SUPPLEMENTARY INFORMATION FOR

Early Post-operative Urine and Serum Biomarkers Predict Acute Kidney Injury and Poor Outcomes after Pediatric Cardiac Surgery

Supplementary Table 1: STROBE checklist

	Item No	Recommendation	Reported on Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	12
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	12
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	12
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	12-15
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	12-15
Bias	9	Describe any efforts to address potential sources of bias	12-14
Study size	10	Explain how the study size was arrived at	Below
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14,15
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14,15
		(*b*) Describe any methods used to examine subgroups and interactions	14,15
		(c) Explain how missing data were addressed	NR
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	14,15
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	Supplementary Figure 1
		(b) Give reasons for non-participation at each stage	Supplementary Figure 1

		(c) Consider use of a flow diagram	Supplementary Figure 1
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NR
		(c) Summarize follow-up time (e.g., average and total amount)	4,5
Outcome data	15	Report numbers of outcome events or summary measures over time	Table 2 Figures 1, 2, 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(*b*) Report category boundaries when continuous variables were categorized	Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6,7
Discussion			
Key results	18	Summarize key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-10
Generalizability	21	Discuss the generalizability (external validity) of the study results	8-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

Our sample size calculations were based upon detecting the odds ratio of the 5th biomarker quintile developing AKI compared to the 1st biomarker quintile. Assuming an overall AKI rate of AKI of 17%, our sample of 311 patients provided over 80% power to detect an odds ratio of at least 3.5 or more using a two-tailed alpha of 0.05.

Supplementary Table 2: Summary Statistics of biomarkers by Severe AKI*

	Severe AKI					No AKI					
	P25*	**Mean**	**Median**	**P75***	**SD**	**P25***	**Mean**	**Median**	**P75***	**SD**	**P-value†**
Urine IL-18 (pg/mL)											
Pre-op	10.41	80.06	32.69	61.80	141.35	7.33	73.74	19.86	46.77	248.57	0.0387
Day 1 0-6 Hours	62.63	645.85	244.00	612.31	1059.12	17.33	238.30	53.47	200.22	570.62	<0.0001
Day 1 6-12 Hours	108.91	278.41	201.96	317.12	310.59	35.06	129.28	64.12	140.70	210.38	<0.0001
Day 1 12-18 Hours	48.74	416.66	114.41	315.80	812.94	22.40	106.96	51.63	116.59	196.61	<0.0001
Day 2	7.58	205.00	25.22	85.57	675.28	6.27	39.99	14.92	47.40	62.55	0.0369
Day 3	4.85	59.96	12.55	27.17	195.75	4.02	31.30	8.42	24.98	72.57	0.2905
Urine NGAL (ng/mL)											
Pre-op	3.87	8.89	5.58	9.23	10.39	1.96	36.48	4.40	9.45	248.91	0.1028
Day 1 0-6 Hours	16.05	349.70	40.70	216.03	686.93	3.23	119.43	9.62	34.38	471.54	<0.0001
Day 1 6-12 Hours	9.81	130.51	17.31	59.16	468.18	4.45	58.36	8.31	18.93	323.95	<0.0001
Day 1 12-18 Hours	8.70	60.24	20.06	58.81	135.45	3.10	42.24	7.84	17.72	186.37	<0.0001
Day 2	4.97	116.38	10.61	33.00	575.54	3.99	29.74	7.85	15.60	115.38	0.0441
Day 3	3.83	53.75	8.70	37.79	195.35	4.25	22.91	8.58	19.73	43.47	0.6020
Plasma NGAL (ng/mL)											
Pre-op	60.00	98.64	60.00	135.90	63.83	60.00	94.70	75.83	106.42	54.76	0.2295
Day 1 0-6 Hours	95.36	218.71	169.76	266.22	201.05	88.64	171.04	144.95	212.57	105.74	0.1774
Day 2	63.04	171.02	119.49	201.36	163.95	60.00	126.49	91.84	163.54	92.47	0.1238
Day 3	60.00	171.88	117.03	182.79	186.38	60.00	126.01	91.18	150.73	98.31	0.2334
Serum Creatinine (mg/dL)											
Pre-op	0.3	0.351	0.3	0.4	0.162	0.3	0.441	0.4	0.5	0.155	<.0001
Day 1 0-6 Hours	0.4	0.545	0.4	0.6	0.298	0.4	0.509	0.5	0.6	0.173	0.3749
Day 2	0.5	0.776	0.7	0.9	0.403	0.4	0.517	0.5	0.6	0.187	<.0001
Day 3	0.4	0.624	0.5	0.6	0.53	0.3	0.445	0.4	0.5	0.165	0.0111

*P25 = 25th percentile, P75 = 75th percentile

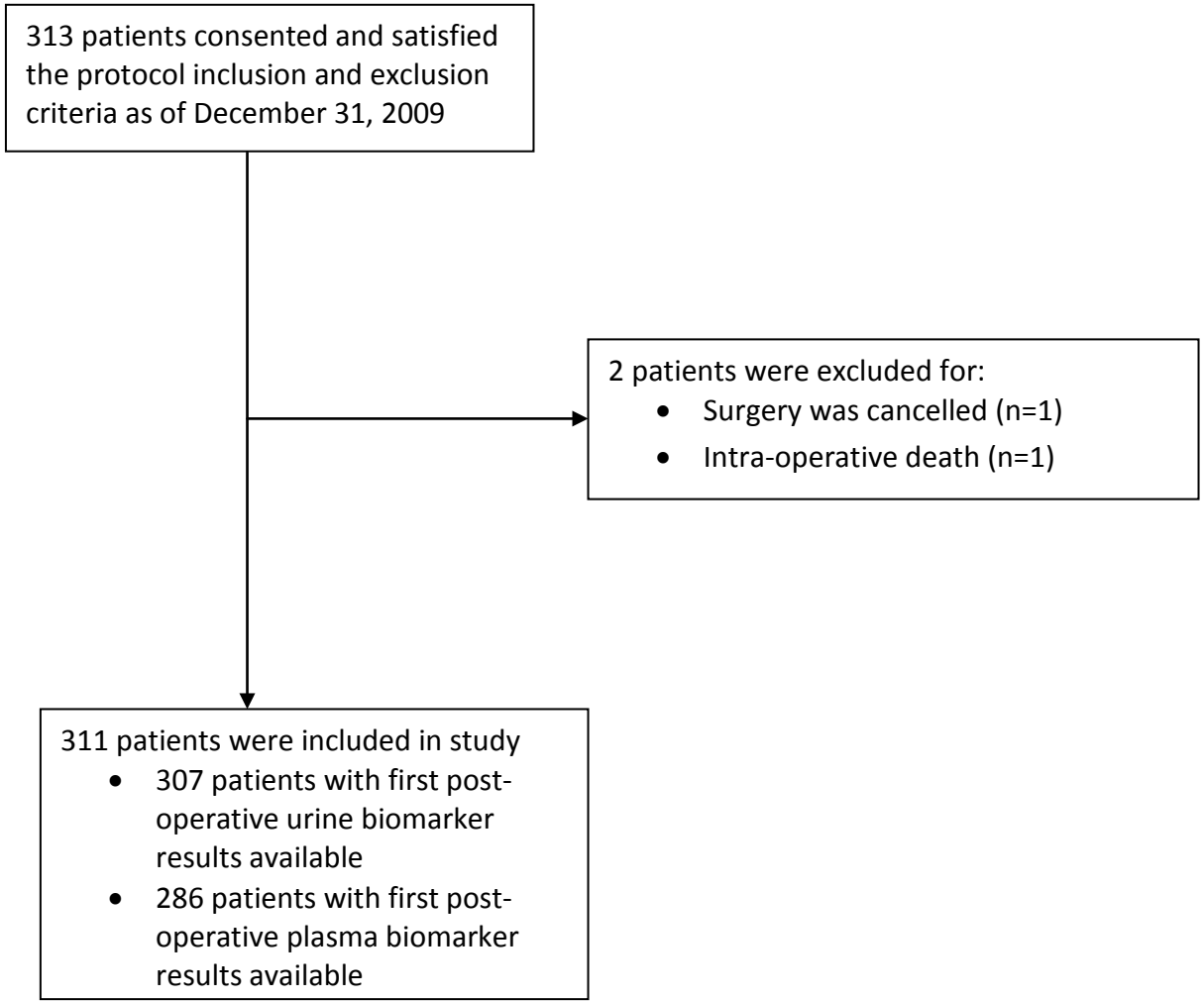
†P-value from Wilcoxon rank sum test

* AKI was defined as the receipt of acute dialysis or the doubling of serum creatinine during hospitalization.

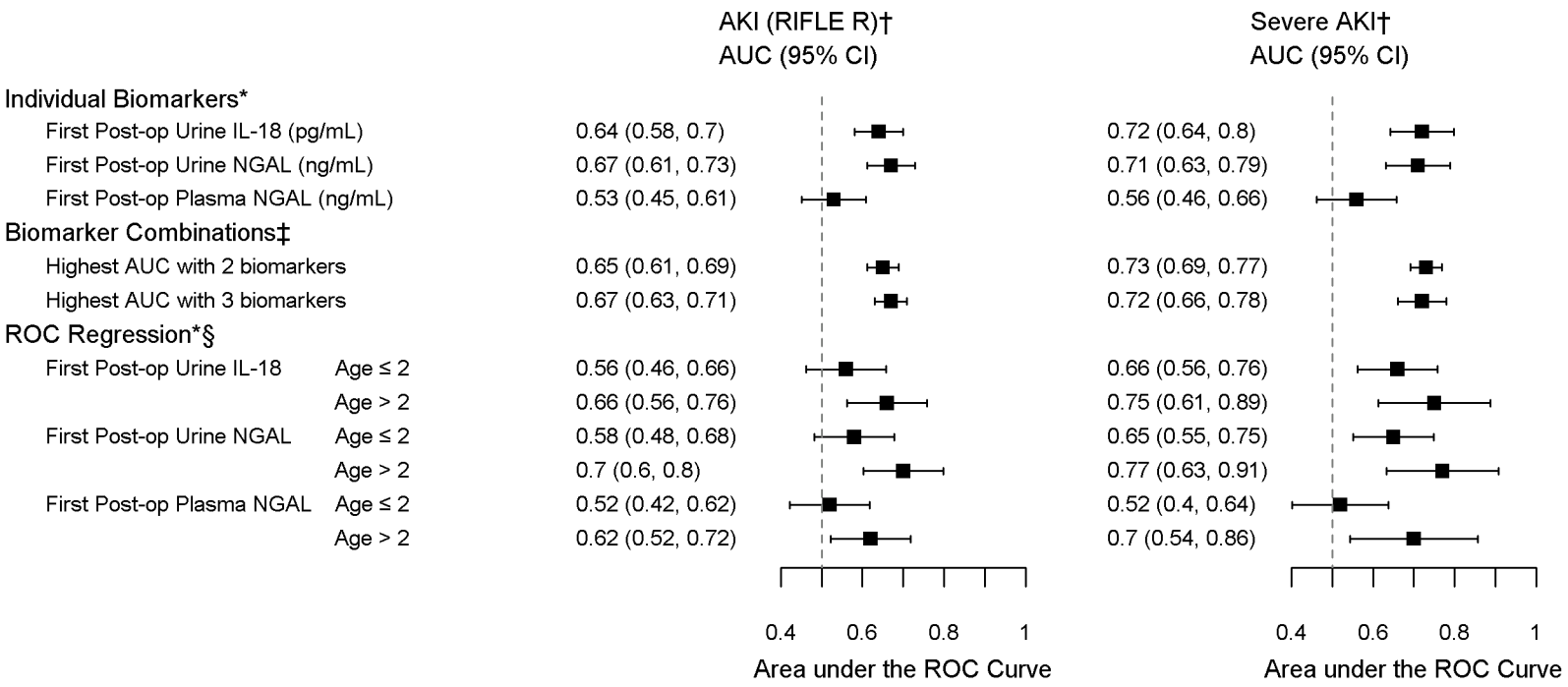
Supplementary Table 3: Performance of first post-operative biomarkers by site for Severe AKI

AUC (SE)	Cincinnati	Montreal	Yale	All
Urine IL-18	0.74 (0.05)	0.76 (0.09)	0.72 (0.11)	0.72 (0.04)
Urine NGAL	0.71 (0.05)	0.76 (0.00)	0.67 (0.12)	0.71 (0.04)
Plasma NGAL	0.58 (0.06)	0.55 (0.10)	0.51 (0.12)	0.56 (0.05)
Serum Creatinine	0.46 (0.05)	0.51 (0.09)	0.48 (0.12)	0.46 (0.04)

Supplementary Figure 1: Patient Flow of Study Population



Supplementary Figure 2: Performance of Biomarker Combinations and Subgroup Analysis



†AKI (RIFLE R) was defined by the receipt of acute dialysis or an increase of 50% in serum creatinine during the hospital stay. Severe AKI was defined by the receipt of acute dialysis or a doubling in serum creatinine during the hospital stay.
*Individual Biomarkers and ROC Regression results are from the first post-operative biomarker sample.
‡Biomarker Combinations: Highest AUC with 2 biomarkers for AKI and Severe AKI is Urine IL-18 on Day 1 6-12 Hours and Urine IL-18 Day 1 12-18 Hours. Highest AUC with 3 biomarkers for AKI is Urine IL-18 Day 1 6-12 Hours, Urine NGAL 12-18 Hours and Plasma NGAL Day 2; for Severe AKI is Urine IL-18 Day 1 0-6 Hours, Urine IL-18 Day 1 6-12 Hours and Urine IL-18 Day 1 12-18 Hours.
§Although higher AUCs are in the groups of Age ≥2 years, this difference is not statistically significant.