ORIGINAL ARTICLE

Outcomes of lung transplantation for pulmonary sarcoidosis across multiple eras: A 25-Year experience from a US center

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ABSTRACT

Background and aim: Sarcoidosis is a systemic condition with various clinical manifestations including end-stage lung disease. The aim of this study was to evaluate the characteristics and outcomes of patients with sarcoidosis undergoing lung transplantation.

Methods: A single center retrospective review was performed of 63 sarcoidosis patients who underwent lung transplantation between January 1, 2000 and April 30, 2025. Patients were divided into arbitrary eras by year (Era 1 2000-2007; Era 2 2007-2013; Era 3 2013-2025).

Results: The median age of the cohort was 53 years, 51% were female, 79% were black, 33% had blood type A, and the median body mass index was 24.4 kg/m^2 (21.3-28.2). The majority (93%) of patients had pulmonary sarcoidosis stage IV by Scadding staging, and 89% had pulmonary hypertension. Baseline median six-minute walk test distance (6MWD) was 235 m (133-306). The median FVC% was 45% (34-50), median FEV_1 was 37% (26-45), median FEV_1/FVC was 73% (62-83) and median DLCO% was 26% (18-32). The median mean pulmonary artery pressure (mPAP) was 35 (26-44) mmHg, and the median pulmonary vascular resistance (PVR) was 4 (3-6) Wood Units (WU). Chronic lung allograft dysfunction (CLAD) occurred in 38% of patients at a median 85 months post-transplant. Overall survival was 87.6%, 66% and 50.6% at 1, 3, and 5 years, respectively. There was no statistically significant difference in mortality across eras: era 1 vs era 3 (HR 0.888, 95% CI 0.407-1.94, p=0.766).

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Conclusions: Outcomes of sarcoidosis patients who undergo lung transplantation are similar to patients with other underlying diagnoses. Timely referral should be made to specialized centers.

Key words: pulmonary sarcoidosis, lung transplantation, pulmonary fibrosis, pulmonary hypertension

Introduction

Sarcoidosis is a heterogenous disease that can present with a spectrum of clinical pulmonary manifestations ranging from asymptomatic to severe pulmonary fibrosis and pulmonary hypertension. Lung transplantation can be a last resort option for select patients with end stage lung disease from sarcoidosis with good outcomes (1). Of those lung transplants performed between 1995 until June 2014, 2.5% were for sarcoidosis (2). An Organ Procurement and Transplantation Network (OPTN) database query of 695 patients from 1987 to 2012 described a 72% one year survival, 47% 5-year survival, and 26% 10-year survival in this cohort (3). A more recent analysis of the OPTN database evaluated outcomes of 950 patients during the Lung Allocation Score (LAS) era, which prioritizes lung transplantation candidates based on medical urgency, between 2005-2022 (4). Survival in this cohort was 84% and 54% at 1 year and 5 years, respectively, suggesting improved outcomes during the LAS era (4). A retrospective review of sarcoidosis lung or heart-lung recipients at 16 European centers between 2006 and 2019 included 112 patients and found a 1, 3, and 5- year survival of 86%, 76%, and 69%, respectively (1). While survival at 1 year post-transplantation is worse in sarcoidosis compared to non-sarcoidosis, survival at 5 years was higher in these patients (4). In 2023, the Composite Allocation Score (CAS) replaced the LAS and utilized continuous distribution to improve equity and efficiency in organ allocation. The aim of this study is to describe the characteristics and outcomes of patients undergoing lung transplantation over a 25-year period at a single, intermediate-sized lung transplantation center in the United States. Prior to transplantation, patients were treated with standard therapies including antifibrotic agents and/or immunosuppressive agents.

Methods

Adult patients ages 18 and older who had a diagnosis of pulmonary sarcoidosis and underwent lung transplantation at a single, intermediate-volume lung transplantation center in Virginia, USA were included in this study. Demographic data, donor data, and outcome data were collected, where available. Patient age, gender, race, blood type, World Health Organization (WHO) functional class (FC), height, body mass index (BMI), smoking history, presence of parenchymal fibrosis, presence of pulmonary hypertension (PH) by right heart catheterization (RHC), and presence of extrapulmonary sarcoidosis were collected. Six minute walk test distance (6MWD), pulmonary function test results (PFT) at time of listing were collected. RHC data closest to the timing of transplantation were included. Data regarding use of ex-vivo lung perfusion (EVLP), cardiopulmonary bypass (CPB), organ ischemic time, use of induction, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) donor-recipient mismatch, transfusion requirements, post-operative pressor requirement, post-op inhaled vasodilator use, need for return to operating room and reason for return, need for post-operative extracorporeal membrane oxygenation (ECMO), presence of post-operative bleeding complications, and need for dialysis during index hospitalization were collected. Outcomes including primary graft dysfunction (PGD), human-leukocyte (HLA) antigen crossmatch results, tracheostomy requirement, one-month readmission, need for treatment for acute rejection within one year, chronic lung allograft dysfunction (CLAD) at last follow up, need for re-transplantation, and cause of death were collected. PGD was defined based on the International Society of Heart and Lung Transplantation (ISHLT) definition based on PaO2/FiO_2 ratio and presence of

infiltrates on chest imaging. CLAD was defined based on the ISHLT definition of a persistent decline in FEV1 of at least 20% from baseline for longer than 3 months and not attributable to a reversible cause. Institutional Review Board (IRB) approval was obtained from the Inova Fairfax Hospital (IRB U21-02-4389). Consent was waived. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) checklist was utilized to ensure adherence to recommended reporting.

Eras

Patients were arbitrarily split into three eras by year: Era 1-early (years 2000-2007); Era 2- middle (years 2007-2013); Era 3- recent (years 2013-2025). Of note, the LAS was implemented on May 4, 2005 and updated to the CAS on March 9, 2023. Thus, the early cohort represents the pre-LAS era, the middle and recent cohorts include the LAS era, and the most recent includes a majority LAS but some CAS era.

Statistical analysis

Descriptive statistics were utilized to describe baseline demographics at time of listing including medians and quartiles for continuous variables and percentages for categorical variables. Baseline features at time of listing were compared using Kruskal-Wallis rank sum test, Pearson's Chi-squared test, and Fischer's exact test. Kaplan-Meier test was used to evaluate survival. Cox proportional hazard test was utilized for univariate and multivariate analysis to compare survival across eras, adjusting for age and gender. A p-value of <0.05 was considered to be statistically significant. A listwise (case deletion) approach was utilized for missing data. All statistical analysis was completed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 63 patients underwent lung transplantation (single or bilateral) between January 1, 2000 and April 30, 2025. The median age of the cohort was 53 years (interquartile range (IQR) 46-59) (Table 1). Fifty-one percent of patients were female, 79% were black, and 33% had blood type A. The median height was 67 inches (65-69 inches) and median BMI was 24.4 kg/m^2 (21.3-28.2) (Table 1). The majority (88%) of patients were classified as WHO FC III (Table 1). Forty-five percent of the patients were prior smokers (Table 1). The median wait time between listing and transplant was 141 days, and the median survival was 59 months. In comparing baseline characteristics, age and race were statistically significantly different across the eras (p=0.002 and 0.047, respectively) (Table 1).

All patients had parenchymal fibrosis, and pulmonary hypertension was present in 89% of patients (Table 2). Extrapulmonary sarcoidosis manifestations included cardiac (5%), skin (3%), ocular (10%), and hepatic (3%). At the time of listing, the median 6MWD was 235 m (133-306). The 6MWD was statistically significantly different across the eras (p = 0.023).

The majority of patients used 1-6 L/min of supplemental oxygen with exertion (56%) (Table 3). The median forced vital capacity (FVC) was 45% of predicted (IQR: 34-50), median forced expiratory volume at 1 second (FEV_1) was 37% (IQR:26-45), FEV_1/FVC was 73% (IQR:62-83), and total lung capacity (TLC) 45% (IQR:41-59) (Table 3). The median diffusion capacity of the lungs for carbon monoxide (DL_{CO}) was 26% (IQR:18-32). All the patients underwent RHC as a part of the lung transplant evaluation. The median right atrial pressure (RAP) was 5 mmHg (IQR: 4-8), median systolic pulmonary artery pressure (sPAP) was 56 mmHg (IQR: 40-68), median diastolic pulmonary artery pressure (dPAP) was 23 mmHg (IQR:16-31), and the median mean pulmonary artery pressure (mPAP) was 35 mmHg (IQR:26-44) (Table 3). The median pulmonary capillary wedge pressure (PCWP) was 10 mmHg (IQR:9-15), with median cardiac index (by thermodilution, if available; otherwise, by Fick) of 3.1 (IQR:2.2-3.5) L/min/m^2, median CO of 6.25 L/min, and median pulmonary vascular resistance (PVR) of 4 (IQR:3-6) Wood Units (WU).

Forty-four (70%) patients underwent bilateral lung transplantation and 19 patients (30%) underwent single lung transplantation (Table 4). No patients received donation after circulatory arrest (DCD) donors, one patient received lungs placed on EVLP, and 76%

Table 1. Baseline characteristics

Characteristic		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
Age Median (IQR)		53 (46-59)	50 (45-58)	48 (45-54)	59 (52-64)	**0.002**
Gender N(%)						0.8
	Female	32 (51)	10 (48)	12 (57)	10 (48)	
	Male	21 (49)	11 (52)	9 (43)	11 (52)	
Race N(%)						**0.047**
	Black	50 (79)	13 (62)	18 (86)	19 (90)	
	Caucasian	4 (6)	1 (5)	1 (5)	2 (10)	
	Other	1 (2)	1 (5)	0	0	
	Unknown	8 (13)	6 (29)	2 (10)	0	
Blood type N (%)						0.3
	A	16/49 (33)	5/8 (63)	6/20 (30)	5 (24)	
	AB	4/49 (8)	0	2/20 (10)	2 (10)	
	B	14/49 (29)	3/8 (38)	5/20 (25)	6 (29)	
	O	15/49 (31)	0	7/20 (35)	8 (38)	
	Missing	14	13	1	0	
WHO Functional Class N(%)						0.6
	III	29/33 (88)	2/2 (100)	8/10 (80)	19 (90)	
	IV	3/33 (9)	0	2/10 (20)	1 (5)	
	NA	1/33 (3)	0	0	1 (5)	
	Missing	30	19	11	0	
Height (inch) Median (IQR)		67 (65-69)	67 (65-71)	66 (64-67)	69 (65-69)	0.3
BMI (kg/m^2) Median (IQR)		24.4 (21.3-28.2)	24.4 (19.7-29.0)	25.7 (21.9-27.8)	23.0 (21.3-30.3	>0.9
Ever smoker N(%)		19 (45%)	1 (33%)	6 (33%)	12 (57%)	0.4

Abbreviations: IQR: interquartile range; LAS: lung allocation score; WHO: world health organization

of patients were placed on cardiopulmonary bypass (Table 4). No patients required pre-operative ECMO. Median ischemic time was 214 min (178-291) on the right and 209 min (143-250) on the left. The majority received induction therapy with basiliximab. There was a 76% EBV donor-recipient mismatches and 52% CMV mismatches (Table 4). Postoperatively, 65% of patients required blood product transfusions, 49% required continued vasopressor use, and 43% received inhaled vasodilators (Table 4). Of the patients in this cohort, 9 patients (20%) required return to the operating room (Table 4). Of those 9 patients, 5 patients (83% of the 9 patients and 8% of total cohort) returned due to hematoma or hemothorax and 17% (one patient)

Table 2. Clinical and functional characteristics at listing

Characteristic		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
Parenchymal fibrosis present N(%)		46 (100)	5 (100)	20 (100)	21 (100)	
	Missing	17	16	1	0	
Pulmonary hypertension present N(%)		40/45 (89)	4/4 (100)	18/20 (90)	18/21 (86)	>0.9
	Missing	18	17	1	0	
Extrapulmonary sarcoidosis N (%)						
	Cardiac	2 (5)	0	0	2 (10)	0.5
	Skin	1 (3)	0	0	1 (5)	>0.9
	Ocular	4 (10)	0	0	4 (19)	0.2
	Liver	1 (3)	0	1 (6)	0	0.5

Table 3. Hemodynamic parameters at listing

		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
6MWT results		(Total N=41)				
	Distance (m) Median (IQR)	235 (133-306)	240 (107-372)	167 (102-239)	252 (229-377)	**0.023**
Amount of supplemental oxygen required with exertion (L/min)						0.2
	>6L	13/41 (32)	0/2	5/18 (28)	8 (28)	
	1-6	23/41 (56)	1/2 (50)	9/18 (50)	13 (62)	
	Room air	5/41 (12)	1/2 (50)	4/18 (22)	0 (0)	
	Missing	22	19	3	0	
PFT results Median (IQR)						
	%pred FVC	45 (34-50)	48 (41-55)	45 (33-49)	45 (36-48)	0.9
	% pred FEV1	37 (26-45)	40 (28-51)	38 (28-42)	34 (25-45)	0.8
	% FEV1/FVC	73 (62-83)	64 (55-73)	72 (63-80)	75 (52-83)	0.8
	% pred DLCO	26 (18-32)	NA	29 (22-34)	23 (18-31)	0.4
	% pred TLC	45 (41-59)	NA	49 (43-63)	44 (38-53)	0.11
Right heart catheterization results Median (IQR)						
	RAP (mmHg)	5 (4-8)	4 (2-5)	5 (3-11)	5 (4-7)	0.4
	sPAP (mmHg)	56 (40-68)	65 (43-86)	60 (35-77)	53 (42-62)	0.8

Table 3 (*Continued*)

		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
	dPAP (mmHg)	23 (16-31)	35 (20-50)	25 (15-35)	22 (17-29)	0.6
	mPAP (mmHg)	35 (26-44)	43 (30-56)	40 (24-49)	34 (26-40)	0.7
	PCWP (mmHg)	10 (9-15)	10 (9-10)	9 (8-15)	10 (9-15)	0.5
	CO (L/min)					
	CI (L/min/m^2)	3.1 (2.2-3.5)	2.9 (2.2-3.5)	3.1 (2.0-3.6)	3.2 (2.7-3.4)	0.8
	PVR (WU)	4.0 (3.0-6.0)	6.3 (3.7-8.9)	4.7 (2.2-8.9)	3.9 (3.0-5.4)	0.6

Abbreviations: %pred: percent of predicted; 6MWT: six minute walk test; CI: cardiac index; DLCO: diffusion capacity of the lungs for carbon monoxide; dPAP: diastolic pulmonary artery pressure; FEV1: forced expiratory volume at one second; FVC: forced vital capacity; mPAP: mean pulmonary artery pressure; PCWP: pulmonary capillary wedge pressure; PFT: pulmonary function test; PVR: pulmonary vascular resistance; RAP: right atrial pressure; sPAP: systolic pulmonary artery pressure; TLC: total lung capacity; WU: Wood units

Table 4. Operative Considerations and Postoperative Complications

		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
Type Transplant						>0.9
	Bilateral	44 (70)	15 (71)	14 (67)	15 (71)	
	Single	19 (30)	6 (29)	7 (33)	6 (29)	
EVLP		1 (2)	0	0	1 (5)	>0.9
CPB		48 (76)	14 (67)	16 (76)	18 (86)	0.3
Ischemic time (minutes)						
	Right Median (IQR)	214 (178-291)	184 (163-214)	197 (148-282)	261 (204-300)	**0.033**
	Left Median (IQR)	209 (143-250)	194 (128-236)	192 (136-229)	247 (180-350)	**0.028**
EBV mismatch		19 (76)	NA	2 (33)	17 (89)	**0.015**
CMV mismatch		32 (52)	8 (40)	9 (43)	15 (71)	**0.081**
Transfusion required		32 (65)	11 (73)	6 (43)	15 (75)	0.14
Pressors required		31 (49)	9 (43)	11 (52)	11 (52)	0.8
Inhaled vasodilators		22 (43)	6 (43)	5 (28)	11 (58)	0.2
Return to OR		9 (20)	6 (46)	3 (23)	0	**0.003**
Reason for return to OR						>0.9
	Hematoma/ hemothorax	5 (83)	2 (67)	3 (100)	NA	

Table 4 (*Continued*)

		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
	Sternal dehiscence	1 (17)	1 (33)	0	NA	
	Unknown/ missing	3	3	0	NA	
ECMO post-tx		1 (2)	0	0	1 (5)	>0.9
All bleeding complications (hemothorax, hematoma, wound site bleeding)						
		8 (13)	6 (29)	2 (10)	0	**0.022**
Dialysis at index hospitalization		6 (15)	2 (50)	1 (6)	3 (14)	0.12
	Missing	22	17	5	0	

Abbreviations: ATG: anti-thymocyte globulin; CPB: cardiopulmonary bypass; CMV: cytomegalovirus; EBV: Epstein-Barr Virus; ECMO: extracorporeal membrane oxygenation; EVLP: ex-vivo lung perfusion; OR: operating room

returned due to sternal dehiscence. ECMO was required post-transplantation in one patient (2%). Bleeding complications, including hematoma, hemothorax, or other bleeding occurred in 8 patients (13% of the overall cohort). Dialysis was required during index hospitalization in 15% of the patients (Table 4). There was a statistically significant difference in ischemic times (right p=0.033, left p=0.028), EBV mismatch rate (p=0.015), need for return to operating room (p=0.003), and bleeding complication (p=0.022) among the eras (Table 4), though these are limited by significant missing data.

The majority of PGD was grade 1 (50% of those with PGD), and grade 3 PGD occurred in 28% of patients. (Table 5). A crossmatch test was positive in 2% of the patients. Three patients required tracheostomy, 16% required readmission within one month of discharge, and 41% of patients were treated for rejection within the first-year post-transplant (Table 5). The majority of patients did not have CLAD at the last clinic visit assessed (63%) at an average of 85 months post-transplant; 13% developed grade 1 CLAD, 6% developed grade 2 CLAD, 13% developed grade 3 CLAD, and 6% had grade 4 CLAD. The cause of death was respiratory failure in 35% of patients, septic shock in 7% of patients, and unknown or other in 58% of patients (Table 5). CLAD was significantly different at last follow up among the eras (p=0.013), though the significance of this is difficult to interpret in the setting of significant missing data in era 1. Cause of death was not statistically significant different (p=0.072) among the eras (in era 1, cause of death was respiratory failure in 4 patients; in era 2, cause of death was respiratory failure in 6 patients and septic shock in 1 patient; in era 3, cause of death was respiratory failure in 5 patients and septic shock in 2 patients). HLA crossmatch was significantly different (p<0.001) among the eras, but there was a large amount of missing data in the early era (Table 5).

The patients remained in the intensive care unit a median of 3.5 days (IQR 3-7), and median hospital length of stay was 13 days (IQR 10-21). Overall survival for the cohort was 87.6%, 66% and 50.6% at 1, 3, and 5 years, respectively (Figure 1). Kaplan-Meier curves comparing the survival across the three eras showed no statistically significant different (p=0.72) (Figure 2). Cox proportional hazard test showed no association between era and survival. Mortality was not statistically significantly different in era 1 compared with era 2 (HR 0.668, 95% CI 0.31-1.40, p=0.288),

Table 5. Main Short and Long Term Outcomes

		Overall N=63	Era 1 (2000-2007) N=21	Era 2 (2007-2013) N=21	Era 3 (2013-2025) N=21	p-value
PGD		24 (80)	1 (50)	6 (67)	17 (89)	0.2
PGD grade at 72 hours		(N=18)				
	1	9/18 (50)	NA	1/4 (25)	8/14 (57)	
	2	4/18 (22)	NA	1/4 (25)	3/14 (21)	
	3	5/18 (28)	NA	2/4 (50)	3/14 (21)	
	Missing	45	21	17	7	
Final HLA Crossmatch						**<0.001**
	Negative	38 (60)	9 (43)	10 (48)	19 (90)	
	Positive	1 (2)	0	0	1 (5)	
	Unknown	24 (38)	12 (57)	11 (52)	1 (5)	
Tracheostomy		3	1	0	2	
Readmission within 1 month		(Total N=27)				>0.9
	No	22/27 (81)	2/2 (100)	6/8 (75)	14/17 (82)	
	Yes	5/27 (19)	0	2/8 (25)	3/17 (18)	
	Missing	36	19	13	4	
Treated for rejection within 1 year		(Total N=34)				
		14/34 (41)	1/2 (50)	7/16 (44)	6/16 (38)	>0.9
Cause of death						0.072
	Respiratory failure	15 (35)	4 (22)	6 (40)	5 (50)	
	Septic shock	3 (7)	0	1 (7)	2 (20)	
	Unknown/other/ missing data	45 (71)	17 (81)	14 (67)	14 (67)	
Retransplant		1 (2)	0	1 (5)	0	>0.9
CLAD at last follow up (mean 85 months)	Grade	(N=34)				**0.013**
	0	20/32 (63)	1/2 (50)	3 (27)	16/19 (84)	
	1	4/32 (13)	0	2 (18)	2/19 (11)	
	2	2/32 (6)	0	2 (18)	0	
	3	4/32 (13)	1/2 (50)	3 (27)	0	
	4	2/32 (6)	0	1 (9)	1/19 (5)	
	Missing/NA	31	19	10	2	

Abbreviations: CLAD: chronic lung allograft dysfunction; HLA: human leukocyte antigen; PGD: primary graft dysfunction

adjusted for age and gender. Mortality was not statistically significantly different in era 1 compared with era 3 (HR 0.888, 95% CI 0.407-1.94, p=0.766), adjusted for age and gender.

Discussion

We report the result of a single center experience transplanting patients with sarcoidosis over a period of

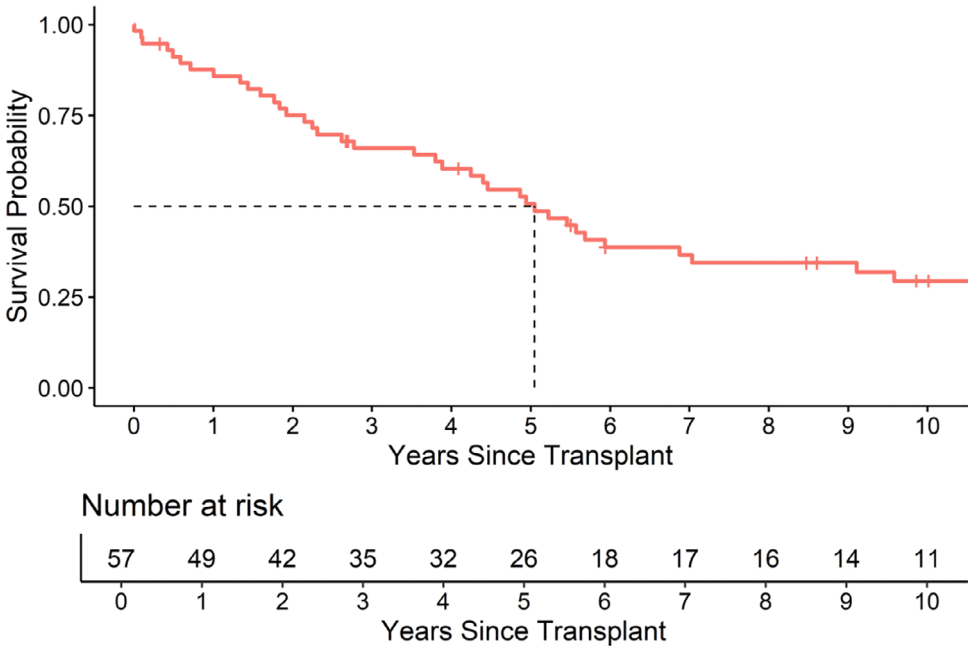

Figure 1. Overall survival after lung transplantation. Kaplan-Meier Curve demonstrating overall survival after lung transplantation in sarcoidosis patients. Overall survival for the cohort was 87.6%, 66% and 50.6% at 1, 3, and 5 years, respectively.

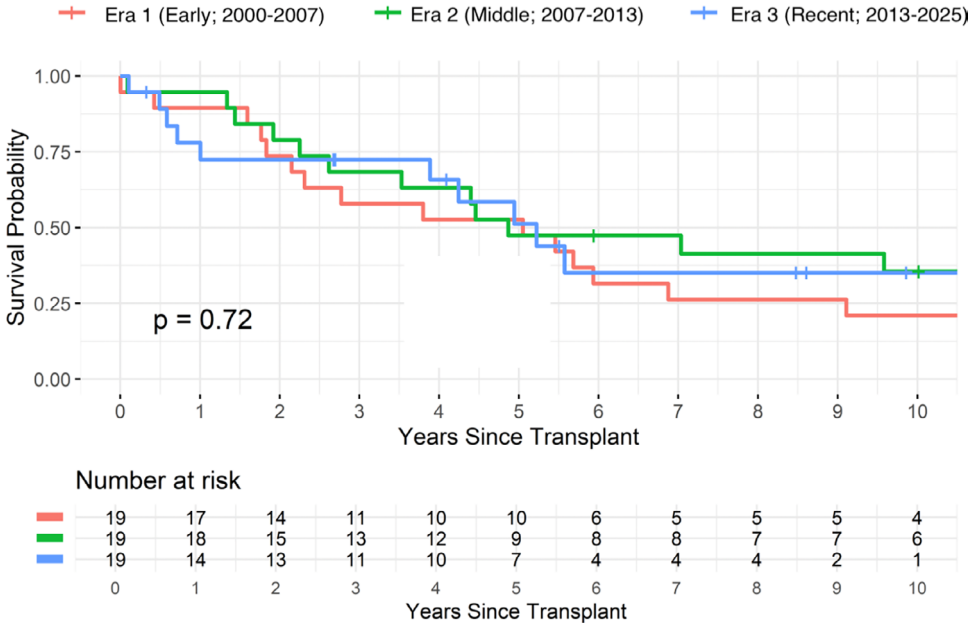

Figure 2. Survival after lung transplantation by era. Kaplan-Meier survival curves comparing survival across the three eras. Red (era 1, years 2000-2007); green (era 2, years 2007-2013); blue (era 3, 2013-2025). There was no statistically significant difference in survival among the eras (p=0.72). Cox proportional hazard test showed no statistically significant difference between era 1 compared with era 2 (HR 0.668, 95% CI 0.31-1.40, p=0.288) or between era 1 and era 3 (HR 0.888, 95% CI 0.407-1.94, p=0.766), adjusted for age and gender.

25 years including three different periods of lung allocation prioritization. The baseline demographic characteristics of our cohort are similar to those that have previously been reported (1). The majority of patients in this cohort were black (79%), and literature suggests advanced radiographic sarcoidosis is more frequent in this population, as is greater organ involvement (5, 6). The patients in this cohort were primarily classified as WHO FC III and IV and sarcoidosis stage IV on imaging, with very poor baseline median 6MWD and DLCO. The population therefore represents a cohort of patients with advanced disease. The majority of patients had sarcoid associated pulmonary hypertension (SAPH), but only 5% of patients had cardiac sarcoidosis identified. The patients generally had moderate pre-capillary pulmonary hypertension. The evaluation of PH was limited in era 1 due to lack of availability of RHC data for review for the majority of patients, and comparison among the eras was not possible. Therefore, PH data in the cohort reflects only era 2 (2007-2013) and era 3 (2013-2025). Postoperatively, 65% of this cohort required blood product transfusion and 20% required return to operating room for either hematoma/hemothorax or sternal dehiscence. We highlight this post-operative complication given the known increased risk of hemothorax and bleeding in patients with sarcoidosis, related to more difficult surgical dissections, due to increased pleural adhesions as well as mediastinal adenopathy and fibrosis (7). Notably, there was significantly less need for return to the operating room rate among the more recent eras and in bleeding, which may be attributable to improvement in perioperative management (8), although our sample size renders this conclusion difficult. PGD is very common in sarcoid lung transplant recipients, and our 28% rate of grade 3 PGD is consistent with the prior literature which has demonstrated about a one-third rate of this most severe form of PGD (9, 10). However, the data for PGD in the patients in era 1 was limited, with many missing variables, which may limit the interpretation of these results. Despite these increased immediate post-operative complications, the findings of this study reiterate that survival outcomes are similar in sarcoidosis patients undergoing lung transplantation to those patients with other underlying lung diseases. In one study of patients with IPF undergoing lung transplantation, one-year survival in 2005 was estimated at 80% compared with about 90% in 2020 (11). The 1-year survival of 87.6% for this cohort is comparable to outcomes reported in the literature (4). In comparison, our overall center patient 1 year survival (adjusted for patient and donor characteristics) was 88.18% for the cohort of patients transplanted between 7/1/2022 and 12/31/2024, based on Scientific Registry of Transplant Recipient data. The risk of CLAD and bronchiolitis obliterans syndrome (BOS) in sarcoidosis patients is not well characterized. Retrospective data evaluating 15 sarcoidosis patients who underwent lung transplantation found that 31% of patients developed BOS (12). Similarly, data from 1987 to 2012 suggests 31.9% of sarcoidosis patients developed BOS, which was similar to the rate of BOS in patients without sarcoidosis (3). In our study, 38% of patients were identified to have CLAD grade 1 or higher at their last clinic visit assessed, a median of 85 months post transplantation, and only 19% had CLAD grade 3 or higher. This study is limited by the number of missing data points for CLAD in the earliest era of patients and therefore results must be interpreted carefully in that context. In addition, whether CLAD was restrictive or obstructive in pattern was not described in this cohort, further limiting interpretability. The comparison of outcomes across the eras highlights that baseline age was significantly different among the eras, with a median age of 59 years in Era 3 compared with a median age of 50 in Era 1, highlighting the advancing age of all lung transplant recipients. The time period included in this study cannot as yet provide reliable information about outcomes during the CAS era, since this was only implemented in March of 2023, so only 2 years of this cohort represent CAS era data. Future studies will be needed to compare outcomes with LAS compared to CAS in this patient population. However, early outcomes from the CAS era suggest lower waitlist mortality and higher transplant rates compared to the pre-CAS era (13). The findings of this study have an important limitation in the large amount of missing data, particularly in the early cohort of patients

and prior to January 2012 when the electronic medical record was implemented at this institution. Therefore, comparison with the earlier eras cannot be reliably extrapolated to other populations of patients. Furthermore, while lung transplantation can improve quality of life and reduce mortality in sarcoidosis patients, recurrence of sarcoidosis in the allograft is a notable complication. Several studies have described histologic evidence of granulomas and disease recurrence as well as increased severity of acute rejection in the early post-transplant period (14, 15). Our study did not evaluate the risk of recurrence of sarcoidosis in this cohort. The global burden of pulmonary sarcoidosis has increased from 1990 to 2021, in part due to advancements in the developed world in imaging modalities, serologic testing, and diagnostic procedures that allow for pathologic identification of disease (16). Thus, the role of lung transplantation in patients with advanced lung disease and fibrosis will continue to increase (9). The World Association for Sarcoidosis and Other Granulomatous Diseases (WASOG) designates WASOG Sarcoidosis Centers of Excellence to multidisciplinary teams of specialized professionals with a shared specialized facility that focus on providing care to sarcoidosis patients. WASOG currently designates 33 of these centers, of which only 24 (73%) also have a lung transplantation program at the same center. Since a number of centers do not have lung transplantation programs, identifying a center for collaboration and timely referral is crucial. This is particularly important as there is suggestion that patients with sarcoidosis on the lung transplantation list have a disproportionate risk of dying compared to patients with other diagnoses (17). Given the paucity of WASOG Centers and access to these, it is likely that the majority of sarcoid patients are managed outside of such centers and there might be many sarcoid patients who could be good transplant candidates but who are never referred. Our center is a designated WASOG Sarcoidosis Center of Excellence, which has allowed transplantation of a significant number of sarcoidosis patients. In fact, sarcoidosis accounts for 6% of the primary diseases for which our patients undergo lung transplantation, which is significantly higher than the national average of 2.5%. Centers which provide these specialized services may be able to provide more timely care, including providing access to multidisciplinary teams, advanced therapies, pulmonary rehabilitation and other support services. Moreover, special considerations for ensuring appropriate preoperative management, including minimizing steroid use and addressing any pre-existing comorbid conditions, is essential in optimizing post-transplant outcomes.

Conclusion

We describe a relatively large cohort of sarcoidosis patients who underwent lung transplantation including their demographics and donor characteristics. Outcomes for these patients are similar to outcomes in transplant patients with other underlying diagnoses, which is consistent with prior reports. Timely referral of sarcoidosis patients to specialized centers with both sarcoidosis and lung transplantation programs is crucial for ensuring access to comprehensive care and enabling appropriate patients the opportunity for this last resort life-saving procedure.

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Ethics Approval: Institutional Review Board (IRB) approval was obtained from the Inova Fairfax Hospital (IRB U21-02-4389).

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Declaration on the use of AI: No AI was utilized for any portion of this study or manuscript.

Abbreviations:

6MWD- six-minute walk test distance
BOS- bronchiolitis obliterans syndrome
CAS- Composite Allocation Score
CLAD- Chronic lung allograft dysfunction
CMV- cytomegalovirus
DLCO- diffusion capacity of the lungs for carbon monoxide
dPAP- diastolic pulmonary artery pressure
EBV- Epstein-Barr Virus
ECMO- extracorporeal membrane oxygenation
EVLP- ex vivo lung perfusion
FEV1- forced expiratory volume at 1 second
FC- functional class
FVC- forced vital capacity
IRB- Institutional Review Board
LAS- Lung Allocation Score
mPAP- mean pulmonary artery pressure
OPTN- Organ Procurement and Transplantation Network
PCWP- pulmonary capillary wedge pressure
PGD- primary graft dysfunction
PVR- pulmonary vascular resistance
RAP- right atrial pressure
sPAP- systolic pulmonary artery pressure
TLC- total lung capacity
UNOS- United Network for Organ Sharing
WASOG- World Association for Sarcoidosis and Other Granulomatous
WHO- World Health Organization

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