Fungal Prophylaxis and Chronic Lung Allograft Dysfunction

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BACKGROUND

- In 2019 there were >2,700 lung transplants in the US
- Opportunistic infection following solid organ transplantation is not uncommon
- Invasive mold infections confer a high burden of morbidity and mortality
- Lung transplant recipients (LTR) experience the highest rate of invasive mold infections among all transplant recipients with an incidence of 8-16% 12 months post-transplant
  - → aspergillosis is the most common culprit pathogen
- Aspergillus colonization and invasive disease have been associated with the development of to chronic lung allograft dysfunction (CLAD)
- There are currently no guidelines regarding antifungal prophylaxis (ppx) strategy or agent selection

OBJECTIVE

- To examine the relationship between post-transplant antifungal ppx and freedom from CLAD

METHODS

- Single-center, retrospective analysis
- 567 adult LTRs 07/2005-12/2015 at UCLA evaluated
- Fungal ppx practices evolved during study period from targeted antifungal ppx (TAP) to universal antifungal ppx (UAP) (voriconazole or posaconazole x6 months post-transplant)
- Kaplan-Meir analysis and Cox regression were performed to estimate freedom from CLAD at 3 years for the TAP versus UAP groups
- Relationship between freedom from CLAD and discharge antifungal (none, voriconazole, or posaconazole) also examined

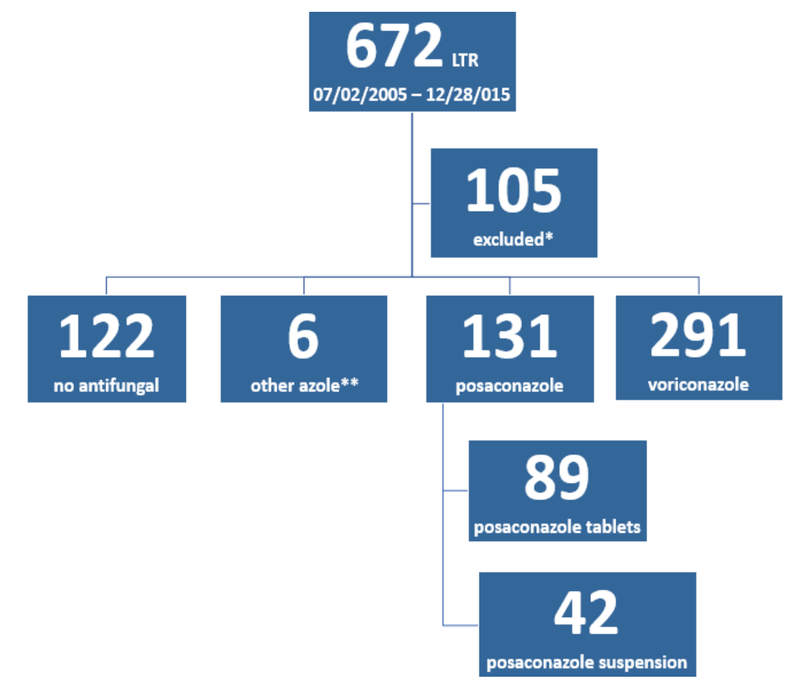

Figure 1. Screening, Exclusion, and Patient Numbers by Group.
*Exclusion Criteria: discharged >28 days post-transplant, re-transplants, multi-organ transplants, lost to follow-up
**Fluconazole or Anidulafungin

RESULTS

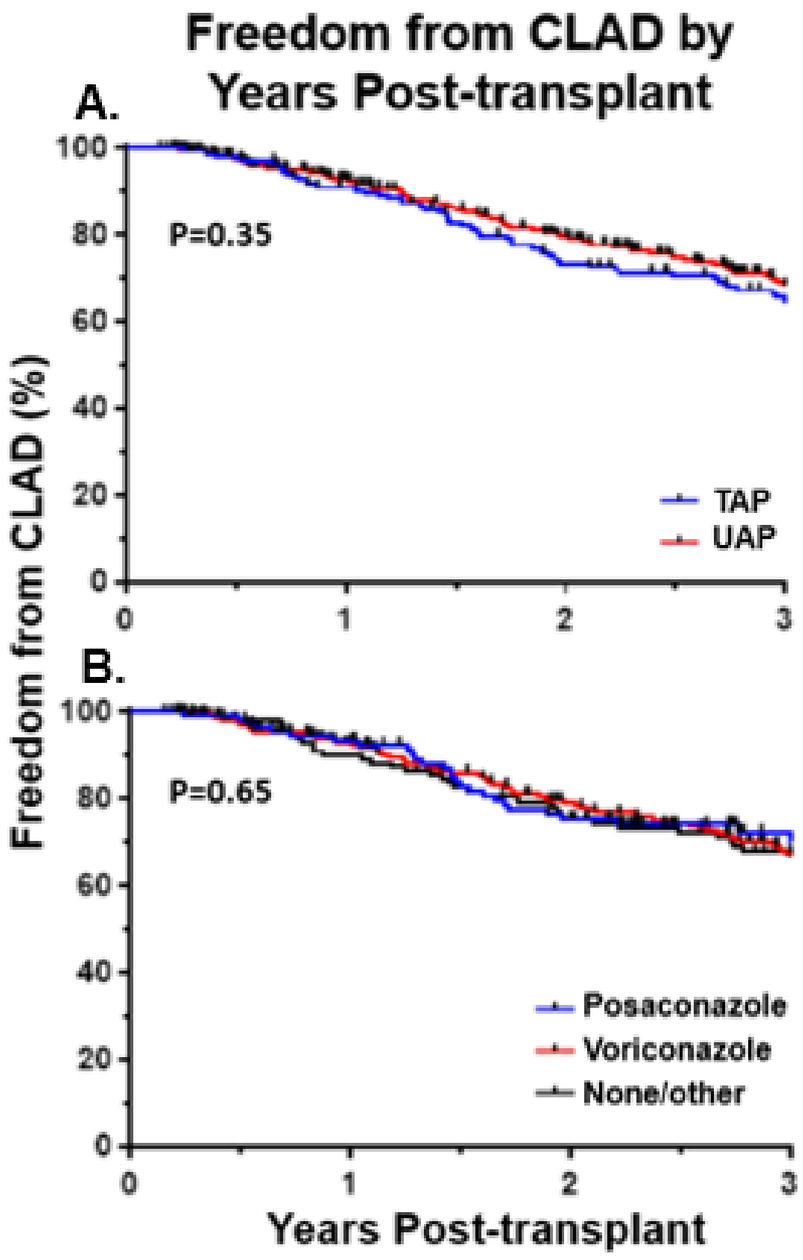

Figure 2. Kaplan-Meier Analysis of Post-transplant Freedom from CLAD. (A) Freedom from CLAD at 3 years post-transplant in the TAP versus UAP cohorts was 65% and 68%, respectively (P=0.35). (B) Freedom from CLAD at 3 years post-transplant with patients grouped by discharge antifungal regimen was as follows: no prophylaxis 67%, voriconazole 68%, and posaconazole 70% (P=0.65).

- The relative risk of CLAD was not significantly reduced in the UAP cohort (hazard ratio 0.83; 95% confidence interval 0.63-1.13; P=0.24)

DISCUSSION

- The absence of significant difference in freedom from CLAD rates in LTRs managed post-transplant with variable antifungal ppx strategies was unexpected
- This finding raises multiple concerns regarding the benefits, consequences and utility of antifungal ppx in LTRs
  - Azoles are not without risk, and their common side effects have been well established
  - Prior work has also highlighted the increased rate of squamous cell carcinoma in LTRs based on cumulative voriconazole exposure
- Next steps will focus on defining the relationship between antifungal ppx and incidence of fungal colonization, invasive disease, and CLAD

CONCLUSION

- There was no significant difference in freedom from CLAD at 3 years post-transplant for LTRs managed under a TAP versus UAP strategy or for these patients when grouped by discharge antifungal regimen
- Further investigation is needed to fully understand the utility and benefits of antifungal ppx in the LTR population

DISCLOSURES

- The authors have no disclosures.

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