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Lung transplantation for scleroderma lung disease: An international, multicenter, observational cohort study

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BACKGROUND: Due to its multisystemic nature, scleroderma is considered a relative contraindication to lung transplantation at many centers. However, recent studies suggest similar post-transplant outcomes in patients with scleroderma compared to those with other causes of interstitial lung disease (ILD). Furthermore, it remains unknown whether scleroderma-associated pulmonary arterial hypertension (PAH) influences post-transplant outcomes. Our objective in this study was to assess the indications, survival, and prognostic factors of lung or heart–lung transplantation for scleroderma lung disease.
METHODS: We retrospectively reviewed the data of 90 patients with scleroderma who underwent lung or heart–lung transplantation between 1993 and 2016 at 14 European centers. International criteria were used to diagnose scleroderma. Pulmonary hypertension (PH) was diagnosed during right heart catheterization based on international guidelines.
RESULTS: Survival rates after 1, 3, and 5 years were 81%, 68%, and 61%, respectively. By univariate analysis, borderline-significant associations with poorer survival were found for female gender (hazard ratio 2.11; 95% confidence interval [CI] 0.99 to 4.50; $p = 0.05$) and PAH as the reason for transplantation (hazard ratio 1.90; 95% CI 0.96 to 3.92; $p = 0.06$). When both these factors were present in combination, the risk of death was 3-fold that in males without PAH. The clinical and histologic presentation resembled veno-occlusive disease in 75% of patients with PAH.
CONCLUSIONS: Post-transplant survival rates and freedom from chronic lung allograft dysfunction in patients with scleroderma were similar to those in patients with other reasons for lung transplantation. Female sex and PAH in combination was associated with lower survival.
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Scleroderma is a rare autoimmune disease characterized by fibrosis and obliterative microangiopathy of the skin and internal organs.[1] Before the introduction of angiotensin-converting enzyme (ACE) inhibitors, renal crisis was the most common life-threatening complication.[2] Now, however, lung disease is the main source of morbidity and mortality.[3,4] Thus, complications of interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH) account for up to 60% of scleroderma-related deaths.[3,5] The prevalence of clinically relevant ILD is 40% to 45% overall and up to 60% in patients with anti-Scl70 antibodies. Median survival in patients with ILD is 5 to 8 years.[6,7] PAH is found in 10% to 12% of patients with scleroderma and has a median survival of only 2 to 3 years, despite the introduction of PAH-targeted therapy.[8,9] Survival is shortest, with a median of <2 years, in patients who have pulmonary hypertension (PH) associated with ILD (PH-ILD).[8,10] Although the earlier detection and more comprehensive management of organ complications have provided some survival gains,[11] a substantial proportion of patients progress to end-stage respiratory failure. In this situation, lung transplantation may constitute a life-saving treatment.

Lung transplantation is rarely performed in patients with scleroderma, however. In the 2016 international registry report, scleroderma accounted for only 1.1% ($n = 404$) of all lung transplants.[12] In general, survival after lung transplant is lower than after other solid-organ transplants. Thus, 5-year survival reported by the Organ Procurement and Transplantation Network (OPTN) was 47% for lung transplants compared with about 80% for deceased donor kidney transplant and 72% for heart or liver transplant.[13–15] Concern exists that the complex and often severe extrapulmonary manifestations of scleroderma may further decrease survival after lung transplantation. More specifically, advanced gastrointestinal dysmotility, poor nutritional status, and renal disease may negatively impact post-transplant outcomes. As a result, many centers are reluctant to perform lung transplantation in patients with scleroderma.

In contradiction with these concerns, several retrospective observational cohort studies

suggest that selected patients with scleroderma can experience acceptable short- and long-term outcomes after lung transplantation.[16] Lung transplantation may therefore deserve a greater role in the treatment of scleroderma. However, large gaps exist in our understanding of the evaluation and selection of patients with scleroderma for lung transplantation.

The purpose of this study was to assess patient selection for lung transplantation to treat scleroderma lung disease, to evaluate survival, and to identify prognostic factors. Toward this end, we conducted a retrospective observational study of 90 patients who received lung transplants at 14 European transplant centers.

Methods

The methods involved in our study approach are described in detail in the Supplementary Material (available online at www.jhltonline.org/). The institutional review board of each participating center approved the study protocol and waived the need for informed consent.

Study design

We retrospectively reviewed the medical files of consecutive patients with scleroderma who underwent cadaveric heart–lung or lung transplantation between February 1993 and June 2016 at 14