

POST-TRANSPLANT SURVIVAL IN PATIENTS WITH INTERSTITIAL LUNG DISEASE: A REAL WORLD COHORT FROM ARGENTINA

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Received: 22-V-2026

Accepted: 29-IX-2026

Abstract

Introduction: Lung transplantation is a therapeutic option for patients with advanced interstitial lung disease (ILD). However, data regarding post-transplant outcomes in Latin America remain limited. The aim of this study was to evaluate overall post-lung transplant survival, survival according to ILD etiology, and factors associated with mortality at an Argentine referral center.

Materials and methods: We conducted a retrospective cohort study including ILD patients who underwent lung transplantation at a single center in Argentina between 2010 and 2023. Overall survival was estimated using Kaplan–Meier analysis. Survival according to ILD etiology was compared using the log-rank test. Factors associated with mortality were evaluated using a Cox proportional hazards model.

Results: Forty-nine patients were included: 16 with idiopathic pulmonary fibrosis, 7 with connective tissue disease-associated ILD, and 26 with other ILDs. Median age was 56 years, and 69.4% were male. Median follow-up was 1.8 years. Overall survival at 1, 3, and 5 years was 68.5%, 51.8%, and 35.6%, respectively. Conditional 5-year survival among 1-year survivors was 48%. No significant differences in survival were observed according to ILD etiology. In multivariable analysis, post-transplant extracorporeal membrane oxygenation use was independently associated with increased mortality (HR 3.85; 95% CI 1.37–10.8; $p = 0.011$).

Conclusion: In this Argentine cohort, post-transplant survival among ILD patients was lower than that report-

ed in international registries, with no significant differences according to ILD etiology. These findings highlight the need for region-specific data on lung transplantation outcomes in patients with ILD.

Key words: interstitial lung disease, lung transplantation, survival analysis, connective tissue disease, ECMO, Latin America

Resumen

Supervivencia postrasplante pulmonar en pacientes con enfermedad pulmonar intersticial: experiencia de vida real en Argentina

Introducción: El trasplante pulmonar es una opción terapéutica para pacientes con enfermedad pulmonar intersticial (EPI) avanzada. Los datos sobre resultados postrasplante en América Latina son limitados. El objetivo fue evaluar la supervivencia global postrasplante, la supervivencia según la etiología de la EPI y los factores asociados con mortalidad en un centro argentino.

Materiales y métodos: Estudio de cohorte retrospectivo de pacientes con EPI sometidos a trasplante pulmonar en un centro de Argentina entre 2010 y 2023. La supervivencia global se estimó mediante análisis de Kaplan–Meier y se comparó según etiología de EPI mediante *log-rank*. Los factores asociados con mortalidad se evaluaron mediante regresión de Cox.

Resultados: Se incluyeron 49 pacientes: 16 con fibrosis pulmonar idiopática, 7 con EPI asociada a enferme-

dad del tejido conectivo y 26 con otras EPI. La mediana de edad fue de 56 años y el 69.4% fueron hombres. Mediana de seguimiento: 1.8 años. La supervivencia global al año, 3 y 5 años fue de 68.5%, 51.8% y 35.6%, respectivamente. La supervivencia condicional a 5 años entre los supervivientes al primer año fue del 48%. No hubo diferencias significativas según la etiología de la EPI. En el análisis multivariado, el uso de oxigenación por membrana extracorpórea postrasplante se asoció independientemente con mayor mortalidad (HR 3.85; IC 95% 1.37-10.8; $p = 0.011$).

Conclusión: En esta cohorte argentina, la supervivencia postrasplante en pacientes con EPI fue menor a la reportada en registros internacionales, sin diferencias según la etiología de la EPI.

Palabras Clave: enfermedad pulmonar intersticial, trasplante de pulmón, análisis de supervivencia, enfermedades del tejido conectivo, oxigenación por membrana extracorpórea, América Latina

KEY POINTS

Current knowledge

- Lung transplantation is an established therapeutic option for selected patients with advanced interstitial lung disease. Most available survival data derive from international registries, while information from Latin America remains limited.

Article's contribution to current knowledge

- This study provides real-world data on lung transplantation outcomes in patients with interstitial lung disease from an Argentine referral center. Post-transplant survival was lower than that reported in international registries, with no significant differences according to ILD etiology. Post-transplant ECMO use was independently associated with mortality.

Interstitial lung diseases (ILDs) are a heterogeneous group of parenchymal lung disorders characterized by varying degrees of inflammation and fibrosis of the pulmonary interstitium¹. Among these, idiopathic pulmonary fibrosis (IPF) and ILDs associated with connective tissue diseases (CTD-ILDs) are leading indications

for lung transplantation in many transplant centers worldwide^{2,3}. As these conditions often progress despite antifibrotic or immunosuppressive treatment, lung transplantation remains the only therapeutic option with proven survival benefit for patients with advanced disease⁴.

Although lung transplantation improves quality of life and extends survival in selected patients with ILD, outcomes remain heterogeneous. Factors such as ILD etiology, age, lung allocation score, and pre-transplant functional status have been associated with differences in post-transplant prognosis⁵. Furthermore, patients with CTD-ILD, previously considered suboptimal candidates due to extrapulmonary involvement, are increasingly undergoing transplantation. While several studies suggest that their post-transplant survival is comparable to that of patients with IPF, other reports show worse outcomes in specific subgroups such as those with polymyositis/dermatomyositis^{6,7}. Patients with systemic sclerosis-associated ILD may also experience distinct outcomes due to extrapulmonary manifestations and a higher incidence of gastrointestinal complications⁸. Moreover, the development of chronic lung allograft dysfunction (CLAD) remains a major determinant of long-term morbidity and mortality in this population⁹.

Most of the available evidence arises from large multicenter registries in North America and Europe. However, regional differences in patient selection, transplant practices, and healthcare access underscore the importance of complementary data from single-center cohorts, particularly from underrepresented regions such as Latin America. The generalizability of findings from European, North American, or Asian populations to these settings remains uncertain^{10,11}.

The primary objective of this study was to estimate the post-transplant survival of adult patients with ILD and to assess whether survival differed according to ILD etiology. Secondary objectives were to describe the characteristics of the transplanted ILD cohort, to identify factors associated with post-transplant mortality, and to evaluate the time to adverse outcomes and the development of CLAD.

Materials and Methods

Study design and population

A retrospective cohort study was conducted at a tertiary university hospital in Buenos Aires, Argentina, between 1 January 2010 and 30 November 2023. Follow-up was conducted until June 6, 2024. All adult patients with ILD who underwent lung transplant during the study period were eligible. Patients with re-transplantation or incomplete data were excluded.

Data on demographics, clinical characteristics, pulmonary function tests, and comorbidities were collected from electronic medical records. All information was extracted from a single clinical data repository (CDR) fed by the hospital's electronic health record. The CDR integrates data from test results, clinical notes, imaging, outpatient and inpatient care.

The primary outcome was time to all-cause mortality, defined as the interval from the date of lung transplantation to the date of death from any cause.

Secondary outcomes included post-transplant survival by ILD etiology, comparing outcomes among patients with IPF, CTD-ILD, and other ILDs. Another secondary outcome was time to the first adverse event, defined as a composite endpoint of initiation of long-term oxygen therapy or development of CLAD during the study period.

CLAD was defined as a persistent forced expiratory volume in one second (FEV1) decline of at least 20% compared to the mean of the two best post-transplant values after exclusion of other identifiable causes⁹.

Statistical analysis

Continuous variables were summarized using mean (standard deviation) or median (interquartile range), as appropriate. Categorical variables were described using absolute and relative frequencies. For comparisons among ILD subgroups, one-way ANOVA or the Kruskal–Wallis test was used for continuous variables, and the Chi-square or Fisher's exact test for categorical variables. Follow-up time was defined as the interval from lung transplantation to death or censoring.

Overall survival was estimated using Kaplan–Meier curves and compared across ILD etiologies using the log-rank test. Cumulative survival probabilities at 1, 3, and 5 years were reported. Conditional 5-year survival given 1-year survival (CS5/1) was calculated using the Kaplan–Meier method as $S(6)/S(1)$. Event-free survival for the composite endpoint of CLAD or long-term oxygen therapy was also estimated using Kaplan–Meier analysis, with

censoring at death or last follow-up.

To identify factors independently associated with post-transplant mortality, a multivariable Cox proportional hazards model was constructed. Covariates included age, extracorporeal membrane oxygenation (ECMO) use during the immediate postoperative period, hospitalization at transplant (≥ 3 days prior), and acute rejection (modeled as a time-dependent covariate). The proportional hazards assumption was assessed using Schoenfeld residuals (global test $p = 0.456$), and multicollinearity was ruled out ($VIF < 2$). Influential observations were examined using DFBETA residuals.

A two-sided p -value < 0.05 was considered statistically significant. All statistical analyses were conducted using Stata version 16 (StataCorp LLC, College Station, TX, USA).

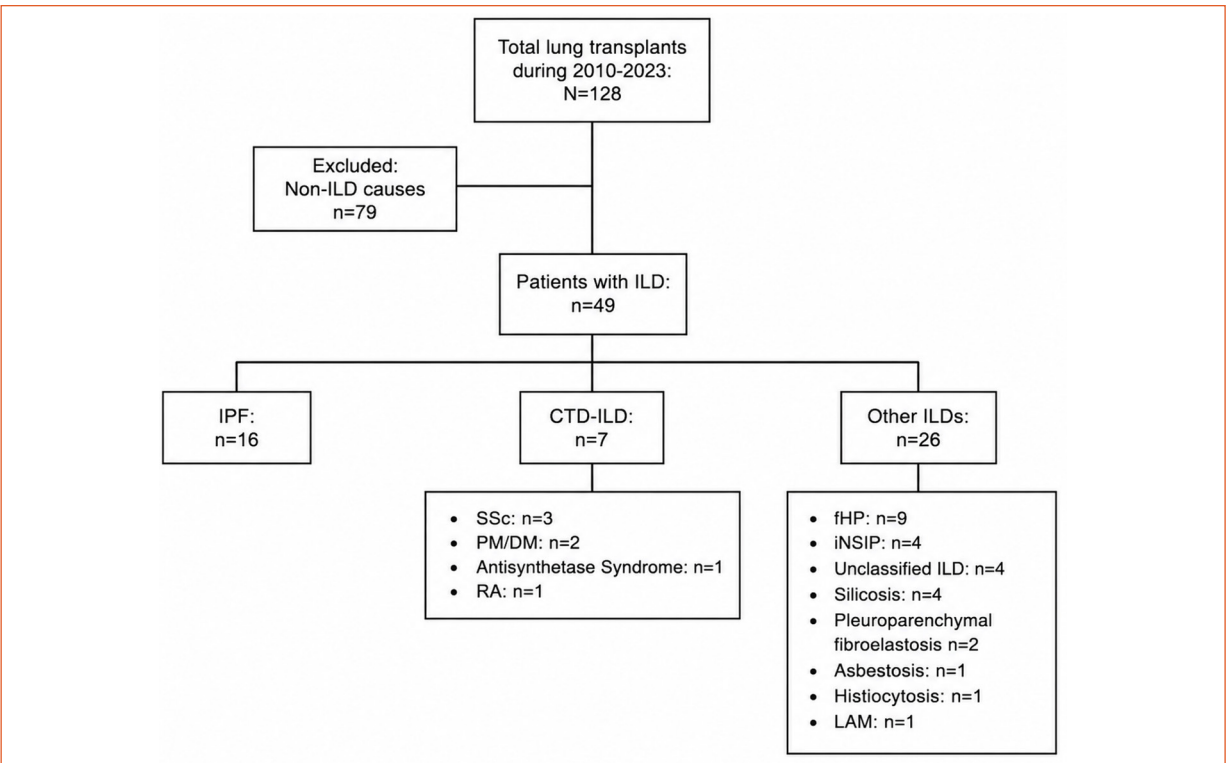
The study followed the Helsinki Declaration of Ethical Principles for Medical Research Involving Human Subjects and the Good Clinical Practice guidelines. The study was approved by the Research Protocols Ethics Committee of the *Hospital Italiano de Buenos Aires*.

Results

Baseline characteristics

Forty-nine patients with ILD were included: 16 (32.7%) with IPF, 7 (14.3%) with CTD-ILD, and 26 (53.1%) with other ILDs. The flow of patient selection is shown in Figure 1, and baseline characteristics stratified by ILD etiology are summarized in Table 1. Most were male (69.4%) and former smokers (63.3%), with a median age of 56 years (IQR 45–62). Pulmonary hypertension was the most common comorbidity (77.6%), followed by cardiovascular disease (20.4%). Patients with IPF were significantly older at transplant than those in other groups ($p < 0.001$). Lung function was severely impaired at listing, with median FVC and DLCO values of 43.5% and 28% predicted, respectively. The majority underwent non-elective transplantation, with 79.6% hospitalized at the time of surgery and 85.7% receiving a single-lung graft. No significant differences were observed between groups in pre-transplant status or procedure. No patients were lost to follow-up. The median follow-up was 1.8 years (IQR 0.4–4.4), and waitlist time was 5.3 months (IQR 2.0–15.4). ECMO was used intra- or postoperatively in 65.3% of recipients. Median post-transplant hospitalization was 36 days (IQR 23–72).

Figure 1 | Flow diagram of patient selection and classification by ILD etiology



ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; CTD-ILD: connective tissue disease–associated ILD; fHP: fibrotic hypersensitivity pneumonitis; iNSIP: idiopathic non-specific interstitial pneumonia; LAM: lymphangioleiomyomatosis; SSc: systemic sclerosis; PM/DM: polymyositis/dermatomyositis; RA: rheumatoid arthritis

The figure outlines the total number of lung transplant recipients with ILD included in the analysis and their distribution into three etiologic groups: IPF, CTD-ILD, and other ILDs

Survival analysis

Kaplan–Meier survival curves are shown in Figures 2 and 3. Figure 2 displays overall survival for the entire cohort, with the steepest decline occurring within the first 3 to 5 years’ post-transplant. Median overall survival was 3.78 years. Among patients surviving the first year, conditional 5-year survival was 48% (CS5/1 = 0.48). Figure 3 shows survival by transplant indication, with no significant differences between groups (log-rank $p = 0.600$). No significant differences were found by transplant era (2010–2023; $p = 0.248$) or sex ($p = 0.787$). Survival at 1, 3, and 5 years was 68.5%, 51.8%, and 35.6%, respectively (Table 1). Although survival was numerically lower in the CTD-ILD group, differences by ILD etiology were not statistically significant ($p = 0.600$, Log-rank test).

Risk factors for mortality

In univariate Cox regression analysis, only post-transplant ECMO use was significantly associated with increased mortality (HR 4.08, 95% CI 1.51–11.02; $p = 0.006$). Age, BMI, ischemic time, transplant era, hospitalization at transplant, acute rejection, single-lung transplantation, and ILD etiology were not significantly associated with mortality. In the multivariable model, ECMO remained independently associated with higher mortality (HR 3.85; 95% CI 1.37–10.8; $p = 0.011$). The proportional hazards assumption was met (global test $p = 0.456$; all individual $p > 0.23$). Univariate and multivariable results are summarized in Table 2.

CLAD and airway stenosis were the most frequent complications, each occurring in 18.4% of recipients. Acute rejection was treated in 14.3%,

Table 1 | Baseline characteristics and Kaplan–Meier survival estimates at 1, 3, and 5 years' post-transplant, by ILD etiology

Variable	Overall N=49	IPF N=16	CTD N=7	Others N=26	p-value
Recipient demographics					
Age years, median (IQR)	56 (45-62)	64 (59-67)	46 (43-55)	49 (38-61)	<0.001
Female sex, n (%)	15 (30.6)	3 (18.8)	3 (42.9)	9 (34.6)	0.396
BMI kg/m ² , mean (SD)	26.4 (4.7)	27.5 (4.4)	28.9 (4.5)	24.9 (4.7)	0.074
Comorbidities, n (%)					
Former smoker	31 (63.3)	13 (81.3)	2 (28.6)	16 (61.5)	0.058
Diabetes mellitus	9 (18.4)	5 (31.3)	2 (28.6)	2 (7.7)	0.096
Cardiovascular disease	10 (20.4)	6 (37.5)	2 (28.6)	2 (7.7)	0.055
PH	38 (77.6)	12 (75%)	7 (100)	19 (73.1)	0.369
Pre-transplant clinical status					
Hospitalization Pre-Transplant, n (%)	39 (79.6)	13 (81.3)	6 (85.7)	20 (76.9)	1.000
Waitlist time, days - median (IQR)	158 (59-462)	159 (48-210)	152 (91-542)	175 (57-600)	0.610
PAPm mmHg, median (IQR)	29 (20-39)	28 (21-36)	38 (30-44)	25 (19-36)	0.118
FVC %, median (IQR)	43.5 (34-50)	42 (35-63)	50 (32-69)	42.5(31-50)	0.360
DLCO %, median (IQR)	28 (21-34)	23 (19-29)	34 (26-41)	28 (20-34)	0.057
Transplant procedure					
Single lung transplantation n (%)	42 (85.7)	16 (100)	5 (71.4)	21 (80.8)	0.082
Ischemic time, min, median (IQR)	290 (240-390)	288 (238-383)	330 (275-403)	275 (226-390)	0.490
Transplant status, n (%)					0.911
Urgent	39 (79.6)	13 (81.3)	6 (85.7)	20 (76.9)	
Elective	10 (20.4)	3 (18.7)	1 (14.3)	6 (23.1)	
Transplant period >=2018, n (%)	24 (49.0)	10 (62.5)	3 (42.9)	11 (42.3)	0.459
Cumulative Survival post-Tx					0.600
1 year, Estimated Survival %	68.5	75.0	71.4	64.0	
3 years, Estimated Survival %	51.8	45.0	47.6	54.8	
5 years, Estimated Survival %	35.6	15.0	*	49.8	

BMI, body mass index; CTD, connective tissue disease; DLCO, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; IQR, interquartile range; PH, pulmonary hypertension; PAPm: mean pulmonary artery pressure; SD, standard deviation; Tx, transplant *, the 5-year survival estimate for the connective tissue disease group could not be calculated due to the absence of patients at risk at that time point (i.e., all patients were either deceased or censored before year 5).

and 12.2% required long-term oxygen therapy. Incidence rates per 100 patient-years were 7.06 (CLAD), 8.10 (stenosis), 5.62 (rejection), and 4.45 (oxygen). Table 3 summarizes cumulative incidence and event rates for major post-transplant complications.

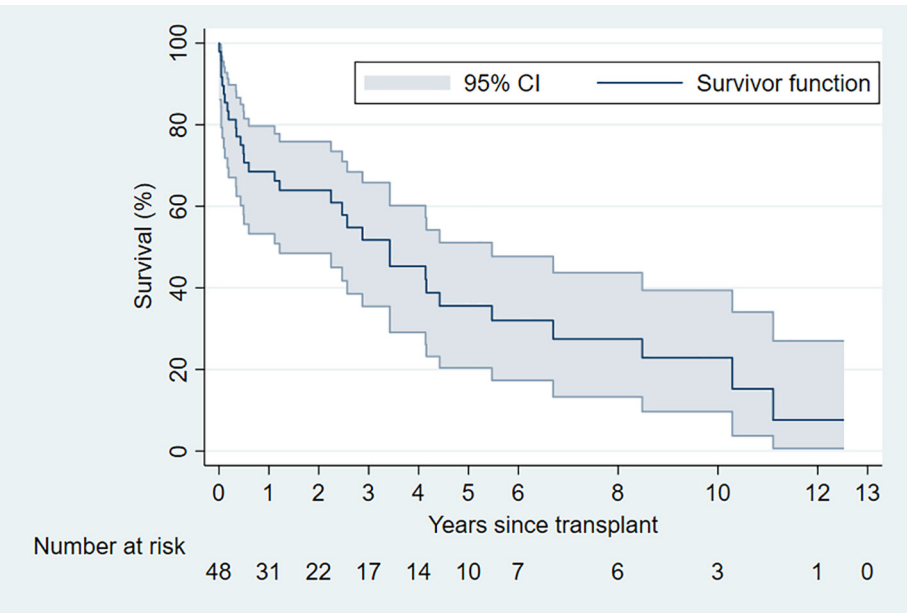
Supplementary Figure 1 shows freedom from CLAD or oxygen use over 12 years' post-transplant. Event-free survival was approximately 93% at 1 and 2 years, 87% at 3 years, and 64% at 4 years. The most pronounced decline occurred within the first 3 years, followed by a progressive decrease to below 30% by year 9. Confidence intervals widened over time due to increasing censoring and a declining number of patients at risk.

A total of 32 patients died during follow-up. The causes of death were as follows: infections in 34.4% (n = 11), hemorrhage in 18.8% (n = 6), graft failure in 18.8% (n = 6), malignancy in 9.4% (n = 3), airway complications in 9.4% (n = 3), and other causes in 9.4% (n = 3).

Discussion

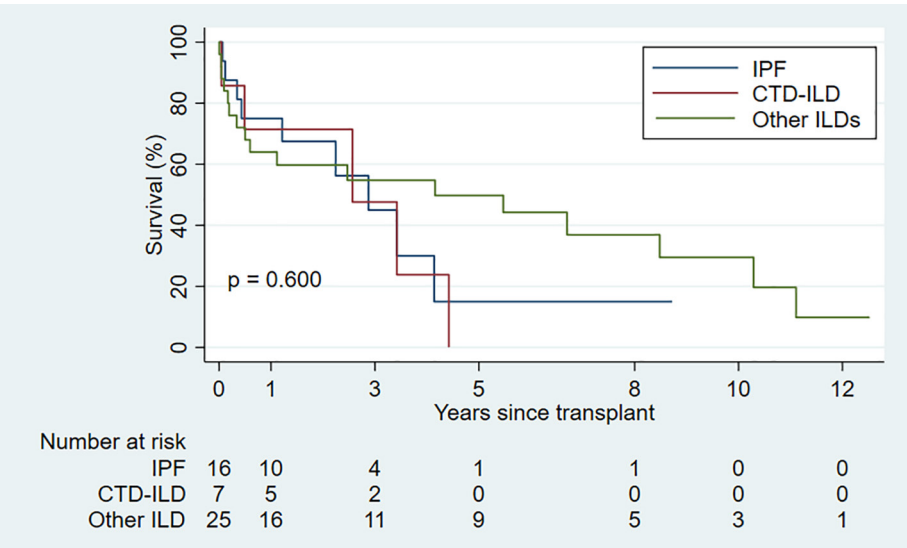
This study provides real-world data on post-transplant outcomes in patients with ILD, highlighting three main findings. First, overall survival was modest, with the highest mortality occurring within the first years following transplantation, although conditional survival analysis showed that patients surviving the first year

Figure 2 | Kaplan-Meier overall survival curve of the study cohort



The figure shows the overall survival function for all lung transplant recipients with interstitial lung disease. The number of patients at risk at specific time points (1, 3, 5, 8, and 12 years) is displayed below the curve. Note: Survival analysis included 48 recipients. One patient who died intraoperatively, prior to graft function establishment, was excluded from analysis in accordance with ISHLT methodology.

Figure 3 | Kaplan-Meier survival curves stratified by ILD etiology



ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; CTD-ILD: connective tissue disease-associated ILD. The survival functions are shown for patients with IPF, CTD-ILD, and other ILDs. Although numerical differences were observed, no statistically significant difference in survival was found between groups (Log-rank test, $p = 0.5997$).

Table 2 | Cox Proportional Hazards Model for Factors Associated with Post-Transplant Mortality

Variable	HR (95% CI) unadjusted	p-value	HR (95% CI) adjusted	p-value
ECMO use post-Transplant	4.08 (1.51-11.02)	0.006	3.85 (1.37-10.8)	0.011
Acute Rejection	1.82 (0.77-4.3)	0.176	1.60 (0.62-3.90)	0.343
Hospitalization Pre-Transplant (Yes vs No)	1.89 (0.71-5.1)	0.205	1.13 (0.39-3.26)	0.817
Age (per year)	1.00 (0.97-1.03)	0.909	1.00 (0.97-1.03)	0.805
Transplant era >=2018	0.82 (0.37-1.85)	0.638		
Ischemic Time (Per hour)	1.01 (0.84-1.36)	0.639		
BMI (per 5 kg/m ² increase)	1.20 (0.54-2.58)	0.648		
Single Transplant	0.96 (0.37-2.52)	0.934		
Etiology (IPF vs Others)	1.00 (0.42-2.36)	0.993		

ECMO: extracorporeal membrane oxygenation; BMI: body mass index; IPF: idiopathic pulmonary fibrosis; CI: confidence interval; HR: hazard ratio

Proportional hazards assumption was verified using Schoenfeld residuals. No violations were detected (global test $p = 0.456$)

Table 3 | Frequency, cumulative incidence, and incidence rate of post-transplant complications

Event	N events	N total	Cumulative incidence (%)	Person- years	Incidence rate (per 100 PY)
Acute rejection	7	49	14.3	124.5	5.62
Chronic rejection (CLAD)	9	49	18.4	127.5	7.06
Long-term oxygen requirement	6	49	12.2	134.9	4.45
Airway stenosis	9	49	18.4	111.1	8.10

PY: person-years CLAD, chronic lung allograft dysfunction

Cumulative incidence is reported as the proportion of patients affected during the study period. Incidence rates are expressed per 100 person-years of follow-up, accounting for variable follow-up duration and censoring.

had a substantially improved prognosis. Second, no significant differences in survival were observed across ILD etiologies, suggesting that, with careful candidate selection, patients with CTD-ILD may achieve outcomes comparable to those with IPF or other ILDs. Third, post-transplant ECMO use was the only independent predictor of increased mortality, underscoring the impact of early perioperative complications.

Our results showed lower 5-year survival (35.6%) compared with international registry data, such as the ISHLT 2023 report, which documented approximately 50% 5-year survival among lung transplant recipients¹¹ and a national cohort study from China in ILD patients, which reported a 5-year survival of 55%¹². This discrepancy may reflect a combination of factors, including a higher proportion of single-lung

transplants, frequent use of post-transplant ECMO, low annual transplant volume, and real-world variability in perioperative care. Single-lung transplantation has been associated with worse long-term outcomes in ILD patients compared with bilateral transplantation, particularly in older or comorbid populations¹³, as evidenced by improved outcomes in IPF cohorts receiving bilateral transplants¹⁴. Similarly, ECMO use has been consistently linked to increased perioperative complications and mortality¹⁵. Furthermore, low-volume transplant centers tend to report inferior short- and long-term outcomes¹⁶, potentially due to limited resources, experience, and multidisciplinary infrastructure.

In our cohort, the estimated 5-year survival conditional on 1-year survival was approximately 48%. These findings suggest that nearly

half of the patients who survive the first year after transplantation can be expected to reach five-year survival, underscoring the prognostic relevance of early post-transplant outcomes. This rate is considerably lower than the ~85% reported in the 2023 ISHLT Registry¹⁷, but is comparable to a Colombian single-center study that reported a conditional 5-year survival of approximately 47%¹⁸.

Few studies have reported post-lung transplant survival from Latin American centers, and available data suggest outcomes may differ from those observed in high-income countries. A 25-year retrospective study from a Colombian center reported 1- and 5-year survival rates of 50% and 31%, respectively, lower than those reported in international registries¹⁸. Similarly, in Mexico 30-day survival was reported at 65.7%¹⁹ and national data from Brazil showed 1-, 3-, 5-, and 10-year survival rates of 70%, 54%, 44%, and 22% for unilateral lung transplants²⁰. These findings underscore the variability and limitations in long-term outcomes across the region, and highlight the importance of generating and analyzing region-specific data to better understand local realities, identify context-specific barriers, and design strategies aimed at improving long-term survival in Latin American transplant programs.

Despite historical concerns about poorer outcomes in CTD-ILD due to systemic involvement, our findings demonstrated no statistically significant difference in post-transplant survival across ILD etiologies. These results are in line with emerging evidence suggesting that CTD-ILD patients, when carefully selected, can achieve similar outcomes to those with IPF^{12,21–23}. This supports a growing consensus that ILD etiology alone should not constitute an exclusion criterion in lung transplant candidacy assessment.

In our cohort, ECMO use was the only variable independently associated with increased post-transplant mortality. Patients requiring ECMO had a nearly fourfold higher risk of death, consistent with prior studies identifying it as a marker of perioperative instability and adverse prognosis^{15,24}. This elevated risk likely reflects both underlying disease severity and ECMO-related complications—including bleeding, pulmonary artery thromboembolism, infection, and

kidney failure²⁵. A meta-analysis further identified ECMO as a strong predictor of 1-year mortality (HR 1.91; 95% CI 1.79–2.04), reinforcing its prognostic impact¹⁵. In contrast, other recipient and procedural factors traditionally associated with post-transplant outcomes¹⁵—including age, BMI, ischemic time, transplant era, hospitalization at transplant, acute rejection, and single-lung transplantation—were not significantly associated with mortality in our cohort. While older age, single lung transplant, and transplant era have been linked to outcomes in large registry analyses^{25,26}, the lack of significance in our study may be attributed to sample size limitations and low statistical power. These findings highlight the importance of perioperative management and suggest that minimizing ECMO use—through early referral, optimized care, and careful selection—may help improve outcomes in ILD transplant recipients.

CLAD or long-term oxygen use occurred in approximately 35–40% of patients within the first four years after transplantation, indicating early graft dysfunction in a substantial proportion of recipients. This underscores the importance of close surveillance during this high-risk period and aligns with previous studies reporting CLAD in up to 50% of recipients within five years²⁷.

The most frequent cause of death in our cohort was infection (34.4%), followed by hemorrhage and graft failure (18.8% each). This pattern aligns with international data in patients with ILD, identifying infection and graft-related complications as leading causes of mortality after lung transplantation²⁸.

The relatively short waitlist time observed (median 158 days) likely reflects late referral and listing practices common among patients with advanced ILD^{29,30}. This emphasizes the importance of earlier identification and timely evaluation for transplant candidacy to optimize pre-transplant clinical status and post-transplant outcomes.

This study has several limitations. First, the relatively short median follow-up duration (1.8 years), compared to the estimated median survival (3.8 years) could affect the precision of long-term survival estimates, partly due to the high number of early deaths, which concentrated follow-up time in the first year for many

patients. Nevertheless, the overall censoring rate was acceptable (34.7%), reducing the risk of overestimation bias. Second, although median post-transplant survival did not differ significantly across ILD subgroups in our cohort, this result should be interpreted with caution due to the limited sample size and the low statistical power of the comparison (~9%). Notably, a larger study with adequate power similarly found no significant survival differences between ILD etiologies¹², supporting the robustness of this observation despite our sample size limitations. Third, the generalizability of the findings may be limited by the specific characteristics of the study population. This was a single-center study, and the cohort may not be fully representative of all lung transplant recipients in Argentina. However, the center is among the largest lung transplant programs in the country, performing the second highest number of transplants annually. Fourth, this analysis treated death as a censoring event when evaluating time to CLAD or long-term oxygen use. This approach assumes that censored individuals have the same risk of developing the outcome as those who remain under observation. However, because death precludes the occurrence of CLAD or oxygen re-initiation, it constitutes a competing risk. As such, this methodology may lead to an overestimation of event-free survival, particularly in cohorts with substantial early mortality. Fifth, survival estimates for the most recent transplant era (post-2020) are based on shorter follow-up and should be interpreted cautiously due to potential time-related bias. This form of bias is common in open cohorts and should be considered when interpreting survival estimates at longer time points³¹. Finally, as a retrospective study using electronic medical records, there is a risk of information bias from inconsistent documentation or misclassification.

This study has several strengths. First, it provides real-world data from a cohort of lung transplant recipients with ILD, a population underrepresented in the current literature, particularly in Latin America. Second, the analysis includes both clinical and procedural variables, as well as post-transplant outcomes such as mortality and CLAD, offering a comprehensive evaluation of transplant prognosis in ILD. Third, data collection was performed systematically

and with high completeness, enhancing the reliability of the findings.

These findings have clinical implications. The comparable post-transplant survival across different ILD subtypes supports lung transplantation in a broad range of ILD etiologies, including those traditionally perceived as high risk, such as CTD-ILD. Furthermore, the identification of factors associated with post-transplant mortality may assist clinicians in refining candidate selection and optimizing perioperative management.

From a research perspective, our results highlight the need for larger, multicenter studies—particularly in underrepresented regions such as Latin America—to validate these findings and explore potential regional variations in outcomes. While international registry data, such as those from ISHLT, provide valuable benchmarks, their findings should not be automatically extrapolated to all geographic settings without local validation. Importantly, generating regional evidence is essential to provide patients with prognostic information that reflects local clinical realities, supports shared decision-making, and guides resource allocation in Latin American transplant programs. In this context, strengthening data collection and outcome reporting in emerging transplant centers is crucial to ensure that clinical decisions are based on regionally relevant evidence and to promote equity in transplant care globally. The association between ECMO and mortality likely reflects the severity of the underlying clinical course, and future research should aim to better differentiate prognostic implications based on ECMO indication, timing, and duration.

In conclusion, this study provides real-world data on lung transplantation outcomes in patients with ILD from Argentina. Post-transplant survival was lower than that reported in international registries, though outcomes did not differ significantly across ILD subtypes. These findings support the inclusion of a broad range of ILD etiologies in transplant programs and highlight the need for locally generated evidence to better inform clinical decision-making, patient counseling, and health policy. More broadly, they underscore the importance of strengthening transplant data across Latin America to address regional disparities and improve long-term outcomes.

Conflict of interest: None to declare

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Supplementary Figure 1 | Kaplan-Meier curve showing freedom from chronic lung allograft dysfunction (CLAD) or long-term oxygen requirement up to 12 years post-transplant. The sharpest decline occurred within the first 3 years. Shaded areas represent 95% confidence intervals; numbers at risk are shown below the X-axis

