Pediatric Kidney Transplantation as a Potential Clinical Model of Acute Kidney Injury

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Background

- Ischemia Reperfusion Injury (IRI) is a mechanism of Acute Kidney Injury (AKI)
- Similar to cardiopulmonary bypass, kidney transplantation can be thought of as controlled IRI
- IRI during kidney transplantation results in acute tubular necrosis (ATN) and may lead to delayed graft function (DGF)
- Therefore, we sought to investigate kidney transplantation in pediatric patients as a model of AKI and identify predictors of DGF

Methods

- Retrospective and prospective observational cohort study
- Study timeframe: 11/1/2017 – 11/30/2021
- Prospective Enrollment started 7/1/2020
- Prospective patients had urine collected for future biomarker testing
- Inclusion Criteria:
  - Patients aged 3 months to 26 years
  - Kidney transplantation at CCHMC
- Exclusion Criteria:
  - Multi-organ transplantation
  - Positive urine culture treated for UTI (prospective only)
  - Did not provide informed consent (prospective only)
- DGF defined as receiving hemodialysis or continuous kidney replacement therapy (CKRT) within 7 days of transplantation
- Statistics:
  - Categorical data analyzed using Fischer's Exact Test
  - Continuous data analyzed using Wilcoxon Rank Sum Test
  - Significance level set at 0.05
  - Multivariable analysis completed using univariate predictors with p value <0.2 and of clinical significance

Results

- 10/90 (11%) of patients developed DGF
- Patients with DGF had:
  - Longer warm ischemia times (51 vs 37 minutes)
  - No difference in cold or total ischemia times
- Patients with DGF who received deceased donor organs were less likely to receive machine perfusion prior to transplant
- Multivariable analysis revealed that deceased donor organ and warm ischemia time was associated with the development of DGF

Predictors of Delayed Graft Function

Table 1. Analysis of Patients with and without Delayed Graft Function

	Delayed Graft Function (n=10)	No Delayed Graft Function (n=80)	*Univariate P value*	*Multi-variable P value*
Demographics				
Male	5 (50%)	47 (59%)	*0.74*	
African American	2 (20%)	9 (11%)	*0.35*	
Age at Transplant (y)*	14.3 (9.6 – 17.3)	11.5 (4.1 – 16.3)	*0.18*	*0.85*
BMI at Transplant*	21.6 (16.6 – 29.8)	17.6 (16.3 – 19.9)	*0.17*	*0.1*
Primary Glomerular Diagnosis	5 (50%)	26 (33%)	*0.3*	
Prior Kidney Transplant	0	6 (8%)	*1*	
Pre-Transplant Dialysis	9 (90%)	59 (74%)	*0.44*	
Pre-Transplant cPRA (%)*	0 (0 – 0)	0 (0 – 1.3)	*0.48*	
Deceased Donor Organ	8 (80%)	41 (51%)	*0.1*	***0.047***
Machine Perfusion	0 (0%)	18 (44%)	***0.02***	
KDPI (%)*	20 (10.8 – 26)	11 (5 – 20)	*0.14*	
HLA Mismatch				
Total*	4 (3.3 – 4.8)	3 (2 – 5)	*0.52*	
0 MM	0	1	*1*	
1-5 MM	10	77		
6 MM	0	2		
Ischemia Time*				
Cold Ischemia	442.5 (350.8 – 670.5)	271 (41.3 – 788)	*0.15*	*0.19*
Warm Ischemia	51 (45 – 56.8)	37 (30 – 43)	***0.0009***	***0.0064***
Total Ischemia	497 (397.5 – 738.5)	305.5 (80.3 – 827)	*0.13*	
T-Cell Depleting Induction	2 (20%)	14 (18%)	*1*	

*(median, IQR)

Conclusions

- The 11% of patients who developed DGF were found to have longer warm ischemia times.
- Those with DGF were less likely too have received machine perfusion prior to deceased donor kidney transplantation.
- Predictors of DGF included deceased donor organ and warm ischemia time on multivariable analysis

Future Directions

- Urine collected on serial days for those in the prospective portion of the study
- A total of 30 patients had urine collected
- Urine will be run for Neutrophil Gelatinase-Associated Lipocalin (NGAL) and Kidney Injury Marker 1 (KIM-1)
- Analysis of urinary biomarkers to evaluate IRI during pediatric kidney transplantation