

SUPPLEMENTARY INFORMATION

Performance of Kidney Injury Molecule-1 and Liver Fatty Acid-Binding Protein and Combined Biomarkers of AKI after Cardiac Surgery

Authors: Chirag R. Parikh,* Heather Thiessen-Philbrook,[†] Amit X. Garg[†], Deepak Kadiyala,* Michael G. Shlipak,[‡] Jay L. Koyner,[§] Charles L. Edelstein,[#] Prasad Devarajan,[¶] Uptal D. Patel,^{**} Michael Zappitelli,^{††} Catherine D. Krawczeski,^{¶¶} Cary S. Passik,^{‡‡} Steven G. Coca,* for the TRIBE-AKI Consortium

Affiliations: *Program of Applied Translational Research, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut and Section of Nephrology, Yale University School of Medicine, New Haven, Connecticut, and Clinical Epidemiology Research Center, Veterans Affairs Medical Center, West Haven, Connecticut; [†]Division of Nephrology, Department of Medicine, Western University, London, Ontario, Canada; [‡]Division of General Internal Medicine, San Francisco Veterans Administration Medical Center, University of California, San Francisco, California; [§]Section of Nephrology, Department of Medicine, University of Chicago, Pritzker School of Medicine, Chicago, Illinois; [#] Division of Renal Diseases, University of Colorado, Denver, Colorado; [¶]Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio; ^{**}Duke Clinical Research Institute and Division of Nephrology, Department of Medicine, Duke University School of Medicine, Durham, North Carolina; ^{††}Department of Pediatrics, Division of Nephrology, McGill University Health Center, Montreal Children's Hospital, Montreal, Quebec, Canada; ^{‡‡}Department of Cardiothoracic Surgery, Danbury Hospital, Connecticut.

SUPPLEMENTARY TABLES

Supplementary Table 1 – Summary Statistics of biomarkers by AKI in Adults

Biomarker	Time point	AKI (n=60)					Non-AKI (n=1159)					P-value
		P25	Median	Mean	P75	SD	P25	Median	Mean	P75	SD	
Urine KIM-1 (ng/mL)	Pre-op	0.80	1.92	2.29	3.06	2.14	0.55	1.21	1.99	2.44	2.69	0.06
	Day 1 0-6 Hours	0.50	1.06	1.69	2.45	1.72	0.16	0.42	0.84	0.94	1.49	<0.001
	Day 1 6-12 Hours	1.21	2.52	3.01	3.96	2.28	0.82	1.55	2.17	2.76	2.16	<0.001
	Day 2	2.91	4.44	6.22	8.38	5.19	2.10	4.20	5.62	7.33	5.49	0.14
	Day 3	7.93	16.58	18.81	27.23	13.58	3.40	7.07	9.51	12.99	8.63	<.001
	Day 4	4.64	8.37	10.36	11.64	9.21	2.09	3.88	5.60	7.21	5.29	<.001
	Day 5	2.38	5.27	8.40	10.22	9.86	1.43	2.83	3.75	5.06	3.29	<.001
Urine L-FABP (ng/mL)	Pre-op	1.1	3.3	19.3	9.1	79.3	1.1	2.3	11.1	5.3	36.5	0.11
	Day 1 0-6 Hours	6.7	66.3	455.2	400.0	611.2	4.2	18.4	142.8	100.9	132.5	<0.001
	Day 1 6-12 Hours	6.5	29.7	299.7	193.6	528.3	3.3	8.6	58.8	28.7	86.9	<.001
	Day 2	5.5	27.5	240.2	193.4	451.9	2.5	8.0	31.3	21.2	60.0	<.001
	Day 3	6.5	20.9	241.0	79.7	490.1	3.0	9.6	30.8	25.7	57.3	<.001
	Day 4	13.8	46.9	242.3	328.0	420.8	4.9	12.0	42.4	35.3	68.0	<.001
	Day 5	11.4	89.2	284.1	199.9	472.7	3.9	9.5	34.2	24.4	63.0	<.001

P25 = 25th percentile, P75 = 75th percentile

P-value from Wilcoxon Rank Sum Test

AKI defined by receipt of acute dialysis or a doubling in serum creatinine from the pre-operative serum creatinine value

Supplementary Table 2 – Summary Statistics of biomarkers by AKI in Children

Biomarker	Time point	AKI (n=53)					Non-AKI (n=258)					pvalue
		P25	Median	Mean	P75	SD	P25	Median	Mean	P75	SD	
Urine KIM-1 (ng/mL)	Pre-op	0.25	0.62	1.12	1.13	1.51	0.17	0.54	0.89	1.13	1.43	0.42
	Day 1 0-6 Hours	0.38	0.63	0.91	1.03	0.96	0.17	0.39	0.70	0.81	1.26	0.002
	Day 1 6-12 Hours	0.79	1.82	2.15	2.85	1.63	0.54	0.92	1.63	2.18	2.06	0.003
	Day 2	0.57	2.28	4.94	6.08	6.65	0.27	1.14	1.90	2.79	2.23	0.006
	Day 3	0.12	0.86	3.54	2.45	8.05	0.16	0.61	1.56	1.42	3.24	0.33
	Day 4	0.51	1.20	2.66	2.84	3.49	0.11	0.43	0.87	1.06	1.20	<0.001
	Day 5	0.42	0.94	1.70	2.24	2.41	0.17	0.44	0.98	1.57	1.23	0.05
Urine L-FABP (ng/mL)	Pre-op	1.7	4.93	9.15	13.8	13.6	1.4	3.7	9.9	7.4	31.1	0.23
	Day 1 0-6 Hours	58.1	366.0	539.3	400.0	531.4	19.9	69.1	216.5	257.2	342.5	<.001
	Day 1 6-12 Hours	46.9	154.3	341.5	400.0	414.8	17.7	47.6	143.9	129.4	264.5	<.001
	Day 2	1.7	21.7	180.8	140.7	392.7	0.7	3.6	22.3	14.0	106.2	<0.001
	Day 3	0.3	3.7	21.8	29.2	36.4	0.4	1.7	5.7	5.5	10.9	0.11
	Day 4	1.1	6.4	21.4	26.1	34.1	0.5	2.2	36.4	7.3	180.2	0.01
	Day 5	1.5	7.7	61.1	24.8	201.6	1.0	4.9	41.3	10.3	218.1	0.16

P25 = 25th percentile, P75 = 75th percentile

P-value from Wilcoxon Rank Sum Test

AKI defined by receipt of acute dialysis or a doubling in serum creatinine from the pre-operative serum creatinine value

Supplementary Table 3 - Association of first post-operative biomarkers adjusted for other biomarkers

	Adults Primary Outcome – AKI	
Quintile (cutpoints)	Clinical Model [†]	Clinical Model + Other Biomarkers [‡]
Urine IL-18 (pg/mL)		
Q1 (<3)	1.0 (referent)	1.0 (referent)
Q2 (3 to 8)	1.6 (0.4, 6.7)	2.4 (0.5, 12.7)
Q3 (8 to 17)	2.3 (0.6, 9.3)	3.1 (0.5, 17.7)
Q4 (17 to 60)	2.8 (0.7, 10.5)	3.7 (0.6, 23.5)
Q5 (> 60)	6.8 (1.9, 24.3)	7.7 (1.1, 52.7)
Urine NGAL (ng/mL)		
Q1 (<3)	1.0 (referent)	1.0 (referent)
Q2 (3 to 7)	1 (0.3, 3.0)	0.4 (0.1, 1.5)
Q3 (7 to 16)	0.9 (0.3, 2.9)	0.2 (0.05, 0.9)
Q4 (16 to 102)	1.1 (0.4, 3.3)	0.2 (0.05, 0.9)
Q5 (> 102)	2.5 (0.9, 6.8)	0.4 (0.08, 1.7)
Plasma NGAL (ng/mL)		
Q1 (<105)	1.0 (referent)	1.0 (referent)
Q2 (105 to 158)	1.1 (0.3, 4.1)	1.4 (0.4, 5.5)
Q3 (158 to 218)	2.3 (0.7, 7.4)	3.0 (0.8, 10.3)
Q4 (28 to 292)	1.4 (0.4, 5.1)	1.9 (0.5, 7.0)
Q5 (>293)	5.0 (1.6, 15.3)	5.9 (1.8, 19.5)

[†] Adjusted for age (per year), gender, white race, CPB time > 120 minutes, nonelective surgery, preoperative CKD-EPI eGFR, diabetes, hypertension, and center.

[‡] Adjusted for age (per year), gender, white race, CPB time > 120 minutes, nonelective surgery, preoperative CKD-EPI eGFR, diabetes, hypertension, center, Urine IL-18, Urine NGAL, Plasma NGAL, Urine KIM-1, Urine L-FABP.

The adjusted relative risks for Urine Kim-1 and Urine L-FABP from this model are presented in Table 2.