

**SUPPLEMENTARY DATA**

**Supplementary Table 1a. Plasma IL-6 and IL-10 measurements by AKI status**

	IL-6 (pg/ml)								IL-10 (pg/ml)							
	Pre-op		Day 1		Day 2		Day 3		Pre-op		Day 1		Day 2		Day 3	
	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI
<b>25<sup>th</sup> percentile</b>	0.6	1.9	85.1	121.2	91.0	107.6	75.1	88.8	0.9	0.9	12.2	18.9	0.9	2.9	0.9	0.9
<b>Median</b>	2.7	3.9	145.5	208.4	143.6	179.7	110.7	143.0	0.9	0.9	37.9	53.6	3.8	5.8	0.9	0.9
<b>75<sup>th</sup> percentile</b>	6.4	8.2	255.5	368.1	233.4	297.5	168.3	228.4	0.9	0.9	95.7	134.5	7.8	12.5	0.9	3.4
<b>*P value</b>	0.001		<0.0001		<0.0001		<0.0001		0.5709		0.0005		<0.0001		<0.0001	

**AKI defined as an increase in serum creatinine by >50% or > 0.3mg/dL**

Day 1 refers to postoperative time 0-6 hours after surgery, day 2 corresponds to 48 hours after surgery, and day 3 corresponds to 72 hours after surgery.

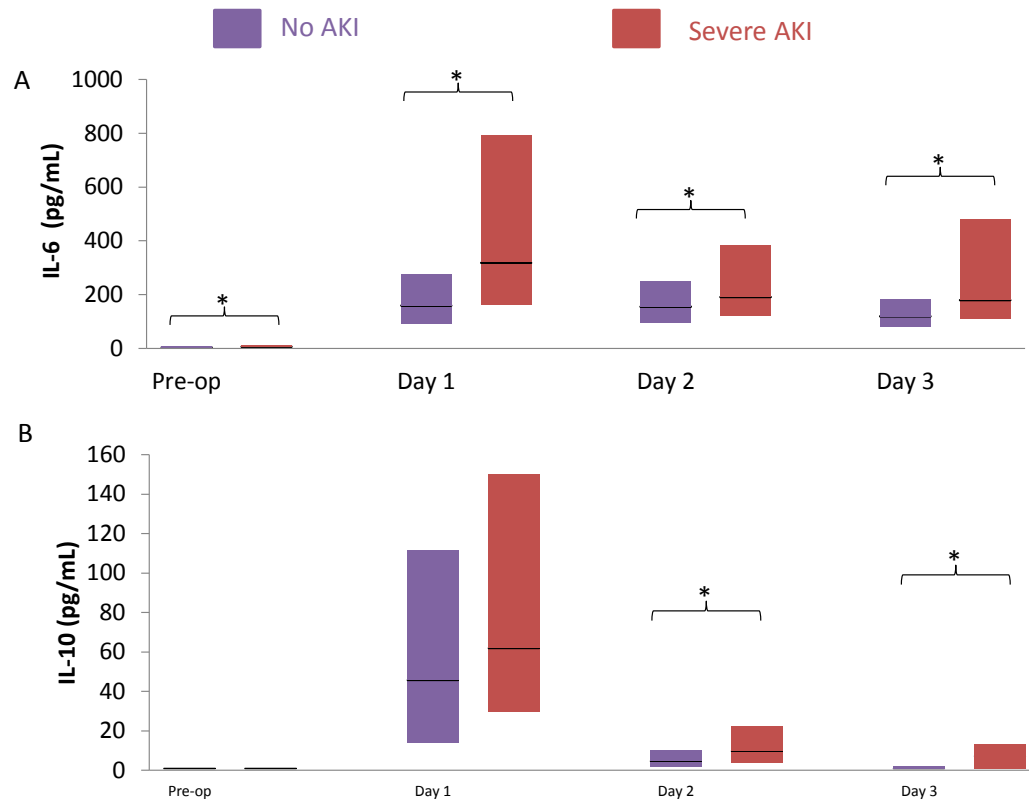
**Supplementary Table 1b. Plasma IL-6 and IL-10 measurements by Severe AKI status**

	IL-6 (pg/ml)								IL-10 (pg/ml)							
	Pre-op		Day 1		Day 2		Day 3		Pre-op		Day 1		Day 2		Day 3	
	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI
<b>25<sup>th</sup> percentile</b>	1.1	2.7	89.1	160	95	119	78.8	112	0.9	0.9	13.8	29.6	1.9	3.6	0.9	0.9
<b>Median</b>	2.9	5.0	159	318	153	189	118	179	0.9	0.9	45.5	61.7	4.5	9.6	0.9	7.2
<b>75<sup>th</sup> percentile</b>	6.8	10.7	277	791	247	379	182	479	0.9	0.9	111	149	9.9	22.2	2.0	13.3
<b>*P value</b>	0.003		<0.0001		0.003		<0.0001		0.90		0.07		0.0003		<0.0001	

**AKI defined as an increase in serum creatinine by >100%**

Day 1 refers to postoperative time 0-6 hours after surgery, day 2 corresponds to 48 hours after surgery, and day 3 corresponds to 72 hours after surgery.

### Supplementary Figure 1



**Plasma biomarker levels by severe AKI status versus rest of the cohort.** In patients with AKI, (A) plasma IL-6 levels were significantly increased both pre- and postoperatively while (B) plasma IL-10 levels were significantly increased only on days 2 and 3. Each bar represents the interquartile range (25<sup>th</sup> percentile to 75<sup>th</sup> percentile), and the horizontal black line represents the median; \*=p<0.05. Day 1 refers to postoperative time 0-6 hours after surgery, day 2 corresponds to 48 hours after surgery, and day 3 corresponds to 72 hours after surgery.

**Supplementary Table 2. Tertiles of inflammatory biomarkers and risk of Severe AKI**

Biomarker	Pre-op				Post-op			
	Tertile (Range)	Severe AKI n (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	Tertile (Range)	SevereAKI n (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
IL-6 (pg/mL)	T1 (0.6-1.9)	8 (2.6%)	1.00 (referent)	1.00 (referent)	T1 (6.2-111)	4 (1.3%)	1.00 (referent)	1.00 (referent)
	T2 (2.0-5.2)	8 (2.6%)	1.01 (0.37, 2.72)	1.09 (0.39, 3.08)	T2 (111-239)	9 (2.8%)	2.28 (0.70, 7.48)	1.51 (0.44, 5.26)
	T3 (5.2-633)	17 (5.5%)	2.20 (0.93, 5.17)	2.17 (0.84, 5.63)	T3 (241-791)	24 (7.5%)	6.41 (2.2, 18.69)	2.99 (0.94, 9.51)
IL-10 (pg/mL)	T1 (0.9)	28 (3.4%)	1.00 (referent)	1.00 (referent)	T1 (0.9-21.7)	8 (2.5%)	1.00 (referent)	1.00 (referent)
	T2 (1.5-168)	3 (3.2%)	0.93 (0.28, 3.10)	0.96 (0.26, 3.61)	T2 (21.8-79.5)	16 (5%)	2.05 (0.86, 4.85)	1.47 (0.53, 4.07)
	...	...	...	...	T3(79.6-841)	13 (4.1%)	1.65 (0.68, 4.04)	1.03 (0.33, 3.18)

**Severe AKI defined as an increase in serum creatinine >100% or dialysis during hospitalization.**

Small cell counts are only presented for data collected by TRIBE-AKI and not from ICES data holdings. OR=odds ratio, CI=confidence interval.

**Pre-op Models:** Adjusted for age, sex, white race, non-elective surgery, pre-op eGFR, diabetes, hypertension, center, congestive heart failure, myocardial infarction, pre-op urine albumin to creatinine ratio, and type of surgery. Number of patients per tertile: IL-6 T1 n=309, T2 n=307 T3 n=308; IL-10 T1 n=814, T2 n=94.

**Post-op Models:** Adjusted for age, sex, white race, non-elective surgery, pre-op eGFR, diabetes, hypertension, center, congestive heart failure, myocardial infarction, pre-op urine albumin to creatinine ratio, and type of surgery. Number of patients per tertile: IL-6 T1 n=318, T2 n=319 T3 n=318; IL-10 T1 n=318, T2 n=319, T3 n=318.

**Supplementary Table 3. Interaction between IL-10 and IL-6 with mortality**

		First Post-operative			
		IL-6			
		Low		High	
		Mortality rate*	Adjusted HR (95% CI)	Mortality rate*	Adjusted HR (95% CI)
IL-10	Low	37.29	1.00 (referent)	70.56	1.52 (0.90, 2.57)
	High	39.30	1.10 (0.82, 1.47)	57.45	1.18 (0.48, 2.92)

**P for interaction = 0.25**

		Peak			
		IL-6			
		Low		High	
		Mortality rate*	Adjusted HR (95% CI)	Mortality rate*	Adjusted HR (95% CI)
IL-10	Low	43.59	1.00 (referent)	60.26	1.13 (0.68, 1.89)
	High	39.35	0.92 (0.62, 1.36)	59.55	1.03 (0.56, 1.88)

**P for interaction=0.87**

\*Mortality rate per 1000 patient years adjusted for site.

Adjusted for age (per year), sex, white race, CPB time > 120 minutes, non-elective surgery, pre-op eGFR, diabetes, hypertension, site, congestive heart failure, myocardial infarction, pre-op UACR, delta serum creatinine, and type of surgery.

Low biomarkers measurements are ≤median value and High biomarker measurements are < median value.

**Supplementary Table 4. First postoperative biomarkers by high and low NGAL**

		High NGAL (defined as > median)				Low NGAL (defined as <= median)				P-value*
Biomarker	Tertile	n	Mortality Rate per 1000 person years	HR (95% CI) unadjusted	HR (95% CI) adjusted	n	Mortality Rate per 1000 person years	HR (95% CI) unadjusted	HR (95% CI) adjusted	
<b>Plasma NGAL</b>										
<b>IL-6 Day 1 0-6 Hours</b>	<b>T1</b>	110	52.74	1.00 (referent)		208	33.2	1.00 (referent)		
	<b>T2</b>	154	51.58	0.98 (0.65, 1.46)	0.89 (0.58, 1.36)	165	36.4	1.04 (0.77, 1.41)	1.05 (0.61, 1.80)	0.61
	<b>T3</b>	211	74.88	1.42 (1.04, 1.95)	1.28 (0.98, 1.67)	107	74.1	2.24 (0.60, 8.40)	1.68 (0.44, 6.44)	0.46
<b>IL-10 Day 1 0-6 Hours</b>	<b>T1</b>	119	63.28	1.00 (referent)		199	31.3	1.00 (referent)		
	<b>T2</b>	164	67.56	1.08 (0.69, 1.68)	0.89 (0.65, 1.23)	155	42.9	1.33 (0.73, 2.44)	1.03 (0.56, 1.89)	0.98
	<b>T3</b>	192	27.03	0.43 (0.31, 0.62)	0.39 (0.27, 0.57)	126	54.1	1.71 (1.15, 2.53)	1.35 (0.90, 2.04)	0.01
<b>Urine NGAL</b>										
<b>IL-6 Day 1 0-6 Hours</b>	<b>T1</b>	108	47.4	1.00 (referent)		210	36.5	1.00 (referent)		
	<b>T2</b>	160	39.27	0.83 (0.74, 0.94)	0.71 (0.56, 0.90)	159	49.4	1.37 (1.01, 1.87)	1.37 (1.04, 1.79)	0.01
	<b>T3</b>	207	71.98	1.55 (0.86, 2.80)	1.14 (0.72, 1.81)	111	74.1	2.03 (0.87, 4.71)	1.82 (0.72, 4.62)	0.36
<b>IL-10 Day 1 0-6 Hours</b>	<b>T1</b>	122	59.84	1.00 (referent)		196	36.5	1.00 (referent)		
	<b>T2</b>	167	52.71	0.91 (0.58, 1.42)	0.92 (0.55, 1.51)	152	59.9	1.63 (0.98, 2.72)	1.24 (0.71, 2.17)	0.44
	<b>T3</b>	186	31.45	0.53 (0.44, 0.65)	0.51 (0.36, 0.73)	132	48.6	1.34 (1.01, 1.76)	1.07 (0.88, 1.30)	0.01

Adjusted for age, sex, white race, CPB time > 120 minutes, non-elective surgery, pre-op eGFR, diabetes, hypertension, center, congestive heart failure, myocardial infarction, pre-op urine albumin to creatinine ratio, and type of surgery. Mortality rates per 1000 person years were site adjusted. \* P value for interaction between tertiles of biomarker and NGAL (high/low). OR=odds ratio, CI=confidence interval, HR=hazards ratio.