

## BACKGROUND

- Everolimus is a mammalian target of rapamycin (mTOR) inhibitor used in immunosuppressive therapy regimens for transplant patients to prevent allograft rejection, with a therapeutic range of 3-8 ng/mL.
- Time in therapeutic range (TTR) has been used to evaluate the effectiveness of calcineurin inhibitors, another class of immunosuppressive medications.
- Chronic lung allograft dysfunction (CLAD) is a substantial and persistent decline ( $\geq 20\%$ ) in measured forced expiratory volume (FEV1) value from the reference (baseline) value. It is also marker of graft dysfunction.<sup>1</sup>

## OBJECTIVE

To evaluate if everolimus percent TTR was associated with progression of CLAD in lung transplant recipients.

## METHODS

### Study Design

- Retrospective cohort study of lung transplant patients at UPMC Presbyterian Hospital
- Obtained IRB approval

### Inclusion & Exclusion Criteria

- **Inclusion:** 18 years old or older, received a lung transplant between January 1, 2011 to December 31, 2021, and at least two everolimus levels
- **Exclusion:** Patients with concurrent sirolimus and everolimus levels and less than two FEV1 values

### Data

- Data were obtained from an electronic health record through an honest broker
- Percent TTR was calculated from everolimus levels for all patients
- Rosendaal linear interpolation method
- Index visit: demographics, comorbidities (ICD-9 and ICD-10)
- Follow up visit: FEV1, everolimus levels

### Primary Endpoint

- New or worsening CLAD identified by changes in FEV1 consistent with ISHLT guidelines

### Statistical Analysis

- IBM SPSS Version 29
- Kaplan-Meier method with log-rank test and Cox regression model to analyze primary outcome

## RESULTS

Figure 1: Inclusion and Exclusion Criteria

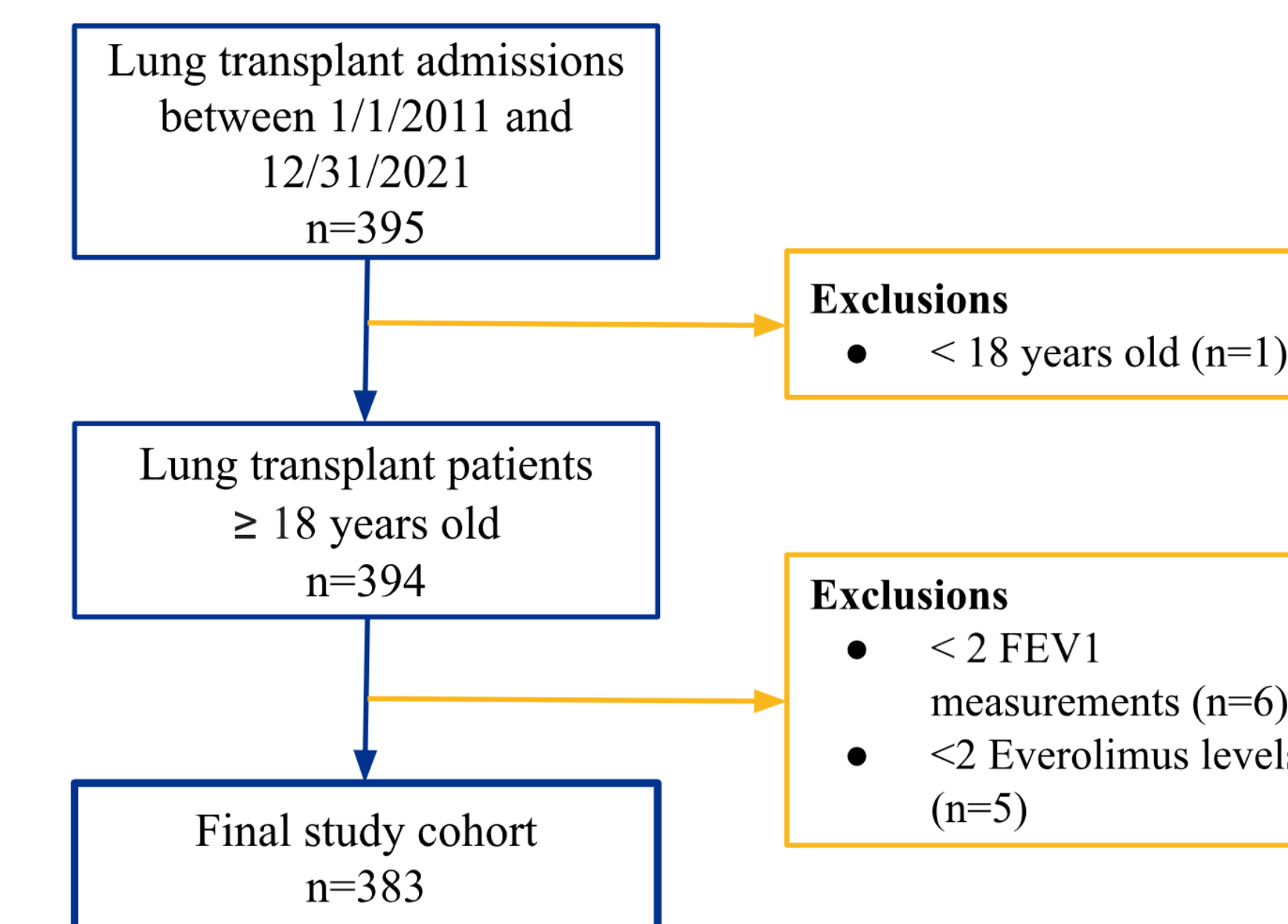


Table 1. Patient Demographics

Characteristic	N (percentage)
Male	220 (57.4)
White	344 (89.8)
Median Age (years)	58 (range: 18-73)
Double Lung Transplant	335 (87.5)
Reason for Transplant	
Chronic obstructive pulmonary disease	116 (30.3)
Idiopathic pulmonary fibrosis	89 (23.2)
Cystic fibrosis	50 (13.1)

Figure 2. Box and whisker plot of percent TTR quartile ranges

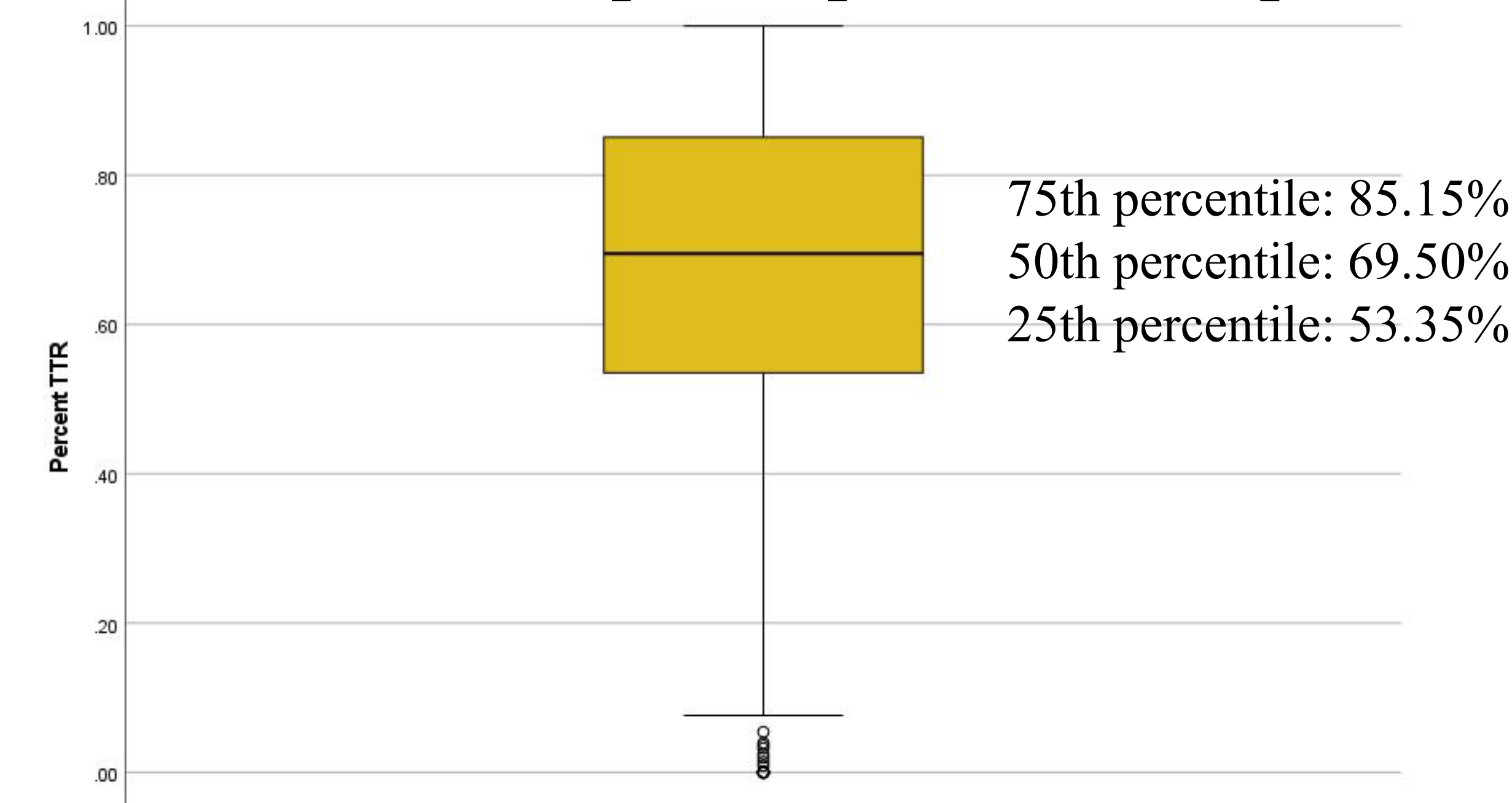
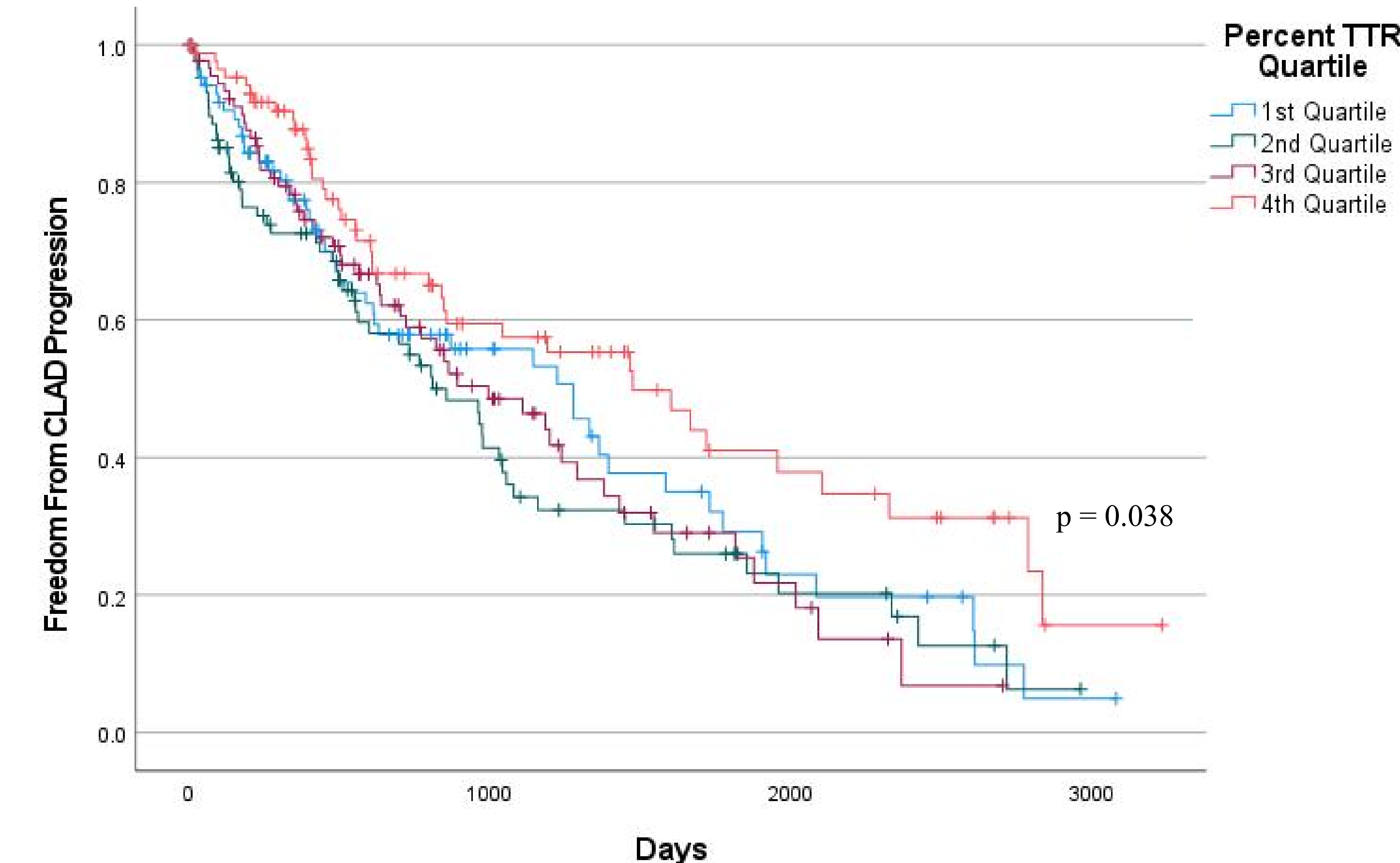


Figure 3. Kaplan Meier curve showing CLAD progression by TTR group



## RESULTS

- Median number of everolimus levels per patient was 17
- Increasing percent TTR was associated with longer time to CLAD progression on Cox regression (HR: 0.532; 95% CI, 0.309 - 0.918)

## LIMITATIONS

- Single site retrospective study
- Variation in initiation of everolimus for each patient
- Concurrent immunosuppressive medications were not evaluated
- Did not include re-transplant patients

## CONCLUSIONS

- Delayed CLAD progression in lung transplant patients was associated with higher percent TTR.
- Further studies are needed to confirm the long-term association of everolimus percent TTR with the development of CLAD.

## REFERENCES

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## DISCLOSURES

Emily Flynn, Madison Kornides, Hannah Meek, Ethan Nguyen and Carlo Iasella do not have any disclosures relevant to this study.

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