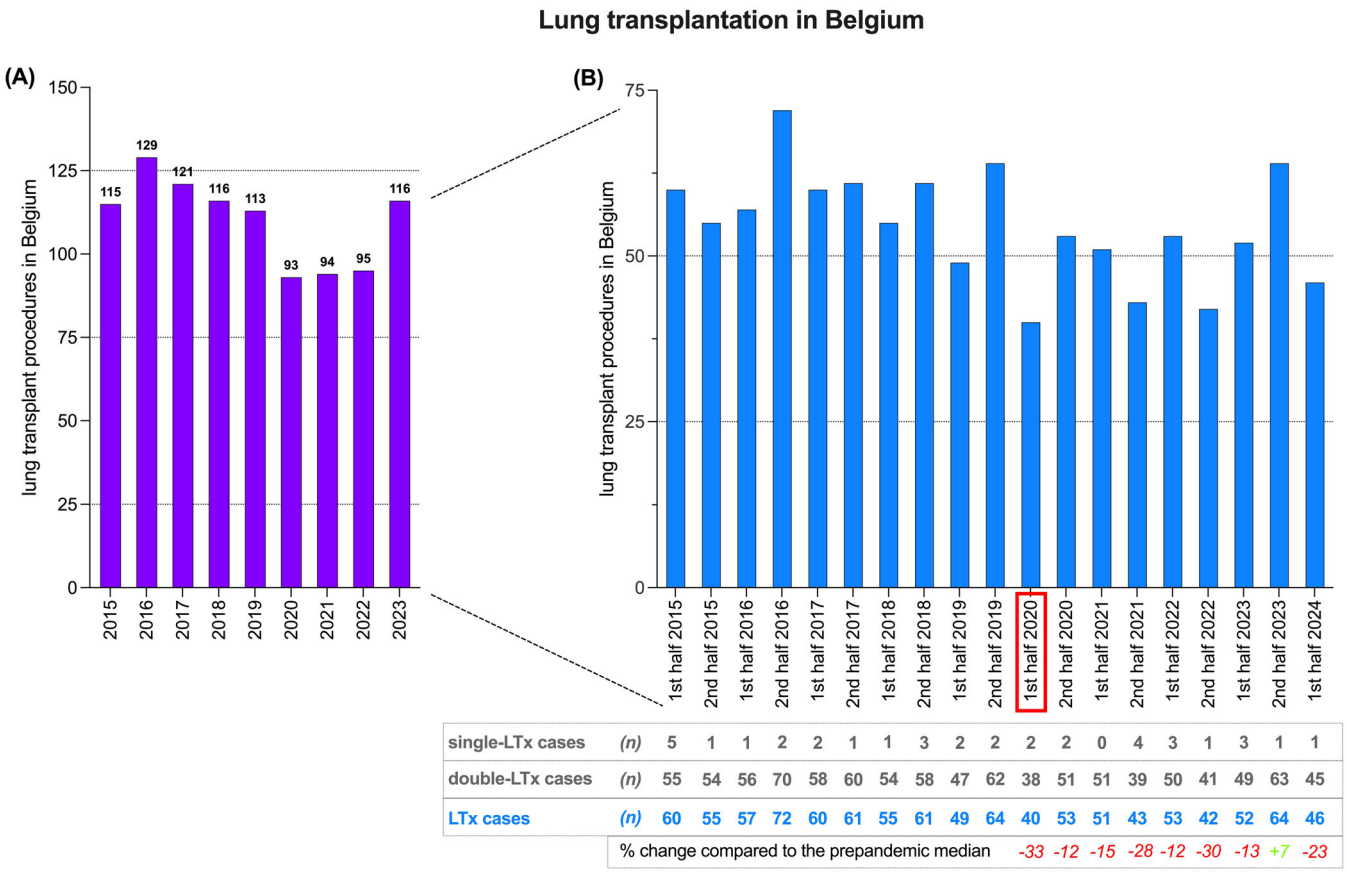


FIGURE 2 | Annual number of lung transplantations in Belgium (A); number of lung transplantations per 6 months (B).

4 | Discussion

This study describes the impact of the COVID-19 pandemic on LTx in Belgium, including lung donation and transplantation, mortality among LTx recipients, and refractory ARDS as a new indication for LTx.

In Belgium, COVID-19 led to a decrease in the total number of deceased organ donors, particularly in the number of available donor lungs. The first pandemic wave in the 1st half of 2020 resulted in a 44% decrease in lung donations. Similarly, from March to May 2020 the number of deceased donors in the UK from whom lungs were offered decreased by 48% [14]. The decrease in lung donations may be related to several factors, including a decrease in road traffic injuries and more complicated screening, workup, and family counseling of potential organ donors in overwhelmed ICUs.

Additionally, the lung is the primary target organ of SARS-CoV-2. Therefore, LTx was associated with an increased risk of donor-derived transmission, which can result in severe early postoperative COVID-19 [15, 16]. Candidate donors who died with rather than from SARS-CoV-2, and who had a positive PCR test result within 21 days were initially considered unsuitable for donation [17]. At the onset of a viral epidemic or pandemic, rapid characterization of infection kinetics and persistence of replication-competent virions is therefore essential [18, 19]. Streamlined screening protocols and optimized diagnostic tests could allow the safe selection of donor lungs, preventing both the unnecessary decline of suitable organs and iatrogenic donor-derived transmission. As our understanding of viral kinetics increased, repeated PCR screening of upper and lower respiratory tract samples allowed for a better assessment of the course of the infection and the risk of transmission [4, 5, 16]. A propensity-matched analysis showed that outcomes after LTx were non-inferior for recipients of lungs from selected donors with a positive SARS-CoV-2 test result within 21 days of donation compared to recipients of lungs from donors with a negative test result [20]. Nevertheless, SARS-CoV-2 continues to circulate among the population and LTx remains at considerable risk of donor-derived transmission. Caution with lung donor selection should be maintained. Using portable point-of-care tests and rapid PCR assays to test bronchoalveolar lavage fluid can complement the clinical assessment of the deceased donor's medical history and radiological imaging [5, 7, 21].

The Belgian annual LTx rate decreased from 2020 to 2022 and did not recover until 2023. A 22-country, multicenter study, found that LTx activity decreased by 16.64% in the first year of the pandemic. However, data on subsequent years are lacking [22]. The lower LTx rate may be related to reduced lung donation rates, as well as reduced OR and ICU capacity, where staff and beds were redirected to treat COVID-19 patients.

Specific challenges posed by an overwhelmed healthcare system were difficult to overcome, resulting in impaired transplant

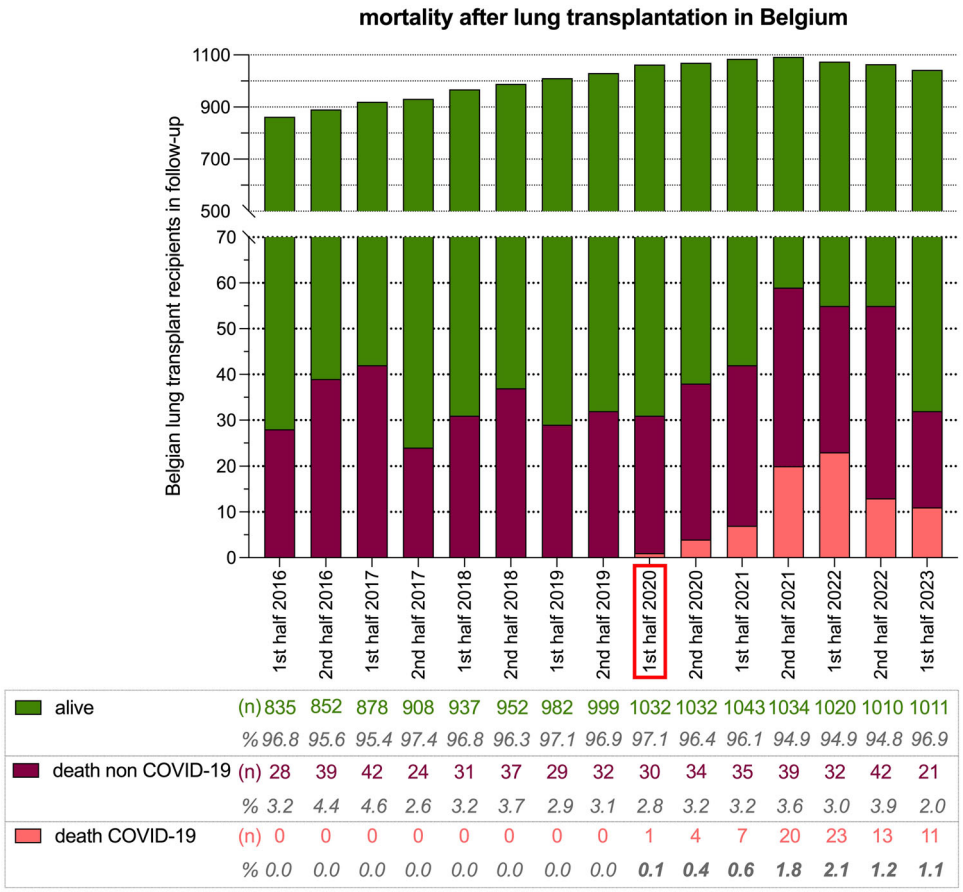


FIGURE 3 | COVID-19 related and non-related mortality per 6 months among Belgian lung transplant recipients.

program functioning [8]. Therefore, in addition to the aforementioned viral workup of lung donors, measures could be taken to ensure a minimum level of ICU and OR capacity to maintain transplant activity in centralized centers.

Additionally, COVID-19 increased mortality among LTx recipients peaked in the 1st half of 2022 with 42% of LTx recipient deaths being related to SARS-CoV-2. At that time, the Omicron variant of concern—known to be more infectious and better at evading pre-existing immunity —was becoming increasingly prevalent. A false sense of security in this later phase of the pandemic—when protective measures were relaxed— may have contributed to the timing of the peak in mortality [23, 24].

Our data reflect the additional mortality caused by SARS-CoV-2 but do not show the proportion of infected recipients who ultimately died, which has been reported to be between 4% and 10% [25, 26]. The severe breakthrough infection rate was highest in LTx recipients (10%), compared with liver (0.9%), heart (4%) or kidney (4%) transplant recipients [9]. The respiratory tract is the primary target of SARS-CoV-2 and LTx recipients are severely immunocompromised due to the triple immunosuppressive regimen, which typically includes steroids, calcineurin inhibitors, and antimetabolites [27]. These factors may explain why an adequate antibody response after the 3rd vaccine dose was observed in only 47% of LTx recipients, compared to 90% of liver transplant recipients [9]. In another study, only 16% of LTx recipients had an adequate response to three vaccine doses [28]. A recent study also confirmed persistently low humoral and cellular immunity after vaccination in LTx recipients [29].

To protect LTx recipients in future epidemics or pandemics, serologic monitoring of the vaccine-induced antibody response and individualized protective measures could prevent severe or fatal breakthrough infections. Prophylaxis and early treatment with monoclonal antibodies can prevent severe breakthrough infections in LTx recipients [30].

ARDS and chronic pulmonary fibrosis due to COVID-19 have emerged as new indications for LTx. In Belgium, three patients with single organ COVID-19 ARDS were selected according to strict criteria and successfully underwent urgent LTx [12, 13, 31]. Interestingly, each patient developed a pulmonary embolism. In the two cases involving early postoperative pulmonary embolisms, the combined sequelae of COVID-19 immunothrombosis, coagulopathy, and transplant-related surgical trauma may have been contributing factors [32–36].

Contrary to earlier expectations, the number of LTx cases for COVID-19 ARDS and pulmonary fibrosis as new indications remained very limited in Belgium [37]. In Austria, 19 LTx procedures were performed in 18% of the patients referred with COVID-19 ARDS [3]. An important number of LTx cases for COVID-19 respiratory failure have been reported in US cohort studies, with 300-400 cases from early 2020 to late 2022 [38–41]. COVID-19 accounted for 0.8% and 10.7% of the LTx volume in

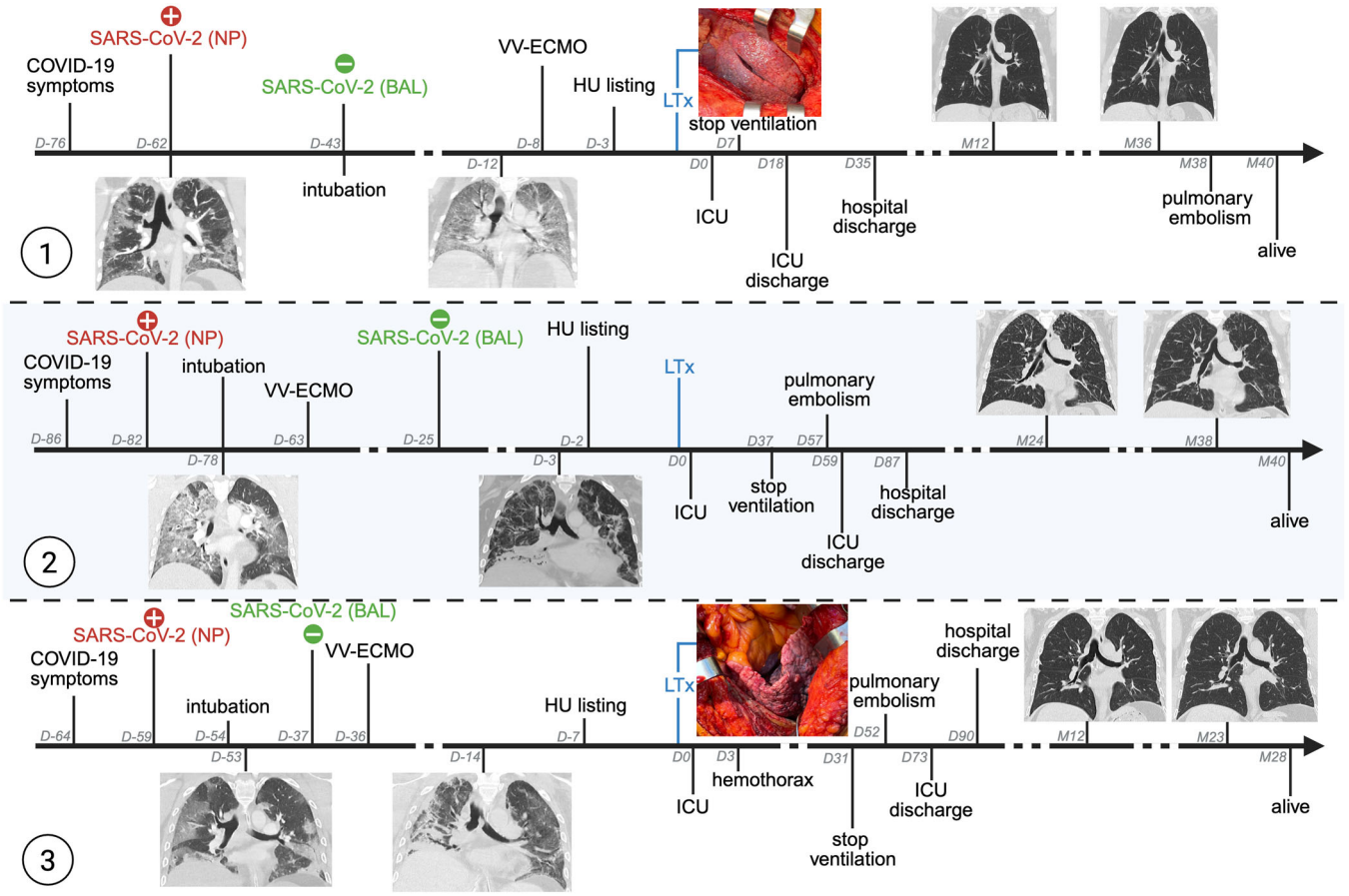


FIGURE 4 | Timeline for the three Belgian cases of lung transplantation for COVID-19 induced acute respiratory distress syndrome. BAL, bronchoalveolar lavage; D, day; ECMO, extracorporeal membrane oxygenation; HU, high-urgency; ICU, intensive care unit; LTx, lung transplantation; M, month; NP, nasopharyngeal; VV, veno-venous.

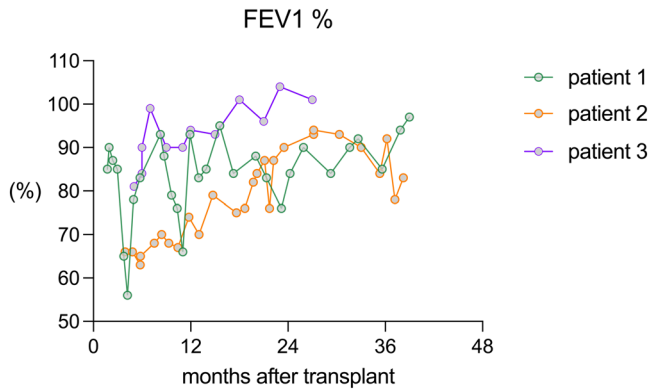


FIGURE 5 | Pulmonary function represented as one-second forced expiratory volume (FEV1) for the three patients who underwent lung transplantation for COVID-19.

2020 and 2021, respectively [41]. One-year survival after LTx for either ARDS or fibrosis due to COVID-19 is similar to non-COVID-19 indications [38–41]. Although the ARDS and fibrosis cohorts are considered separate study groups, clear criteria for both entities were not described and differences in the COVID-19 disease progression and patient status before LTx were not reported. Long-term outcomes after LTx for COVID-19 ARDS are awaited, but available data show a promising trend. Timely referral and rigorous patient selection—aimed at successful postoperative recovery and an acceptable functional status—allows LTx to be a valuable but last resort treatment option.

LTx for COVID-19-related chronic pulmonary fibrosis has not been performed in Belgium. However, successive waves of ICU admissions for COVID-19 ARDS, a second wave of patients with fibrosis requiring LTx was expected [37, 42]. The strong inflammatory response associated with viral pneumonia is thought to trigger pro-fibrotic pathways in the lung parenchyma [43]. Radiological interstitial abnormalities associated with this response were found to be present in 11% of COVID-19 patients within the first year after discharge. However, the proportion of affected lung tissue showed a decreasing trend [35, 44, 45]. Data on persistent abnormalities and progression to end-stage pulmonary fibrosis beyond the first year after COVID-19 are awaited. Several studies have reported on LTx for COVID-19, but criteria for COVID-19 fibrosis and the delay between onset of disease and LTx were not clearly reported [39, 41]. Therefore, data on outcomes after LTx for COVID-19 chronic fibrosis are currently lacking.

A first limitation is that our data are limited to the Belgian setting, where trends may differ from those in other countries. Second, the decrease in LTx activity may have affected waiting list mortality, but this was not addressed in the current study [46]. Third, among LTx recipients, we considered only mortality related to COVID-19, but we did not report the need for hospital or ICU admission or progression to CLAD.

This study is notable because it reports on the impact of COVID-19 in a country with a high annual LTx rate (9.6 per million population in 2019), providing sufficient detail to identify clear trends. Additionally, data were reported on a 4.5-year pandemic period, while providing comparative data from the 5 years before the pandemic.

In conclusion, the COVID-19 pandemic affected the availability of donor lungs, the LTx rate and mortality among recipients. COVID-19 as an indication for LTx remained limited in Belgium. Preparing for future pandemics of respiratory viruses will allow us to better protect the vulnerable populations of candidates on waiting lists and LTx recipients.

Author Contributions

Conceptualization: Jan Van Slambrouck, Robin Vos, and Laurens J. Ceulemans. Data curation: Jan Van Slambrouck, Isabelle Etienne, François Carlier, Veronique Verplancke, Axel Jens, Gauthier Gernay, and Karen Denaux. Formal analysis: Jan Van Slambrouck, and Laurens J. Ceulemans. Resources: Robin Vos, Isabelle Etienne, François Carlier, Veronique Verplancke, Axel Jens, Joost Wauters, Laurens De Saedeleer, Laurent Godinas, Saskia Bos, Maarten Vander Kuylen, Youri Sokolow, Christiane Knoop, Benoit Rondelet, Patrick Evrard, Suresh K. Yogeswaran, Jacqueline Smits, Serge Vogelaar, Dirk Van Raemdonck, and Laurens J. Ceulemans. Visualization: Jan Van Slambrouck, Gauthier Gernay, Laurens J. Ceulemans. Writing – original draft: Jan Van Slambrouck, and Laurens J. Ceulemans. Writing – review & editing: Robin Vos, Isabelle Etienne, François Carlier, Veronique Verplancke, Axel Jens, Gauthier Gernay, Christiane Knoop, Patrick Evrard, Jacqueline Smits, Serge Vogelaar, and Dirk Van Raemdonck. Supervision: Laurens J. Ceulemans. All authors read and approved the final manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data can be obtained from the corresponding author upon request.

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Supporting Information

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