Supplemental Digital Content 12A: Sensitivity Analysis: Multivariable Analysis of Preoperative Characteristics and Postoperative Acute Kidney Injury – Missing Data Handled via Multiple Imputation

Medical Factors	Risk Factor	β Coefficient	Multivariable model p-value	95% Confidence Interval †
Mail Gender	Medical Factors		p-varue	
MM log/mm² 0.017 <.0.001 0.01 - 0.02 Male Gender 0.027 <.0.001 0.023 - 0.303 Patient Medical History		0.0000007	0.29	-0.0000006 - 0.000002
Male Cender	BMI (kg/m²) ^{§§}			
Congest/se Reant Failure	Male Gender	0.027	< 0.001	0.023 - 0.303
Congest/se Reant Failure	Patient Medical History *			
Valvalar Disease		0.018	< 0.001	0.010 - 0.026
Pulmonary Circulation Disorders	Cardiac Arrhythmias	0.010	< 0.001	0.005 - 0.016
Peripheral Vascular Disorders	Valvular Disease	0.007	0.12	-0.002 - 0.016
Hypertension, Uncomplicated	Pulmonary Circulation Disorders	0.016	0.001	0.007 - 0.026
Hypertension, Complicated	Peripheral Vascular Disorders	0.014	< 0.001	0.008 - 0.020
Paralysis/Other Neurological Disorders 0.009 0.01 0.002 - 0.016	Hypertension, Uncomplicated	-0.0008	0.73	-0.005 - 0.004
Chronic Pulmonary Disease	Hypertension, Complicated	0.077	< 0.001	0.068 - 0.086
Diabetes, Complicated 0.008		0.009	0.01	0.002 - 0.016
Diabetes, Complicated	Chronic Pulmonary Disease	0.0008	0.77	-0.005 - 0.006
Hypothyroidism	Diabetes, Uncomplicated	0.008	0.01	0.002 - 0.013
Liver Disease	Diabetes, Complicated	0.065	< 0.001	0.050 - 0.081
Peptic Ulcer Disease Excluding Bleeding	Hypothyroidism	-0.010	0.01	-0.0160.003
AIDS/HIV 0.036	Liver Disease	0.055	< 0.001	0.047 - 0.062
Rheumatoid Arthritis / Collagen Vascular Diseases	Peptic Ulcer Disease Excluding Bleeding	0.002	0.75	-0.013 - 0.018
Coagulopathy	AIDS/HIV	0.036	0.09	-0.006 - 0.078
Lymphoma	Rheumatoid Arthritis / Collagen Vascular Diseases	-0.007	0.21	-0.017 - 0.004
Metastatic Cancer	Coagulopathy	0.062	< 0.001	0.054 - 0.070
Solid Tumor	Lymphoma	0.005	0.52	-0.010 - 0.020
Weight Loss	Metastatic Cancer	-0.0003	0.94	-0.007 - 0.007
Alcohol Abuse	Solid Tumor	-0.0006	0.84	-0.006 - 0.005
Drug Abuse	Weight Loss	0.029	< 0.001	0.022 - 0.035
Psychoses -0.013	Alcohol Abuse	-0.013	0.02	-0.0230.002
Preoperative Chronic Medications ACEI/ARB	Drug Abuse	-0.003	0.68	-0.015 - 0.010
ACEI/ARB	Psychoses	-0.013	0.14	-0.030 - 0.004
Beta Blocker	Preoperative Chronic Medications			
Preoperative hemoglobin (g/dL) \$ -0.0004	ACEI/ARB	-0.004	0.16	-0.010 - 0.002
Preoperative eGFR (mL/min/1.73 m²)** \$ -0.000003	Beta Blocker	-0.009	0.002	-0.0140.003
Preinduction Baseline Mean Arterial Pressure (mmHg) [§] Surgical Factors Surgical Body Region Elevated Risk 0.047 <0.001 0.042 − 0.052 Emergent Surgery 0.030 <0.001 0.024 − 0.036 Anesthetic Factors ASA Class ASA Class ASA Class 1 0 (reference) ASA Class 2 0.0003 0.96 −0.010 − 0.011 ASA Class 3 0.025 <0.001 0.015 − 0.036 ASA Class 4 0.080 <0.001 0.068 − 0.092 ASA Class 5 0.214 <0.001 0.068 − 0.092 Expected Anesthesia Duration ^{§§§} 0.091 <0.001 0.083 − 0.100 General Anesthesia 0.024 <0.001 0.018 − 0.030 Institution (Random Effect), ICC (95% CI) Original Model performance (c-statistic) 0.0000003 0.36 0.0001 0.036 0.0001 0.016 0.001 0.018 − 0.030 0.012 (0.006 − 0.022)	Preoperative hemoglobin (g/dL) §	-0.0004	< 0.001	-0.00050.0004
Commit Sturgical Factors	Preoperative eGFR (mL/min/1.73 m ²)** §	-0.000003	< 0.001	-0.0000030.000002
Surgical Factors	Preinduction Baseline Mean Arterial Pressure (mmHg) §	0.0000003	0.36	-0.0000003 - 0.000001
Elevated Risk	Surgical Factors			
Commonweight Comm	Surgical Body Region			
Ansthetic Factors ASA Class ASA Class 1 ASA Class 2 ASA Class 3 ASA Class 3 ASA Class 4 ASA Class 5 ASA Class 5 ASA Class 5 ASA Class 6 ASA Class 6 ASA Class 7 ASA Class 8 ASA Class 8 ASA Class 9 A		0.047	< 0.001	0.042 - 0.052
ASA Class 1 ASA Class 2 ASA Class 3 ASA Class 3 ASA Class 4 ASA Class 5 ASA Class 5 Capered Anesthesia Duration SSS O.024 Constitutional Factors Non-university Hospital (Fixed Effect) Original Model performance (c-statistic) Occupange 1 O.0000 0.006 Occupange 1 O.004 Occupange 2 O.001 Occupange 2 O.001 Occupange 3 O.004 Occupange 3 O.004 Occupange 3 O.004 Occupange 3 O.004 Occupange 4 O.001 Occupange 4 O.001 Occupange 5 O.004 Occupange 6 O.004 Occupange 6 O.004 Occupange 6 O.004 Occupange 7 O.00	Emergent Surgery	0.030	< 0.001	0.024 - 0.036
ASA Class 1 0 (reference) ASA Class 2 0.0003 0.96 -0.010 -0.011 ASA Class 3 0.025 <0.001 0.015 -0.036 ASA Class 4 0.080 <0.001 0.068 -0.092 ASA Class 5 0.214 <0.001 0.146 -0.248 Expected Anesthesia Duration \$\frac{88}{2}\$ 0.091 <0.001 0.083 -0.100 General Anesthesia 0.024 <0.001 0.018 -0.030 Institutional Factors Non-university Hospital (Fixed Effect) 0.004 0.64 -0.014 -0.023 Institution (Random Effect), ICC (95% CI) 0.075 (0.74-0.76)	Anesthetic Factors			
ASA Class 2 0.0003 0.96 -0.010 -0.011 ASA Class 3 0.025 <0.001 0.015 -0.036 ASA Class 4 0.080 <0.001 0.068 -0.092 ASA Class 5 0.214 <0.001 0.146 -0.248 Expected Anesthesia Duration \$\frac{8}{2}\$\$\$ 0.091 <0.001 0.083 -0.100 General Anesthesia 0.024 <0.001 0.018 -0.030 Institutional Factors Non-university Hospital (Fixed Effect) 0.004 0.64 -0.014 -0.023 Institution (Random Effect), ICC (95% CI) 0.012 (0.006-0.022)	ASA Class			
ASA Class 3 0.025 < 0.001 0.015 – 0.036 ASA Class 4 0.080 < 0.001 0.068 – 0.092 ASA Class 5 0.214 < 0.001 0.146 – 0.248 Expected Anesthesia Duration \$\$\$ 0.091 < 0.001 0.083 – 0.100 General Anesthesia 0.024 < 0.001 0.018 – 0.030 Institutional Factors Non-university Hospital (Fixed Effect) 0.004 0.64 -0.014 – 0.023 Institution (Random Effect), ICC (95% CI) 0.012 (0.006-0.022) Original Model performance (c-statistic) 0.75 (0.74-0.76)	ASA Class 1			
ASA Class 4 0.080 <0.001 0.068 - 0.092 ASA Class 5 0.214 <0.001 0.146 - 0.248 Expected Anesthesia Duration SSS 0.091 <0.001 0.083 - 0.100 General Anesthesia 0.024 <0.001 0.018 - 0.030 Institutional Factors Non-university Hospital (Fixed Effect) 0.004 0.64 -0.014 - 0.023 Institution (Random Effect), ICC (95% CI) 0.012 (0.006-0.022) Original Model performance (c-statistic) 0.75 (0.74-0.76)	ASA Class 2	0.0003	0.96	-0.010 - 0.011
ASA Class 5 0.214 <0.001 0.146 - 0.248 Expected Anesthesia Duration \$\frac{5}{2} 0.091	ASA Class 3	0.025	<0.001	$0.\overline{015} - 0.036$
Comparison Com	ASA Class 4	0.080	< 0.001	0.068 - 0.092
O.024 C.001 O.018 - 0.030		0.214	< 0.001	
Institutional Factors 0.004 0.64 -0.014 - 0.023 Institution (Random Effect), ICC (95% CI) 0.012 (0.006-0.022)	Expected Anesthesia Duration ^{§§§}	0.091	< 0.001	0.083 - 0.100
Non-university Hospital (Fixed Effect) 0.004 0.64 -0.014 - 0.023 Institution (Random Effect), ICC (95% CI) 0.012 (0.006-0.022) Original Model performance (c-statistic) 0.75 (0.74-0.76)	General Anesthesia	0.024	<0.001	0.018 - 0.030
Institution (Random Effect), ICC (95% CI) Original Model performance (c-statistic) 0.012 (0.006-0.022) 0.75 (0.74-0.76)	Institutional Factors			
Original Model performance (c-statistic) 0.75 (0.74-0.76)	Non-university Hospital (Fixed Effect)	0.004	0.64	-0.014 - 0.023
	Institution (Random Effect), ICC (95% CI)			0.012 (0.006-0.022)
New Model performance (c-statistic) 0.75 (0.74-0.75)				
·	New Model performance (c-statistic)			0.75 (0.74-0.75)

 $[\]dagger$ Mixed effects model with anonymized institution ID as random effect; all other covariates fixed effects. *As determined by Elixhauser Comorbidity Enhanced ICD-9-CM/ICD-10 CM Algorithm

§§ Square root transformation

§§§ Logarithmic transformation

 $ACEI = angiotensin\text{-}converting\ enzyme\ inhibitor;\ AIDS = autoimmune\ deficiency\ syndrome;\ AKI = acute\ kidney\ injury;\ ARB = angiotensin\ II\ receptor\ blocker;\ ASA = American\ Society\ of\ Anesthesiologists;\ CKD-EPI = Chronic\ Kidney\ Disease\ Epidemiology\ Collaboration;\ CPT = Current\ Procedural\ Terminology;\ eGFR = estimated\ glomerular\ filtration\ rate;\ HIV = human\ immunodeficiency\ virus;\ ICC = intraclass\ correlation\ coefficient;\ KDIGO = Kidney\ Disease:\ Improving\ Global\ Outcomes;\ WHO = World\ Health\ Organization$

^{**} As determined by CKD-EPI formula, indexed by body surface area. Race assumed non-black for patients with race data unavailable.

[§] Squared transformation

Supplemental Digital Content 12B: Sensitivity Analysis: Risk of Acute Kidney Injury Associated with Intraoperative Hypotension by Preoperative Risk Quartile – Missing Data Handled via Multiple Imputation

Absolute Hypotension - Derivation Cohort					
Intraoperative	Quartile 1*	Quartile 2*	Quartile 3*	Quartile 4*	
Hypotension [†] -	Low Preoperative	Medium	High Preoperative	Highest	
Absolute MAP	Risk	Preoperative Risk	Risk	Preoperative Risk	
Values	(N = 22,806)	(N = 22,802)	(N = 22,791)	(N = 22,793)	
No Absolute	(reference)	(reference)	(reference)	(reference)	
Hypotension					
	n= 13,614	n= 13,510	n= 12,753	n= 12,319	
MAP 60-64	1.04 (0.83-1.30)	1.01 (0.86-1.20)	1.23 (1.09-1.38)	1.15 (1.06-1.16)	
mmHg			Increased AKI	Increased AKI	
	n= 4,698	n= 4,677	n= 4,860	n= 4,864	
MAP 55-59	0.89 (0.67-1.19)	1.30 (1.08-1.57)	1.17 (1.01-1.34)	1.45 (1.32-1.59)	
mmHg		Increased AKI	Increased AKI	Increased AKI	
	n= 2,927	n= 2,980	n= 3,173	n= 3,308	
MAP 50-54	1.28 (0.87-1.90)	1.53 (1.16-2.01)	1.33 (1.09-1.63)	1.61 (1.41-1.83)	
mmHg		Increased AKI	Increased AKI	Increased AKI	
	n= 1,049	n=1,036	n= 1,215	n= 1,349	
MAP <50 mmHg	1.65 (1.02-2.69)	1.63 (1.16-2.29)	1.62 (1.29-2.03)	2.02 (1.74-2.33)	
	Increased AKI	Increased AKI	Increased AKI	Increased AKI	
	n= 518	n= 599	n= 790	n= 953	

Adjusted Odds Ratio – Color Scale [†]				
1.00				
1.20				
1.40				
1.60				
1.80				
2.00				
2.20				
2.40				
2.60				
2.80				
3.00				

Relative Hypotension - Derivation Cohort						
Intraoperative Hypotension† – Relative MAP	Quartile 1* Low Preoperative Risk	Quartile 2* Medium Preoperative Risk	Quartile 3* High Preoperative Risk	Quartile 4* Highest Preoperative Risk		
Values No Relative	(N = 22,806) (reference)	(N = 22,802) (reference)	(N = 22,791) (reference)	(N = 22,793) (reference)		
Hypotension	(Telefelice)	(Telefelice)	(Telefelice)	(Telefelice)		
	n= 7,548	n= 7,294	n= 7,263	n= 8,652		
MAP 20-30%	0.92 (0.73-1.16)	0.92 (0.77-1.09)	0.89 (0.78-1.01)	0.85 (0.78-0.93)		
Below Baseline				Decreased AKI		
	n = 5,846	n = 5,811	n = 5,678	n = 5,472		
MAP 30-40%	1.00 (0.79-1.26)	0.98 (0.82-1.16)	1.01 (0.89-1.15)	0.88 (0.81-0.97)		
Below Baseline				Decreased AKI		
	n = 5,673	n = 5,671	n = 5,636	n = 4,899		
MAP > 40%	1.38 (1.08-1.76)	1.33 (1.11-1.59)	1.25 (1.09-1.42)	1.05 (0.95-1.15)		
Below Baseline	Increased AKI	Increased AKI	Increased AKI			
	n = 3,739	n = 4,026	n = 4,214	n = 3,770		

Values presented as adjusted odds ratio and 95% confidence interval.

Regression within each quartile included all four blood pressure ranges and operative duration (log transformed).

AKI = acute kidney injury; MAP = mean arterial pressure

^{*} Patients were stratified by risk of postoperative AKI using the full multivariable model.

[†] Color scale used only for adjusted odds ratios demonstrating statistically significant associations.