Predicting Risk of Early Readmission in Lung Transplant Recipients Using dd-cfDNA

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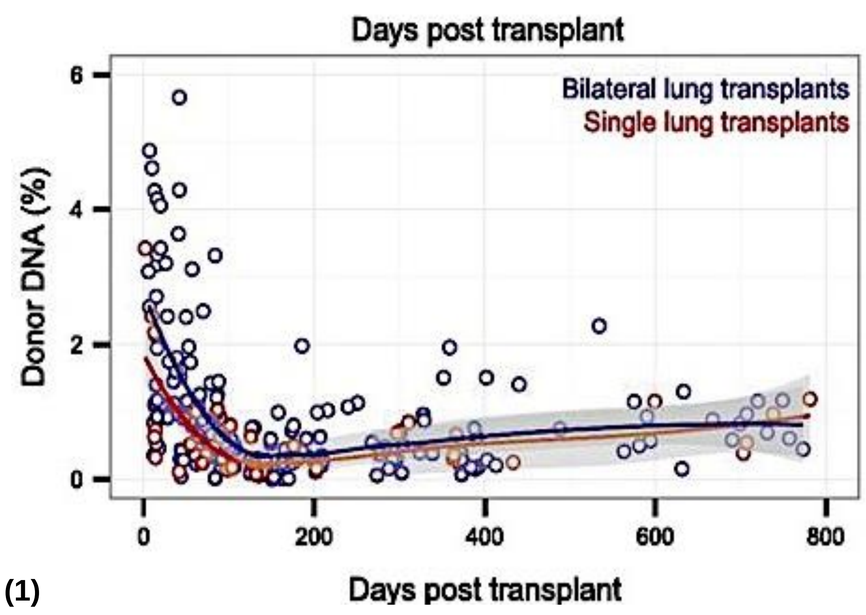
Introduction

Donor derived-cell free DNA (dd-cfDNA) is an emerging biomarker in transplantation. With recent approval of a commercially available assay in kidney transplant, studies to validate a similar technique in other solid organ transplantation are being sought.
Previous trends of the "normal" trends of dd-cfDNA have been reported in the clinical course of lung transplant recipients (1), pointing to the potential use of this biomarker later in the post-transplant period. Levels appear to reflect allograft injury and may aid in identifying clinical outcomes such as rejection or infection.
Additionally, early readmission post transplantation remains a major challenge for lung transplantation, reports of up to 45.4% of patients requiring hospitalization within 30 days of index discharge (2).
Thus, we hypothesized that early measurements of dd-cfDNA may possibly predict early post-transplant complications including the need for readmission after initial discharge.



(1)

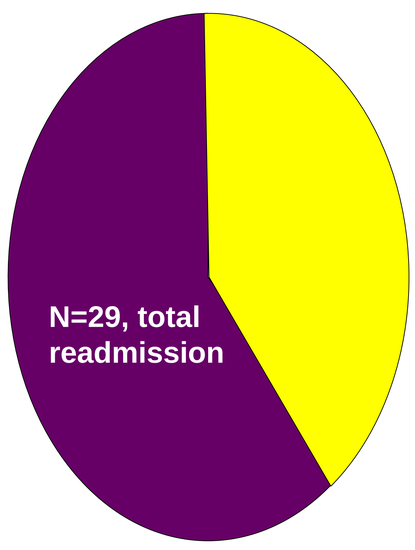
Methods

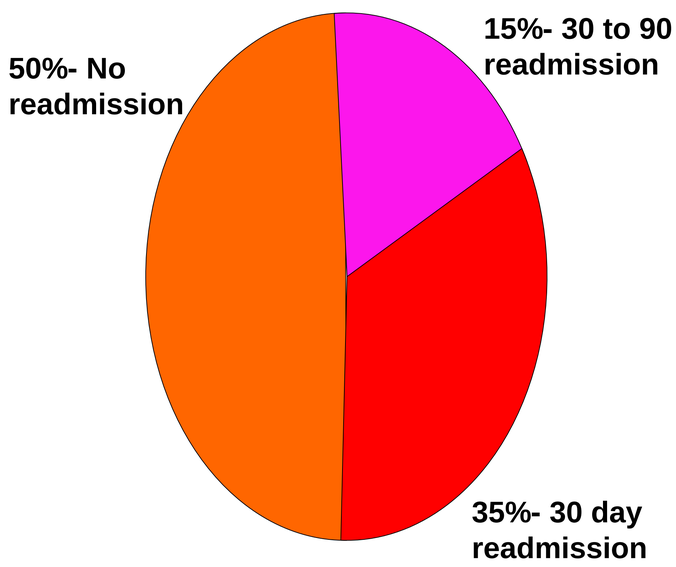
The *GRAfT* study is a multi-center, prospectively collected cohort of heart and lung transplant recipients followed clinically and with serum dd-cfDNA collection. LTx recipients with at least one dd-cfDNA level between post-operative days (POD) 1-10 were included in our analysis (n=50). dd-cfDNA was measured by shotgun sequencing and levels adjusted for procedure type. We evaluated the association between early dd-cfDNA (POD 1, 3, 7, and 10) and time to readmission up to 90 days post initial hospital discharge.

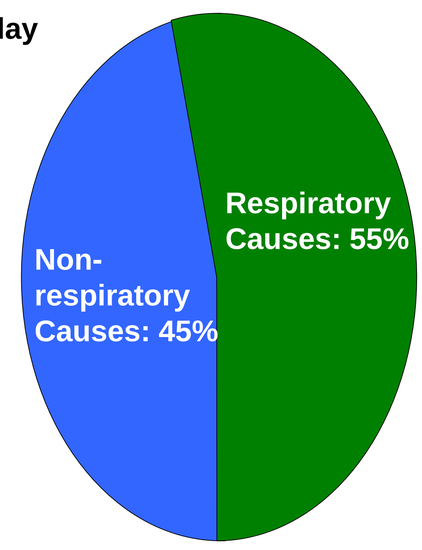
Results

Key Variables Assessed	Peri-operative Course	Index Hospitalization	Post-Discharge
	Intubation Mechanical Ventilation/ Duration ECMO PGD Pre-Admission Length	ICU admission/ duration VTE Pneumonia C. Diff Colitis	Oxygen Requirement Acute Rehabilitation Tracheostomy Percutaneous Feeding Tube

- **Key characteristics of the cohort included median age of 50 years old, 62% female, 78% Caucasian, and the most common primary diagnosis was interstitial lung disease, 67%. Sixty five percent underwent bilateral lung transplantation.**
- **dd-cfDNA measured at POD 1, 3, 7, or 10 did not appear to be associated with the need for hospital readmission, time to readmission, or reason for readmission.**
- **When groups were dichotomized at Day 7 into high/low dd-cfDNA by median, there was an association between low dd-cfDNA and need for hospital readmission, but this association was not significant when adjusted for co-variables.**







Conclusions

Our analysis shows that early dd-cfDNA is unable to identify patients at risk for early (<90 days) readmission:

- **Readmission is common within 90 days of index discharge in lung transplant recipients**
- **There is a high rate of non-respiratory causes of re-admission in our series**
- **Lower level at Day 7 correlated with need for earlier readmission, suggesting that allograft function alone is not a predictor of readmission or good allograft function early on may lead to premature discharge while other issues remain**
- **Limitations of our study include a small sample size and the study was during a high level of variability in dd-cfDNA as per previous reports**
- **Must wait for plateau phase of dd-cfDNA before relying on it to predict clinical outcomes, too early to utilize this biomarker for this purpose**

Citations:
1. De Vlaminck I, Martin L, Kertesz M, et al. Noninvasive monitoring of infection and rejection after lung transplantation. Proceedings of the National Academy of Sciences of the United States of America. 2015; 112(43): 13336-13341.
2. Osho AA, Castleberry AW, Yerokun BA, et al. Clinical predictors and outcome implications of early readmission in lung transplant recipients. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2017;36(5):546-553.ahmad