

Single Versus Double Lung Retransplantation Does Not Affect Survival Based on Previous Transplant Type

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Background. Survival following retransplantation with a single lung is worse than after double lung transplant. We sought to characterize survival of patients who underwent lung retransplantation based on the type of their initial transplant, single or double.

Methods. The United Network for Organ Sharing database was queried for adult patients who underwent lung retransplantation from 2005 onward. Patients were excluded if they underwent more than one retransplantation. The patient population was divided into 4 groups based on first followed by second transplant type, respectively: single then single, double then single, double then double, and single then double. Descriptive analysis and Kaplan-Meier survival analysis were performed. A *p* value less than 0.05 was considered significant.

Results. A total of 410 patients underwent retransplantation in the study time period. Overall mean survival for all patients who underwent retransplantation was 1,213 days. Kaplan-Meier survival analysis demonstrated no difference in graft survival between the 4 study groups (*p* = 0.146).

Conclusions. There was no significant difference in graft survival between recipients of retransplant with single or double lungs when stratified by previous transplant type. These results suggest that when retransplantation is performed, single lung retransplantation should be considered, regardless of previous transplant type, in an effort to maximize organ resources.

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Lung transplantation remains the only definitive treatment for progressive or end-stage pulmonary disease when life expectancy is less than 1 year [1]. Despite donor and recipient specific pretransplant criteria, the 1-, 3-, and 5-year survival lung transplant falls significantly behind other solid organ transplantation at 82.2%, 68.1%, and 55.6%, respectively [1]. In the early postoperative course, mortality is mainly attributed to perioperative complications, primary graft dysfunction, and acute rejection. However, with improvement in immunomodulation and the treatment of acute rejection, a significant portion of failed pulmonary transplantation is ultimately due to the development of bronchiolitis obliterans syndrome, a condition felt to reflect chronic allograft rejection [2].

With a lack of well-defined medical options to curtail these usually progressive situations, lung retransplantation

becomes a therapeutic consideration [2]. However, lung retransplantation carries significantly greater morbidity and mortality than primary transplant, in part, due to the effects of the chronic immunosuppression and subsequent comorbid medical conditions [3]. In the largest outcome study assessing survival after retransplantation, Novick and colleagues [4] in 1997 found a 1-, 2-, and 3-year survival of 47%, 40%, and 33%, respectively. Similarly, Kawut and colleagues [5] in a 2007 modern cohort study demonstrated improvement in survivability in the modern era but with survivability still falling below rates for other solid organ transplantation. There continues to be no widely accepted standard of care with regard to the type of retransplantation procedure (single, double, contralateral, ipsilateral), as there is little data to inform a surgical decision about the appropriate retransplant procedure to perform. In addition, considering the shortage of appropriate donor lungs, ethical questions arise about the appropriateness of retransplantation and potential survival benefit [3].

Therefore, using the United Network for Organ Sharing (UNOS) database, the aim of this study was to

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compare the survival of patients who underwent single or double lung retransplantation with respect to the prior transplant type in the era of lung allocation score (LAS).

Patients and Methods

Data were obtained from the UNOS registry for patients listed for lung transplantation from January 2005 to December 2013. Patients were included in the study if they underwent lung retransplantation and were ≥ 18 years of age. Patients were excluded if they did not undergo retransplantation, underwent three or more transplants, or had missing data.

The study population was then divided into 4 groups based on first followed by second transplant type, respectively: single then single (S-S), double then single (D-S), double then double (D-D), and single then double (S-D). The full study design is shown in Figure 1. The primary outcome of this study was a comparison of graft survival among the 4 groups of patients who underwent lung retransplantation.

Statistical analyses were completed using SPSS v. 22 (IBM, Armonk, NY) and SAS v. 9 (SAS Institute, Cary, NC). All reported results are at time of retransplantation. A normality test was performed and demonstrated a nonnormal distribution of the study subjects. Therefore, Mann-Whitney, Kruskal-Wallis, and chi-square analyses were used to compare study group characteristics. Results are reported as number (percentage) or median (interquartile range). Kaplan-Meier survival analysis with log rank was used to compare survival between study groups. Matching based on age, gender, creatinine, diagnosis, body mass index (BMI), and LAS was performed for the D-S and D-D groups using the gmatch SAS macro from the Mayo Clinic. A match was attempted at a 1:2 ratio; however, this did not yield enough cases. Therefore, after

matching, 63 cases from the D-S and 92 cases from the D-D groups were included. A p value of 0.05 or less was considered statistically significant.

Results

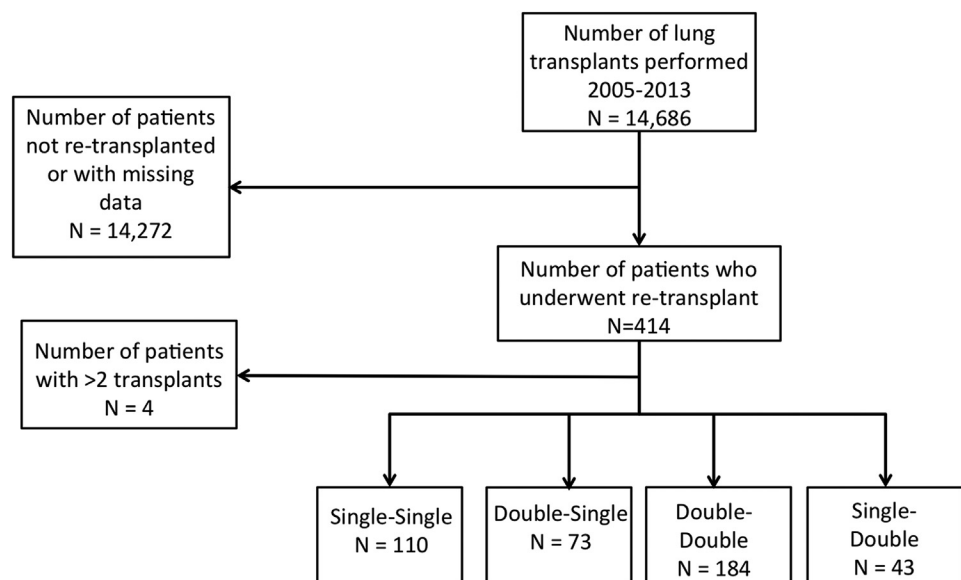
Analysis included a total of 14,686 patients. The groups under investigation included 13,272 patients that did not undergo retransplant or had missing data and 414 patients that did undergo retransplant. The patients that underwent retransplant were subdivided into 4 categories: S-S, S-D, D-S, and D-D.

The annual number of repeat lung transplants is shown in Figure 2 and increased from 14 in 2005 to 68 in 2013. This increase likely reflects changes in distribution of donor organs due to the implementation of the LAS in 2005.

Characteristics of the 4 groups are shown in Table 1. The 4 groups were similar for proportion of men, original waitlist time, and oxygen requirement at time of retransplant. The D-D group was the youngest, had the lowest BMI, had the longest time to retransplant, and had the highest proportion of patients with cystic fibrosis (CF). There were no patients with CF who received a single lung transplant initially. Although creatinine was statistically significantly different among the 4 groups, the difference in values (1.0 to 1.3) is unlikely to be clinically relevant.

Graft survival of recipients of double-lung repeat transplant was significantly better than that of single-lung recipients for repeat transplant ($p = 0.045$). Analysis of graft survival time stratified by the 4 study groups is shown in Figure 3. Overall patient survival for all patients who underwent retransplantation was 1,213 days. There was no statistical difference in graft survival among the 4 groups ($p = 0.146$).

Fig 1. Study design. The 4 study groups were single followed by single, double followed by single, double followed by double, and single followed by double lung transplantation.



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