Peritoneal Dialysis May Modulate the Urine Biomarker Profile in Children Who Undergo Complex Cardiac Surgery Using Cardiopulmonary Bypass Surgery

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BACKGROUND

- AKI is common in children who undergo cardiac surgery with cardiopulmonary bypass (CPB).
- Optimal timing of renal support therapy for children at risk for AKI and fluid overload is unknown.
- We recently showed that compared to passive drainage of abdominal fluid, empiric PD improves fluid balance, hemodynamic measures, decreases time to chest closure, and may be associated with shorter duration of mechanical ventilation.
  (Sasser W, et al. *Congenital Heart Disease* 2013 in press)
- Urine biomarkers can predict CPB-AKI but the impact of PD on urine biomarker levels is unknown.

OBJECTIVES

1) To compare concentrations of 8 urine AKI biomarkers between children with and without AKI.
2) To determine if PD alters urine AKI biomarkers compared to passive drain.

METHODS

- Using a before and after prospective intervention design, we enrolled two groups of patients undergoing complex cardiac surgery with CPB (median age 8 day).
  - Group 1 (drain; n= 9) was enrolled between January and June 2011, and received an abdominal catheter for passive drainage.
  - Group 2 (PD; n=24) were enrolled after June 2011. Subjects were started on active PD shortly after surgery, once hemodynamically stable (median 2.5 hrs. after admission).
- Eight urine biomarkers were analyzed at CICU admission (CICU) and 24 hours after CICU admission
  - Only subjects who had samples at both time points were included in the analysis
- PD was initiated using 1.5% Dianeal,10 cc/kg dwell, dwell time 40 min, and hourly cycles. Dianeal concentration was adjusted for fluid goals.
- AKI was defined if SCr rose ≥ 0.3 mg/dl from baseline in drain group or SCr ≥ 0.2 mg/dl in PD group.
  - Baseline SCr value was determined by the lowest SCr 1 wk. before or 1 wk. after CPB surgery.
- Analysis between biomarkers and AKI status was compared using Kruskal-wallis test.
- Linear regression was performed to model the geometric mean of the log biomarker to determine differences between a) PD vs. Drain groups, b) time (cicu and cicu_24), and c) the interaction of group X time d)AKI.

RESULTS

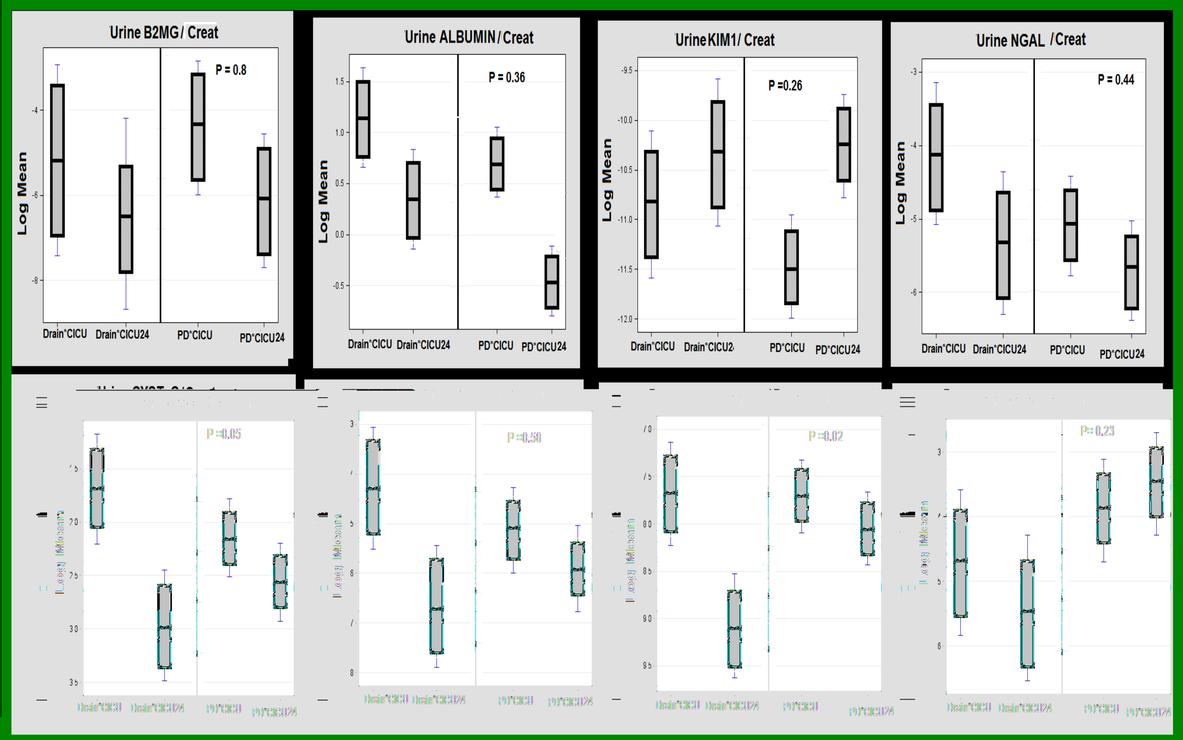
Table 1: Patient Characteristics

	Drainage (N=9)	PD (N=24)	p
Age at surgery (days)	4 (3,1)	10 (3,2)	0.04
Pre-Op Weight (kg)	3.1 (2.0-4.1)	3.3 (2.4-7.1)	NS
Gestation Age (wks)	39 (36,40)	38 (0,41)	0.02
Male (%)	7/9	19/24	0.83
Race			
White (%)	7	13	0.40
Black (%)	2	9	
Other (%)	0	2	
Cardiopulmonary Bypass Time (min)	161 (142,199)	169 (138,210)	0.47
Aoric Cross Clamp (minutes)	83 (58,103)	86 (68,115)	0.51

Table 2: Correlations b/n urine biomarkers and cardiopulmonary bypass / aortic X Clamp time.

	CPB TIME			Aortic Cross Clamp Time		
	Correlation Estimate	95% Conf. Limits	p Value	Correlation Estimate	95% Conf Limits	p Value
NGAL/Cr at CICU	0.58	(0.29,0.77)	<0.001	0.47	(0.15,0.70)	0.004
NGAL/Cr @ CICU 24	0.25	(-0.10,0.55)	0.15	0.17	(-0.19,0.48)	0.48
CYS_C/Cr @ CICU	0.49	(0.16,0.71)	0.003	0.42	(0.08,0.67)	0.01
CYS_C/Cr@ CICU 24	-0.05	(-0.39,0.30)	0.76	-0.01	(-0.35,0.34)	0.96
EFG/Cr@ CICU	-0.22	(-0.52,0.13)	0.22	-0.07	(-0.41,0.28)	0.68
EFG/Cr@ CICU 24	0.05	(-0.30,0.39)	0.78	0.05	(-0.30,0.8)	0.79
B2MG/Cr @ CICU	0.25	(-0.10,0.55)	0.15	0.22	(-0.13,0.53)	0.20
B2MG/Cr @ CICU24	-0.15	(-0.49,0.20)	0.38	-0.18	(-0.50,0.17)	0.3
OPN/Cr @ CICU	0.061	(-0.29,0.40)	0.73	0.15	(-0.20,0.47)	0.40
OPN/Cr @ CICU 24	0.04	(-0.31,0.38)	0.82	0.19	(-0.16,0.50)	0.27
ALB/Cr @ CICU	0.045	(-0.30,0.38)	0.80	0.07	(-0.27,0.41)	0.66
ALB/Cr @ CICU 24	-0.11	(-0.44,0.25)	0.54	-0.18	(-0.5,0.17)	0.3
KIM1/Cr@ CICU	-0.11	(-0.44,0.24)	0.52	0.05	(-0.30,0.39)	0.78
KIM1/Cr @ CICU 24	-0.11	(-0.44,0.24)	0.52	0.05	(-0.30,0.40)	0.76
UMOD/Cr @ CICU	-0.33	(-0.61,0.01)	0.06	-0.15	(-0.47,0.20)	0.39
UMOD/CCr@ CICU24	0.04	(-0.30,0.39)	0.8	0.02	(-0.32,0.36)	0.9

Figure 2: Differences between (Drain; N = 9) vs. group 2 (PD; n = 24) of the changes in urine biomarkers between CICU admission and 24 hours after CICU admission. p-value for interaction of group * time.



Summary/ Conclusions

- Urine Ngal and Cystatin C are associated with increased CPB time and Aortic Cross Clamp time
- We were unable to demonstrate differences in these biomarkers/Cr at CICU admission or CICU _24 possibly due to small sample size or limitations of SCr –based AKI definitions.
- Changes in biomarkers over time differed in Drain Vs. PD group for Urine UMOD/ Cr and epidermal Growth Factor (EGF)/Cr
- This interaction was significant even when controlling for AKI status (p<0.02)
- Possible reasons for these findings include:
  - Changes in inflammation between groups
  - Changes in severity of AKI between groups
  - Changes in renal perfusion
- Studies to delineate the reasons for our findings will be needed to allow proper interpretation of biomarkers in patients receiving RRT.

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