Lobar Lung Transplantation: A Single-Center 10-Year Experience

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ABSTRACT

Background. The shortage of donors for lung transplants is the main limitation of the preceding. Lobar transplantation is an alternative especially useful in patients with short stature and small thoracic cavities. The aim of this study was to perform a descriptive analysis of Portuguese patients who underwent lobar lung transplantation.

Methods. A retrospective study was conducted, and patients submitted to lobar lung transplantation from January 2012 to December 2023 were evaluated. A descriptive analysis was made, including demographic data, lung diseases, waiting list dynamics, pre-transplant evaluations, and post-transplant outcomes.

Results. Sixteen lobar transplants were performed with a predominance of female patients and a median age of 47 years. Most patients had interstitial lung disease or bronchiectasis either due to cystic fibrosis or non-cystic fibrosis. The median predicted total lung capacity (pTLC) ratio was 0.73. The median waiting list time was 6 months with 9 urgent transplants and 1 emergent lobar retransplant. Extracorporeal membrane oxygenation (ECMO) was used in pre-, intra-, and postoperative periods. Most transplanted lobes were the median lobe (ML) + right upper lobe (RUL) and left upper lobe (LUL). The median length of stay was 58 days, with complications such as PDG grade 3, bronchial tree ischemia, and concentrical stenosis of bronchial anastomosis. Six patients died in this period, 1 in the immediate postoperative period and 5 during the post-transplant hospitalization, with a median survival of 20.7 months and a 1-year and 5-year survival rate of 60%.

Conclusion. Our results show a population with an increased waiting list converging in many urgent cases, with an early mortality and high primary graft dysfunction rate. Nevertheless, mid- and long-term survival are promising.

LUNG transplantation is an established therapeutic option in patients with advanced lung disease. With developments in surgical techniques, postoperative care, and immunosuppression, survival after lung transplantation has witnessed a significant improvement over the years. However, the global shortage of donors for transplantation is a major public health concern and a major limitation of lung transplantation [1].

A variety of different strategies have been addressed to increase the lung donor pool. Improved intensive care unit (ICU) management of the donor, extended donor criteria (including increased age donors, more permissive smoking history, more permissive partial pressure of arterial oxygen (PaO2)/fraction of inspired oxygen (FiO2), etc), ex vivo lung perfusion, split lung transplantation, and lobar transplantation

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are some of the strategies that have been successfully adopted [1,2].

Lobar transplantation is one of the strategies that can be used, especially in patients listed for lung transplantation with shorter stature and small thoracic cavities. These patients, typically affected by cystic fibrosis and restrictive lung diseases, female or of pediatric age, tend to have longer waiting list periods [3,4].

In case of worsening of the underlying disease, more frequently observed in long wait listing periods, lung transplantation can become urgent [4]. As a result, lobar transplantation recipients are more frequently bridged to transplantation on ECMO or mechanical ventilation [5]. Accordingly, several studies have been published regarding this practice. It is worth mentioning that post-survival rates have been improving, being similar both in those not requiring and those bridging to veno-venous ECMO [6]. A higher acuity can be associated with decreased survival post−lung transplantation [7].

Even though early complications in this group can be more frequent, long-term survival may be comparable with bilateral lung transplants [8].

For lobar transplants, the lower lobes are most commonly used due to their anatomy and rich vascularization, even though the superior lobes and the middle lobe can be used as well [3].

To improve donor-recipient compatibility, size matching needs to be adequate; the best parameter for this remains controversial. Nevertheless, the pTLC ratio is best supported by the literature [4].

The aim of this study was to perform a descriptive analysis of patients who underwent lobar lung transplantation and respective outcomes (length of stay, complications, and survival) in our center.

MATERIALS AND METHODS

We conducted a retrospective study including patients submitted to lobar lung transplantation in Hospital de Santa Marta, Centro Hospitalar Universitário de Lisboa Central, from January 2012 to December 2023. This is the only lung transplantation center in Portugal.

Patients were referred from different Portuguese hospitals. Before transplant, all of them were evaluated with thoracic computed tomography, pulmonary function testing, clinical and laboratory evaluation, and doppler echocardiogram. Pulmonary function tests included spirometry and plethysmography for measurement of expiratory flow rates and lung volumes; diffusion capacity for carbon monoxide was also estimated, by the single-breath method.

All patients undergoing lung transplantation met the listing criteria for lung transplantation in accordance with International Society for Heart and Lung Transplantation (ISHLT).

A descriptive analysis of this group of patients was made, including demographic data, lung disease, list waiting time, pre-transplant clinical evaluation, donor pTLC (D pTLC), recipient pTLC (R pTLC), type of transplantation, lobes implanted, length of stay, complications related to lung transplantation, and mortality.

Patients requiring admission before lung transplantation due to disease exacerbation (under ECMO support, invasive or non-invasive mechanical ventilation, and high-flow nasal oxygen cannula) were considered urgent.

The decision to perform lobar transplantation was based on donor−recipient height discrepancy. pTLC ratio, and visual assessment of donor lungs and recipient's chest cavity. To calculate lobar donor-to-recipient predicted total lung capacity ratio (pTLC lobar ratio):

- pTLC was calculated based on sex (male or female) and height (cm) [9];
- pTLC ratio was calculated by dividing D pTLC by R pTLC (pTLC ratio = D pTLC/R pTLC);
- Lobar donor pTLC (Ld pTLC) was calculated by multiplying D pTLC by the number of segments transplanted divided by 19 (Ld pTLC = D pTLC × (number of transplanted segments/19));
- pTLC Lobar ratio was calculated by dividing Ld pTLC by R pTLC (pTLC Lobar ratio = Ld pTLC/R pTLC).

Statistical Analysis

Continuous variables, as they do not have a normal distribution, are presented as median and IQRs. Categorical variables are presented in absolute and relative frequency. For survival analyses, the Kaplan−Meier statistics with log-rank testing using SPSS version 19 (IBM SPSS, Inc) was used.

RESULTS

Patient Demographics

During the study period, 355 lung transplants were performed in this center, 16 of which were lobar transplants, which corresponds to 15 patients (1 of them was submitted to lobar transplantation and then lobar retransplantation), all of them from brain-dead donors.

Most patients were female (13 patients; 86.7%), and the observed median age was 47 years (13-61). Three patients were under 18 years of age when the transplant was performed.

Indications for transplantation included 5 patients with fibrotic hypersensitivity pneumonitis, 3 cystic fibrosis, 2 non-cystic fibrosis bronchiectasis, and the rest (1 per disease) idiopathic pulmonary fibrosis, lymphoid interstitial pneumonia, lung fibrosis due to SARS-CoV-2 infection, nonspecific interstitial pneumonia, and bronchiolitis obliterans.

The median waiting list time for transplantation was 6 months (0.5-27), 11 months (3-26) if we exclude urgent transplants.

Nine transplants were urgent, and 1 patient needed an emergent lobar retransplant due to acute allograft rejection 15 days after the first lobar transplant.

As a part of a bridging to transplantation strategy, veno-venous ECMO (ECMO VV) was frequently employed. A total of 6 out of 16 transplants (38%) required this approach, being the most frequently used technique during the preoperative

Table 1. Extracorporeal Circulation Techniques

	Preoperative	Intraoperative	Postoperative
ECMO VV	6 (38%)	3 (19%)	9 (56%)
ECMO VA	1 (6%)	12 (75%)	3 (19%)
CPB	-	1 (6%)	-
No support	9 (56%)	-	4 (31%)
Total	16	16	16

CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VV, venovenous.

Table 2. Days of ECMO Use

		Preoperative, d	Postoperative, d
ECMO VV	Average	37.5	4.9
	Median + SD	12.5 ± 57.25	2 ± 7.36
	IQR	33.5	5.75
	Total days	225	39
ECMO VA	Average	12	7
	Median + SD	12	8 ± 5.57
	Interquartile range	0	5.5
	Total days	12	21

ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VV, venovenous.

period. There was an average period of ECMO VV of 37.5 days and a median of 12.5 days preoperatively. Regarding the intraoperative period, veno-arterial ECMO (ECMO VA) was applied in 12 out of 16 transplants (75%). It is worth considering that all patients required some form of ECMO/cardiopulmonary bypass (CPB) support in the perioperative period, but 6 transplants (37.5%) only required this during the intra-operative period. Finally, concerning the postoperative period, patients also frequently required ECMO VV support, a total of 8 transplants (50%). There was an average duration of ECMO VV of 4.9 days and a median of 2 days post-intervention. The series analysis of ECMO support is detailed in Tables 1 and 2.

Donor Characteristics

Regarding the predictive lung function of the donor and receptor, lobes and number of segments transplanted, lobar donor pTLC and the pTLC lobar ratio, they are described in Table 3.

Most commonly transplanted right lung lobes were the middle lobe + right upper lobe (87.5%) and, on the left, the left upper lobe (62.5%). The mean pTLC Lobar ratio was 0.77 ± 0.1.

Length of Stay and Complications

The median length of stay was 58 days (1-218), with a median mechanical ventilation time of 22 days (1-120).

A total of 8 patients (50%) developed primary graft dysfunction (PGD) grade 3. A1 rejection was observed in 4 patients (25%).

In terms of bronchial complications, 1 patient developed bronchial tree ischemia (9 days post-transplant), and another developed concentrical stenosis of the right and left bronchial anastomosis (2 months post-transplant), treated with rigid bronchoscopy techniques (3 months post-transplant).

Table 3. Lung Function and Number of Segments Transplanted

	D pTLC (mL)	R pTLC (mL)	Lobes Transplanted	Transplanted Segments (n)	Ld pTLC	pTLC Ratio	pTLC Lobar Ratio
	6900	3000	ML + RUL/LLL	9	3268.4	2.3	1.09
	6900*	4570	LLL	4	1452.4	1.5	0.67
	6500	4500	RLL/LLL	9	3078.9	1.4	0.68
	6800	4970	ML + RUL/LUL	10	3578.9	1.4	0.72
	6500	4500	ML + RUL/LUL	10	3421.1	1.4	0.76
	6600	4190	ML + RUL/LLL	9	3126.3	1.6	0.75
	6900	4190	ML + RUL/LUL	10	3631.6	1.6	0.87
	6900	4760	ML + RUL/LLL	9	3268.4	1.4	0.69
	6100	4570	ML + RUL/LUL	10	3210.5	1.3	0.70
	5400	4470	ML + RUL/LUL	10	2842.1	1.2	0.64
	6600	4240	ML + RUL/LUL	10	3473.7	1.6	0.82
	6900	4440	ML + RUL/LUL	10	3631.6	1.6	0.82
	6300	5630	ML + RUL/LL with lingular wedge resection	12	3978.9	1.1	0.71
	7400	4040	ML + RUL/LUL	10	3894.7	1.8	0.96
	6500	4510	ML + RUL/LUL	10	3421.1	1.4	0.76
	5500	4310	ML + RUL/LUL	10	2894.7	1.3	0.67
Median	6550	4455		10	3344.7	1.4	0.73
Average (L) +SD	6.32 ± 9.3	4.3 ± 0.75		9.5	3.3 ± 0.6	1.5 ± 0.3	0.77 ± 0.1
IQR	500	342.5		1	477.625	0.225	0.1325

D, donor; Ld, lobar donor; LLL, left lower lobe; LUL, left upper lobe; ML, median lobe; R, recipient; RLL, right lower lobe; RUL, right upper lobe.

* Single lung lobar transplant.

Table 4. Causes of Death

Cause of Death	N
Septic shock due to respiratory infection	2
Refractory alveolar hemorrhage	2
Allograft disfunction	1
Atypical mycobacteria infection (*Mycobacterium fortuitum*)	1

No patient developed chronic lung allograft dysfunction.

Mortality

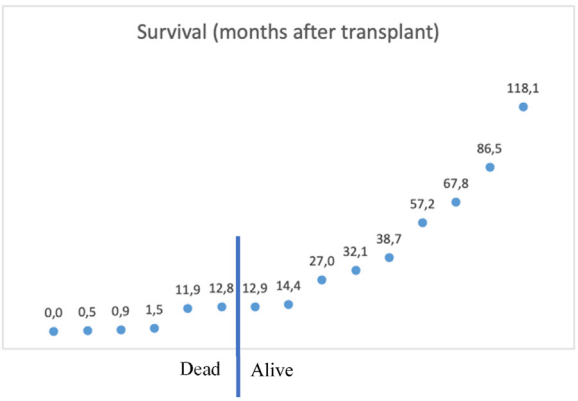
In terms of mortality, 6 patients died in this period: 1 in the immediate postoperative period and 5 during the post-transplant hospitalization. The causes of death are shown in Table 4.

The median survival time was 20.7 months, and among 9 patients who survived the postoperative period, no deaths were observed afterward. The post-transplant survival, in months, is described in Graph 1, and the relation between mortality in lobar transplant with the teams' experience in both lung transplant and lobar transplants is exemplified in Graph 2. The median follow-up time was 13.02 months. Kaplan Meier shows a 1-year survival of 60%, and a 5-year survival of 60% as is illustrated in Graph 3, and even though more deaths have occurred in the urgent transplants subgroup, no statistically significant difference was observed (*P* value 0.730), as illustrated in Graph 4.

DISCUSSION

In 10 years, less than 5% of our center's lung transplants were lobar transplants. Our results show a median waiting list time of 6 months, 11 months excluding urgent patients, with a maximum waiting list time of 29 months. These results underscore the fact that these patients tend to remain a longer period on waiting list, which in turn can reflect on an increased acuity of lung transplantation as observed in other series [4,5,10].

Pediatric patients are an additional challenge because of their low stature and small chest wall, which can affect donor-recipient compatibility. In this series, 3 patients were pediatric, and



Graph 1. Survival per patient

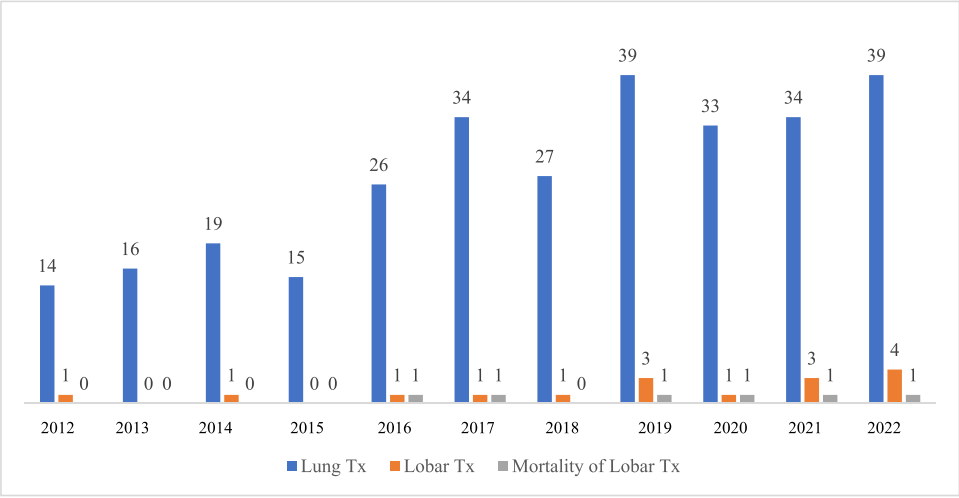
all of them had cystic fibrosis. Two of them were in ECMO as a bridge to transplantation, and the other was submitted to lung transplantation under CPB. This last case was performed in 2012 when ECMO was yet to be defined as the standard of care for extracorporeal support during lung transplantation [11,12]. One of the patients needed an emergent retransplant and died after the second surgery. The other 2 are still alive. According to the literature, the overall survival after lung transplant in the pediatric population is similar to adults, as it improves over time due to better surgical techniques, experience, and better postoperative care in the ICU [13,14]. Some studies suggest that in pediatric patients with cystic fibrosis, lung transplant was associated with an improvement in survival when compared with non-transplanted pediatric patients [15].

Like children, women and patients with restrictive disease have smaller chest walls, and a donor can be difficult to find, thus resulting in longer waiting list time. In this study, all patients were either female, under 18, or had restrictive lung disease. Nevertheless, lobar lung transplant can virtually be used in any pulmonary disease, including obstructive diseases like noncystic fibrosis, bronchiectasis or bronchiolitis obliterans, as our series demonstrates.

Our results show an average pTLC ratio of 1.5 ± 0.3 and, as anticipated, when adjusted for the number of segments transplanted, a decrease to 0.77 ± 0.1 (pTLC Lobar ratio) which is consistent with results shown in a lung lobar transplantation systematic review (pTLC Lobar ratio 0.76 ± 0.2) [4].

Questions remain about the optimal pTLC recipient-donor ratio that should be aimed for when performing lung transplantation. A study of subjects from the Scientific Registry of Transplant Recipients in the United States identified the pTLC ratio as an independent predictor of death in the 1st year post−lung transplantation, showing a nonlinear association with declining risk of death with a higher pTLC ratio from 0.5 to about 1.3 (with a rising risk of death above this value) [16]. Another study shows a decreased risk of PGD grade 3 in oversized (pTLC > 1) allografts [17]. Despite these possible advantages, oversized allografts raise concerns as hemodynamic compromise on chest closure operatively and in the immediate postoperative period, as well as atelectasis, which in turn can undermine oxygenation and increase the risk of infection [4,10]. However, in another study, oversized allografts were not associated with postoperative complications but with shorter lengths of stay [18]. Taking this into consideration, some authors suggest that lobar transplantation could be an important option in cases with severely oversized allografts (pTLC ratio > 1.4) [4]. In our results, we present an average pTLC ratio of 1.5 ± 0.3, which goes in line with this evidence, showing an appropriate selection of cases for lobar lung transplantation in our center.

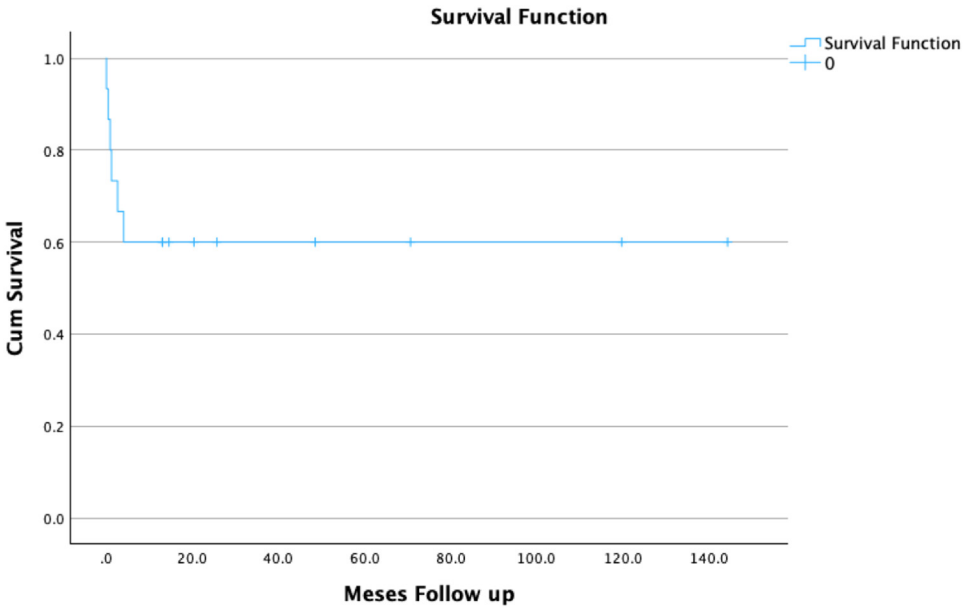
A great proportion of these transplants were made in urgent or semi-urgent settings due to the rapid deterioration of patients' clinical conditions, which can also be observed in larger series. In our series, most (56.25%/9 out of 16) were considered urgent, including the re-transplant. The fact that patients needed ECMO or different forms of ventilatory support, like continuous noninvasive ventilation or high flow nasal oxygen when the respiratory insufficiency is refractory to conventional therapies,



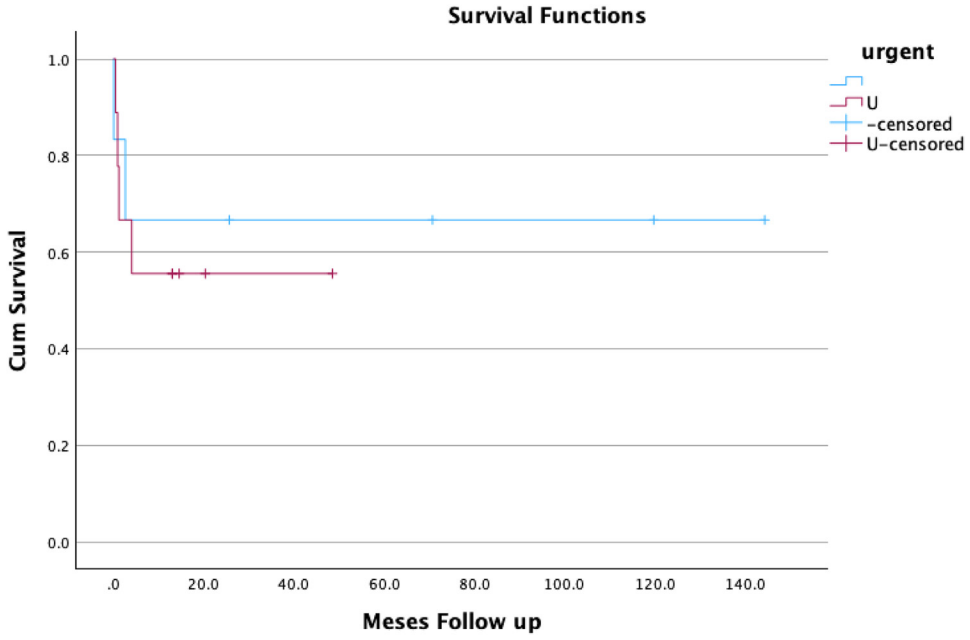
Graph 2. Proportion of lobar transplants and related mortality in comparison with number of transplants per year

puts them in an upward position in the waiting list, and the lobar transplant was an effective technique to provide them with a new and functional lung from donors presenting a significant size mismatch. Despite the absence of a statistically significant difference, the group of urgent transplants had a superior number of deaths (66.7%/4 out of 6 deaths). Acuity of transplantation has been related to decreased survival [7].

Extracorporeal circulation is an important tool used in lobar transplantation. A total of 15 patients required ECMO support intraoperatively (1 after reperfusion edema and the others from the beginning), and 1 patient required CBP. The use of extracorporeal circulation is important for the prevention or treatment of reperfusion edema that might arise in the first graft due to its diminished vasculature (when compared with a complete lung), receiving the entire cardiac output of the recipient [10]. Some authors defend the use of ECMO as imperative in the setting of lobar transplantation to avert complications and improve outcomes, having the additional advantage of possible prolongation in the postoperative period [5,10]. Postoperative ECMO was used in 11 patients (69%), which is higher than other series.



Graph 3. Kaplan Meier Survival analysis of lobar lung transplants



Graph 4. Kaplan meier survival comparison between urgent (U) and non urgent lobar transplants

This may be related to the elevated number of patients transplanted in urgent manners (9 patients, 8 of them requiring post-operative ECMO).

Regarding complications, a total of 8 patients (50%) developed PGD 3. Some authors describe a range of PGD 3 between 13% and 56% [4] and others describe a significant greater likelihood of PGD 3 in patients submitted to lobar transplantation when compared with the full lung transplants [10].

Bronchial complications are a major concern in lobar transplantation. In our study, 2 patients (12.5%) developed this kind of complication: 1 bronchial tree ischemia (related to acute rejection) and 1 bronchial stenosis. As back table lobectomies are performed for lobar transplantation, special technical considerations must be considered (enough bronchial margins for anastomosis, avoiding thorough dissection, increased difficulty in the dissection of empty vessels, etc) to prevent complications, adding complexity to the procedure [10]. Despite the concerns of bronchopleural fistula in the presence of donor bronchial stump [19,20], in our center, most anastomoses on the right were made with the RUL + ML, with an associated right lower lobe (RLL) bronchial stump. The bronchial stenosis observed occurred on the bronchial anastomosis being successfully treated with endoscopic techniques. Some authors report no complications related to bronchial stumps, which agrees with our findings [21].

Although lower lobes are often favored for lobar transplantations [3], at our center, we typically use upper lobes for such procedures. We find that the upper lobes' anatomy lends itself better to fit the static apex of the thoracic cavity, with the potential for easier adaptation of the diaphragm if necessary. On the other hand, this approach allows the donor-receptor anastomosis of the main pulmonary arteries and bronchi, reducing the likelihood of donor-receptor mismatch.

Concerning mortality, all deaths occurred during hospital stay, with a 30-day mortality of 25%, a 90-day mortality of 31.25%, and a 1-year mortality of 37.5%. A systematic review of lobar transplantations identified that lobar transplant recipients had a 1.85 relative risk of 1-year mortality compared with conventional lung transplantation, although publication bias was identified [4]. Some authors advocate this higher early mortality could be related to the higher acuity of transplantation in this group, as transplantation in urgent matters has been related to decreased survival [4,7]. Despite the absence of a statistically significant difference, the group of urgent transplants in our study presented a superior number of deaths (66.7%/4 out of 6 deaths).

Finally, long-term survival was also taken into consideration. At the time of this report, some of the patients who have reached 1-year survival are yet to reach 3- or 5-year survival milestones. This might be a limitation of our series because only 5 out of 16 transplants have been done more than 5 years prior to the data collection date. A total of 5 out of 11 cases (45%) of 2-year survival and 3 out of 5 cases (60%) of 5-year survival were assessed. Existing evidence supports the use of lobar lung transplantation as a valid alternative to full lung transplantation with similar medium- and long-term outcomes [22].

When performing such a technically demanding procedure on a complex patient, especially in urgent matters, challenges may arise during the peri-operative period, which can justify high perioperative mortality, as also seen in Toronto series with a 41.9% of cases made in rapidly deteriorating patients, and a

Table 5. Comparison With Other Series

		Our Center	Vienna 2014	Eberlein et al (Systematic Review)	Toronto 2019	Schiavon et al 2022
Hospital stay (d)		58 (1-218)	33.5 (1-147)	30-43	45 (27-86)	30 (24-48)
Mechanical ventilation (d)		22 (1-120)	6 (1-61)	-	-	44 (24-83)
pTLC $_{full}$ (ratio)		1.5 ± 0.3	-	1.15 to 1.68 ± 0.4	1.61 ± 0.45	1.2 (1.1-1.4)
pTLC $_{lobar}$ (ratio)		0.77 ± 0.1	-	0.69 ± 0.1 to 0.94 ± 0.3	0.97 ± 0.53	0.8 ± 0.1
ECLS support	Preoperative	7 (44%) – ECMO	No single variable	-	15 (20%) non-specified	-
	Intraoperative – ECMO	15 (94%)	49 (36.6%)	-	26 (34.7%)	-
	Intraoperative – CPB	1 (6%)	4 (3%)	-	38 (50.7%)	-
	Postoperative	11 (69%) – ECMO	3 (2.2%)	20%-36% – ECMO	14 (18.6%) non-specified	0 - ECMO
No support		All patients required during the perioperative period	28 (20.9%)	-	-	-
Retransplantation		1 (6%)	8 (6.2%)	-	-	0
30-d mortality		1 (6%)	14 (10.2%)	-	10 (13.3%)	8%
Long-term survival	1-y	56%	65%	50%-100%	73.2%	73%
	2-y	45%	63%	-	-	63%
	5-y	60%	55%	37.5%-54.9%	56.9%	55%
PGD	Different outcomes evaluated	8 (50%) with PGD 3	61 (44%) with PGD >0	13%-56%	20 (26.7%) with PGD 3	39% with PGD 3
No. of cases		16	138	301	75	49

CPB, cardiopulmonary bypass; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; PGD, primary graft dysfunction; pTLC, predicted total lung capacity; VA, venoarterial; VV, venovenous.

17.3% 90-day mortality [10]. Nevertheless, after surpassing this critical initial period, long-term mortality can be favorable; our results indicate no post-discharge death with a 5-year survival of 60%, comparable with other series published in literature where 5-year survival is about 50% [23].

Concerning lobar transplant recipients' data and outcomes obtained in our center, we further detail our series against the results of other studies, in Table 5.

Our study has several limitations: its retrospective nature which can lead to potential bias. A small sample size and a limited follow-up period. Furthermore, the pTLC ratio was used as the main marker for donor-recipient allocation even though it is imprecise, especially concerning predictions of thoracic cavity size in patients with end-stage lung disease [16].

CONCLUSIONS

In conclusion, in order to overcome the donor shortage, many strategies have been adopted, lobar transplantation being one of them. In a period of 10 years, we report our series of lobar lung transplantations. Our results show a population with an increased waiting list period converging in many urgent cases. An increased early mortality and PGD rate was observed; nevertheless, despite a small sample size and retrospective nature of the study, mid- and long-term survival is promising, making lobar lung transplantation an important and valid option, specifically in small-chested patients, being an effective way to avoid longer waiting list periods and lung transplantation performed in urgent matters. Lobar pTLC ratio can be used as a tool for donor-recipient matching despite exhibiting some limitations. More extensive studies in this area are necessary.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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