# IGFBP7*TIMP2 as an Early Predictor of Acute Kidney Injury After Lung Transplantation

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## Background

- Acute kidney injury (AKI) is a common early postoperative complication of lung transplantation surgery, characterized by deterioration of kidney function, with an incidence as high as 65%.
- AKI is associated with increased postoperative morbidity and mortality, as well as progression to chronic kidney disease, dialysis and potential need for kidney transplantation.
- To date, the gold standard for diagnosing AKI is based on increase in serum creatinine levels, which often leads to delayed diagnosis
- IGFBP7&TIMP2 are cell cycle arrest biomarkers indicative of cellular stress that have been shown to be early predictors of AKI in other surgical and ICU patients

## Research Question

- Are the cell cycle arrest biomarkers IGFBP7 & TIMP2 measured at 6 and 24 hours associated with post-operative acute kidney injury?

## Patient Demographics and Results

| | No AKI n=93 | AKI n=94 |
|---|---|---|
| **Mean Age** | 62 | 52 |
| **Gender** | | |
| Male | 62% | 49% |
| Female | 38% | 51% |
| **Pre-operative diagnosis:** | | |
| Chronic Obstructive Pulmonary Disease (COPD) | 25% | 15% |
| Interstitial Lung Disease (ILD) | 65% | 49% |
| Cystic Fibrosis | 9% | 23% |
| Other | 2% | 13% |
| **Transplant type** | | |
| Unilateral | 28% | 4% |
| Bilateral | 72% | 85% |
| Heart/Lung | 0% | 11% |
| **Mean Lung Allocation Score (LAS)** | 47 | 57 |
| **AKI Stage** | | |
| Stage 1 | | 48% |
| Stage 2-3 | | 52% |
| **In-Hospital Mortality** | 2% | 19% |

Table 1: Patient Demographics

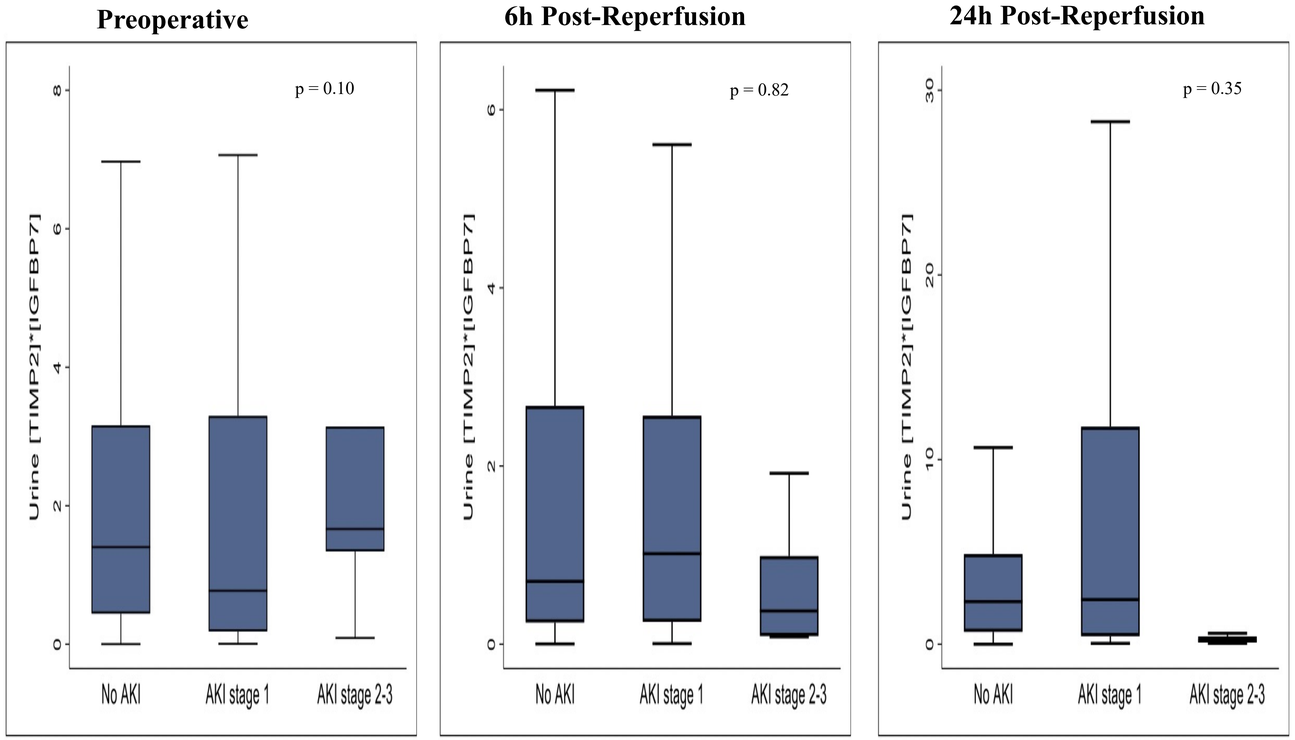



Figure 2: Urine [TIMP2]*[IGFBP7] at multiple perioperative timepoints, by AKI stage. [TIMP2]*[IGFBP7] is calculated as [TIMP2 (ng/ml)]*[IGFBP7 (ng/ml)]/1000, as in prior studies of this biomarker combination. High concentration outliers are not displayed to allow visualization of boxes.

## Methods

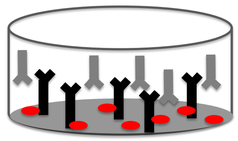
- **Patients:** Consented prior to surgery and enrolled in the 5-center Lung Transplant Outcomes Group Acute Kidney Injury (LTOG-AKI) cohort study between 2017-2019, n=187
- **Samples:** Urine samples collected preoperatively, 6 and 24 hours post allograft reperfusion, stored at -80 degrees Celsius until analysis.
- **Testing:** Commercially available Abcam and Quantikine ELISA to quantify IGFBP7 & TIMP2 concentrations in samples
- **AKI:** KDIGO-defined, during transplant hospitalization

  Stage 1: Cr↑ ≥0.3mg/dL over 48h or ≥50% over 7 days

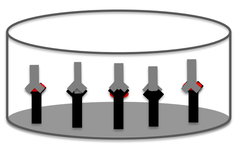
  Stage 2: ≥2-fold to <3-fold Cr↑

  Stage 3: ≥3-fold Cr↑ or renal replacement therapy (RRT)

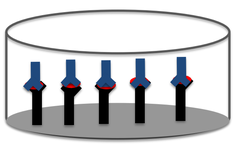
### ELISA for IGFBP7



Add **capture antibody** and **detection antibody** to solution with unknown concentration of IGFBP7



The capture antibody binds to the plate and both the detection and capture antibodies bind to opposite ends of IGFBP7 in a sandwich formation



A substrate is added which changes color when bound to detection antibody, and allows results to be read

## Conclusions & Future Directions

- We did not find a significant association between urinary levels of the biomarkers IGFBP7 and TIMP2 and post-operative acute kidney injury after lung transplantation
- Repeat study on a larger cohort of lung transplant patients to validate results.

## References/Acknowledgements

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