"Double Lung Transplantation in Cystic Fibrosis: The Impact of CFTR Modulators and Evolving Treatment Strategies"

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Introduction

Cystic Fibrosis is an autosomal genetic disease caused by mutations in the *CFTR* gene. CFTR dysfunction results in abnormal chloride transport leading to a multi-organ disease, dominated by respiratory manifestations (Fajac and Pierre-Régis Burgel 2023). Despite advances in therapy, lung transplant remains a key intervention for CF disease.

Objectives

- Evaluate survival outcomes of CF patients treated with lung transplantation (Tx) VS modulators and no transplant.
- Identify the role of timing and associated referral in transplant success.
- Emphasize that lung transplantation remains the most effective long-term treatment.

Method

A literature review was conducted via peer-reviewed studies comparing CFTR modulators and lung transplantation. Key subtopics included transplantation timing, center expertise, survival outcomes, and the roles of mechanical ventilation (MV).

Results

- **Figure 1:** Those patients listed for Tx with an FEV_1 (Forced Expiratory Volume) of ≤ 30%, had reduced survival VS those listed with FEV_1 ≥ 30% (Belkin et al., 2006), showing the importance of early referral and timing in optimizing outcomes of transplant.

- **Figure 2:** UW Transplant Center Data (Spahr et al., 2007) demonstrates 5-year survival of 67% overall VS 75% in (MV) patients. These results show the benefit of transplant at expert centers, with (MV) as early intervention.
- **Figure 3**: Lung transplant had improved 5-year survival in CF patients who were categorized in Group 1, in comparison to those not receiving lung transplant (Liou et al., 2001). Such findings support transplantation as a superior treatment strategy in long-term, even in a current era of CFTR modulators.

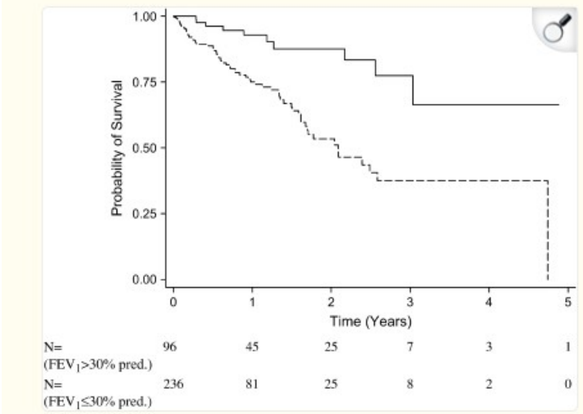

Figure 1: Associated survival by FEV_1 among CF patients listed for Tx. A lower survival observed in patients with FEV_1 ≤ 30%. Data from Belkin et al. 2006 .

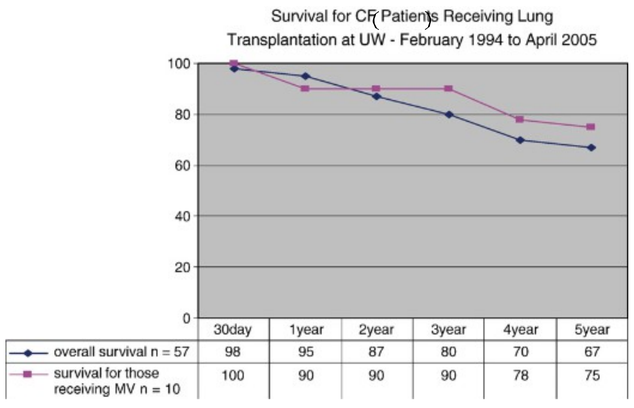

Figure 2: 5-year survival for CF patients receiving lung transplant at UW 1994-2005, including associated outcomes with mechanical ventilation (MV). From Spahr et al.(2007).

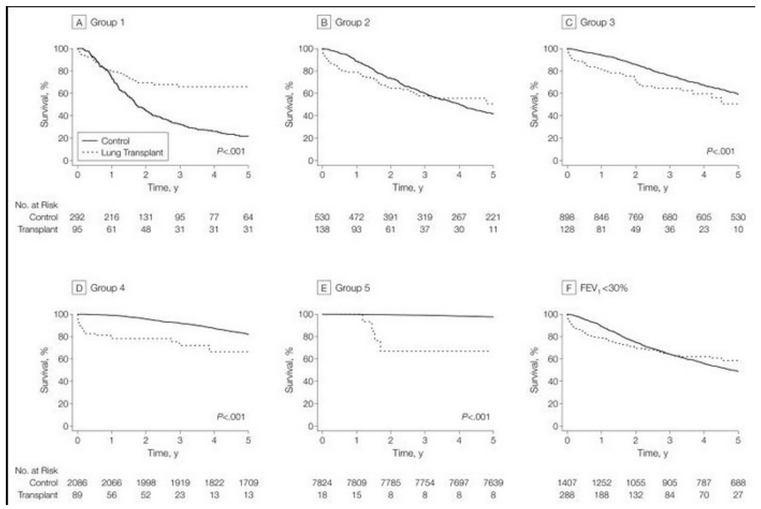

Figure 3: Lung transplant VS no lung transplant survival outcomes in CF patients. Adapted from (Liou et al. (2001).

Conclusion

- Early timing of transplant is vital to improve living outcomes for CF patients.
- Transplant center expertise and supporting interventions such as CFTR modulators and mechanical ventilation (MV) contribute to improved clinical outcomes.
- CF patients who undergo lung transplant demonstrate better long-term survival in comparison to those who do not undergo transplant.

Future Direction

- Refine or improve current modulators by improving exosome-based and stem-cell based therapies.
- Optimize current timing of transplant by improvement of the referral process, i.e. the early referral to experienced centers.
- Early intervention of non-invasive treatments like mechanical ventilation (MV) early in care.

Reference

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