

Chronic Lung Allograft Dysfunction (CLAD), the leading cause for re-transplantation associated with high cost

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Jennifer McGrain, MS RRT, is employee of Zambon USA Ltd
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Background and Method

Background

- Survival after lung transplantation (LTX) is poor in comparison to other solid organs. (1)
- For lung transplant recipients with poor allograft outcome, the last resort intervention is a potential lung re-transplantation (reLTX).
- Our aim was to review re-transplant rates and survival, underlying reasons for reLTX and development of CLAD thereafter.

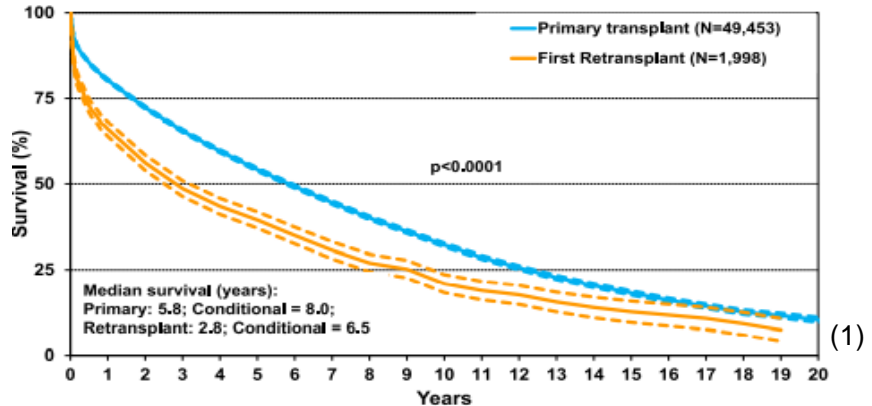
Method

- Systematic review of re-transplantation with a focus on most current publications from the United States and Europe - 2015 to 2021 - was performed in Pubmed.
- International Society of Heart and Lung Transplantation (ISHLT) and United Network of Organ Sharing (UNOS) were screened for specific data on reLTX, causes, outcome and survival.
- CLAD, pre- and post-reLTX, were subject to a closer scrutiny.

Lung Retransplant Rate and Bronchiolitis Obliterans (BOS)

Worse outcome in ReLTX with trend to improvement

- **Average reLTX rate** in the ISHLT Registry as of June 2015 was 4.1%, with 5.1% in single LTX and 3.6% in double LTX. (1)
- **Survival is worse in reLTX** than in primary lung transplant pLTX based on ISHLT registry data (1)
- Median survival for first reLTX recipients in the period of 1990 to 2014 (n=1,998) was 2.8-year, and 6.5-year in those who survived year one, with unadjusted survival rates of 79% at 3-month, at 1-, 3-, 5- and 10-year, 66%, 49%, 39% and 21%. (1)
- A **positive evolution** has been seen in more recent studies: based on UNOS data comparing 3 time periods 1-year survival 2006-09 72.1% vs. 2010-13 76% vs. 2014-17 80.1%. (2), (3)

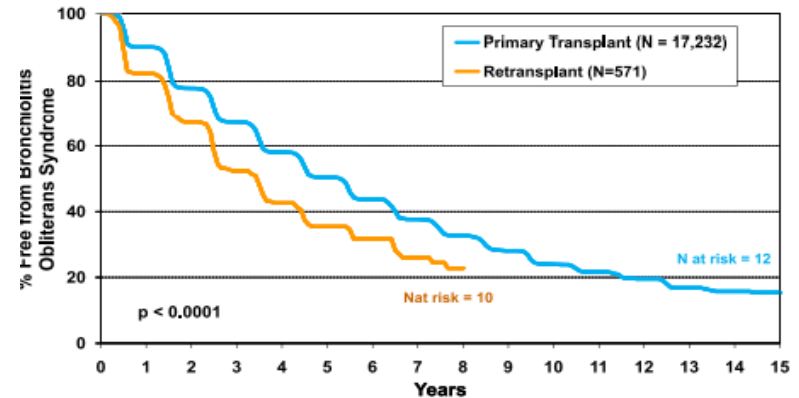


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2. Hall DJ et al. Two Decades of Lung Retransplantation: A Single-Center Experience. Ann Thorac Surg 2017;103:1076-83
3. Wallinder A et al. Outcomes and Long-term Survival After Pulmonary Retransplantation: A Single Center Experience. Ann Thorac Surg 2019;108:1037-44

Lung Retransplant Rate and Bronchiolitis Obliterans (BOS)

**BOS: Major Cause of Death in pLTX and reLTX
CLAD, the leading cause for reLTX**

- CLAD is the major cause of death for pLTX
- CLAD is the major cause of death for reLTX, followed by early rejection and graft failure. (1)
- About 63% to 70% of reLTX patients suffer from CLAD obstructive phenotype (BOS) and 14% to 28% from CLAD-restrictive phenotype (RAS). (1)
- Also, Verleden et al found in their dedicated study to reLTX in CLAD patients n=143 patients BOS in 66% and RAS in 34%. (2)



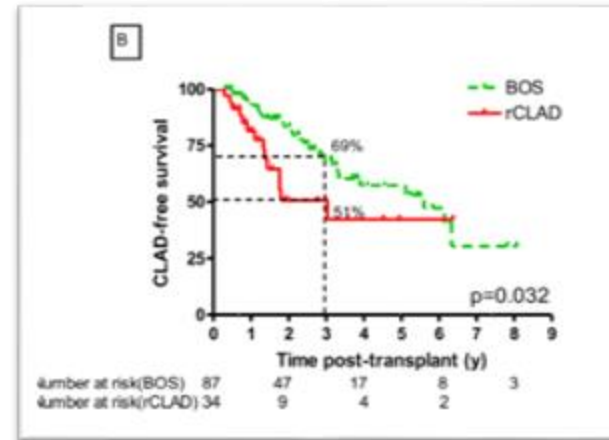
(1)

1. Yusen RD et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-first Adult Lung and Heart-Lung Transplant Report—2014; Focus Theme: Retransplantation. The Journal of Heart and Lung Transplantation, Vol 33, No 10, October 2014
2. Verleden S et al. Impact of CLAD Phenotype on Survival after Lung Retransplantation: A Multicentre study. Am J Transplant. 2015 August; 15(8): 2223–2230.

Time between Primary LTX and ReLTX

Time between pLTX and ReLTX: about 1200 days

- In the ISHLT Registry based on 1597 reLTX recipients, 2005 – 2017, **intertransplant median interval was 1243 days** (IQR: 573 to 2256). (1)
- A dedicated study to reLTX in CLAD examined 143 patients re-transplanted for BOS in 66% and RAS in 34%.
- Time between pLTX and reLTX was respectively 1006 and 1323 days in BOS and RAS.
- 30% reLTX recipients (n=26) redeveloped BOS within a median time of 804 days and n=14 RAS within 444 days. (2)
- Ren et al found underwent reLTX due to CLAD, mean time between the first LT and reLTX was 1460 days



Unadjusted, overall freedom from CLAD analysis (conditional on 90-days survival): rCLAD patients develop CLAD earlier than BOS patients r: Restrictive

1. Harbay MO et al. Epidemiology, Risk Factors, and Outcomes of Lung Retransplantation: An Analysis of the International Society for Heart and Lung Transplantation (ISHLT) Registry. Abs. 392, JHLT 39, No 4S, April 2020
2. Verleden S et al. Impact of CLAD Phenotype on Survival after Lung Retransplantation: A Multicentre study. Am J Transplant. 2015 August; 15(8): 2223–2230.
3. Revilla-Lopez E et al. Lung Retransplantation Due to Chronic Lung Allograft Dysfunction: Results From a Spanish Transplant Unit. Arch Bronconeumol. 2019;55(3):134–138

Economic Burden of Retransplant

Costs paid by Medicare for retransplant are substantially higher:

Per person per year cost for **reLTX**

Year one \$642,354

Year two \$261,330

Per person per year cost for **patients alive with a functioning graft** are

Year one \$195,775

Year two \$40,606

Conclusion

- ReLTX is in the range of 4% both in the USA and Europe based on ISHLT data
- CLAD being the leading cause for ReLTX and the obstructive phenotype, BOS the most prevalent accounting for two thirds
- Median time to reLTX is in the range of 1250 days.
- A high number of reLTX recipients re-develop BOS, for which no approved treatment exists currently
- The burden for reLTX is considerable.
- Treatments for CLAD and particularly, the obstructive phenotype, BOS, are warranted

Thank you for your time.

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Title

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