

Survival after lung transplantation in Europe – CLAD as major cause of death

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Introduction and Objective

Lung transplantation (LTX) outcomes are poor in comparison to other solid organ transplantations. Our aim was to review, with a focus on Europe, survival, leading chronic complications, and major causes of death in Europe. A particular focus was put on Chronic Lung Allograft Dysfunction (CLAD) and its trends.

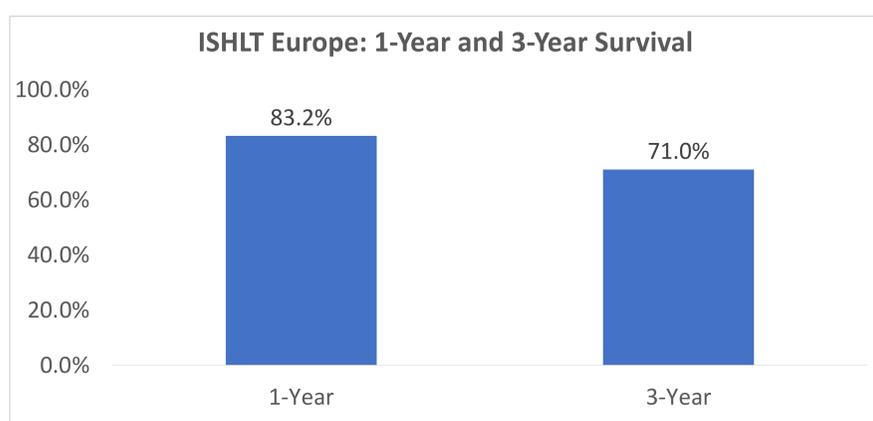
Materials and Methods

There is no dedicated European registry on lung transplantation, outcomes, and complications. Therefore, accessible data from ISHLT registry with focus on the European continent and European Registries were screened for lung transplantation survival data. Furthermore, a dedicated literature research on chronic complications following LTX and particularly CLAD was performed with focus on Europe. In a further step, clinical trial registries were screened for advanced trials addressing the leading form of CLAD – obstructive phenotype - Bronchiolitis Obliterans Syndrome (CLAD-BOS) in Europe.

Results

Survival rate for LTX reaches 83.2% and 71% at 1 and 3 years, based on 3502 cases included between 2013 and 2016 in the ISHLT registry – European Continent – under exclusion of retransplant¹.

Figure 1. Post-Lung Transplantation survival based on 2013-2016 ISHLT – European data n=3502 patients



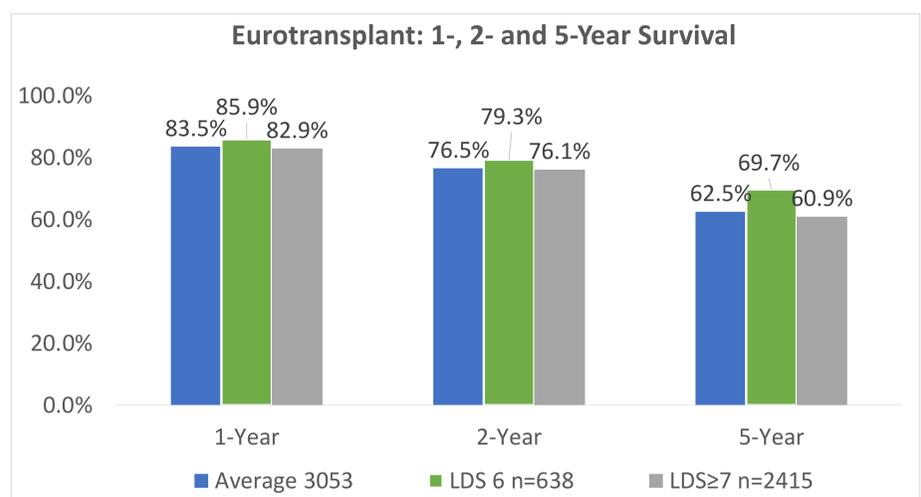
Eurotransplant² data analysis focused on Lung Donor Score 6 n=638 and ≥7 n=2415 from 2012 to 2016 comprising a total of 3053 LTX from Austria, Belgium, Germany, and the Netherlands showed an average survival rates of 83.5%, 76.5% and 62.5% at 1, 2 and 5 years.

CLAD is the major cause of death according to data in the ISHLT registry overall, with no pan-European data.

Large mono- and multicentric European studies report CLAD³⁻⁴⁻⁵⁻⁶ rates ranging from 38% at 3 years to 44%⁴ at longer follow-up. These findings are in line with US data, which are in the range of 42% over a time period of 8 years, from 2011 to 2018⁷.

CLAD-BOS represented consistently the most prevalent phenotype, up to 80% of all CLAD cases in the referenced studies. Although no dedicated European registry data are available, monocentric studies pinpoint CLAD as the single largest cause of death post-LTX. Within CLAD, BOS phenotype accounts for two-thirds of deaths based on reported autopsy analysis⁶.

Figure 1. Post-Lung Transplantation survival based on 2012-2016 Eurotransplant data n=3053 patients



Discussion

The ISHLT registry, European continent, is the only source for pan-European survival data following lung transplantation. Yet, long-term survival data is lacking as well as data on CLAD and the respective phenotypes on a European level.

Some large European studies provide insight on CLAD prevalence and the relevance of CLAD-BOS as a major cause of death, consistent with US data from UNOS.

Currently, two substances for treatment targeting specifically CLAD-BOS are in phase 3 clinical investigation in Europe⁸. Nintedanib, oral delivery, is being studied in LTX, without differentiation being single and double LTX (NCT03283007). L-CsA – Liposomal Cyclosporine A for inhalation use – is being investigated in 2 trials, respectively dedicated to single and double LTX (NCT03657342 and NCT03656926).

Conclusion

In Europe, 3-year post-lung transplantation survival is around 70% and 5-year survival at 63%. CLAD is consistently the most prevalent and fatal complication in lung transplant recipients. CLAD-BOS is the most frequent phenotype. New treatments to address chronic graft failure and primary cause of death in LTX, namely CLAD-BOS, are needed. Currently two therapeutic approaches are under investigation in phase 3 clinical trials aiming at treatment for CLAD-BOS in Europe.

Disclosure

Emilie Hofstetter received honorary fees from Breath Therapeutics GmbH, a Zambon company
Gerhard Boerner, PhD, is employee of Breath Therapeutics GmbH, a Zambon company



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