Figure S1. Overall processes of clinical model feature selection. **Panel A** summarizes the whole process. **Panel B** represents details of intersection of important features identified by different machine learning algorithms.
LR =logistic regression; RF =random forest, SVM =Support Vector Machine; XGBoost =extreme gradient boosting

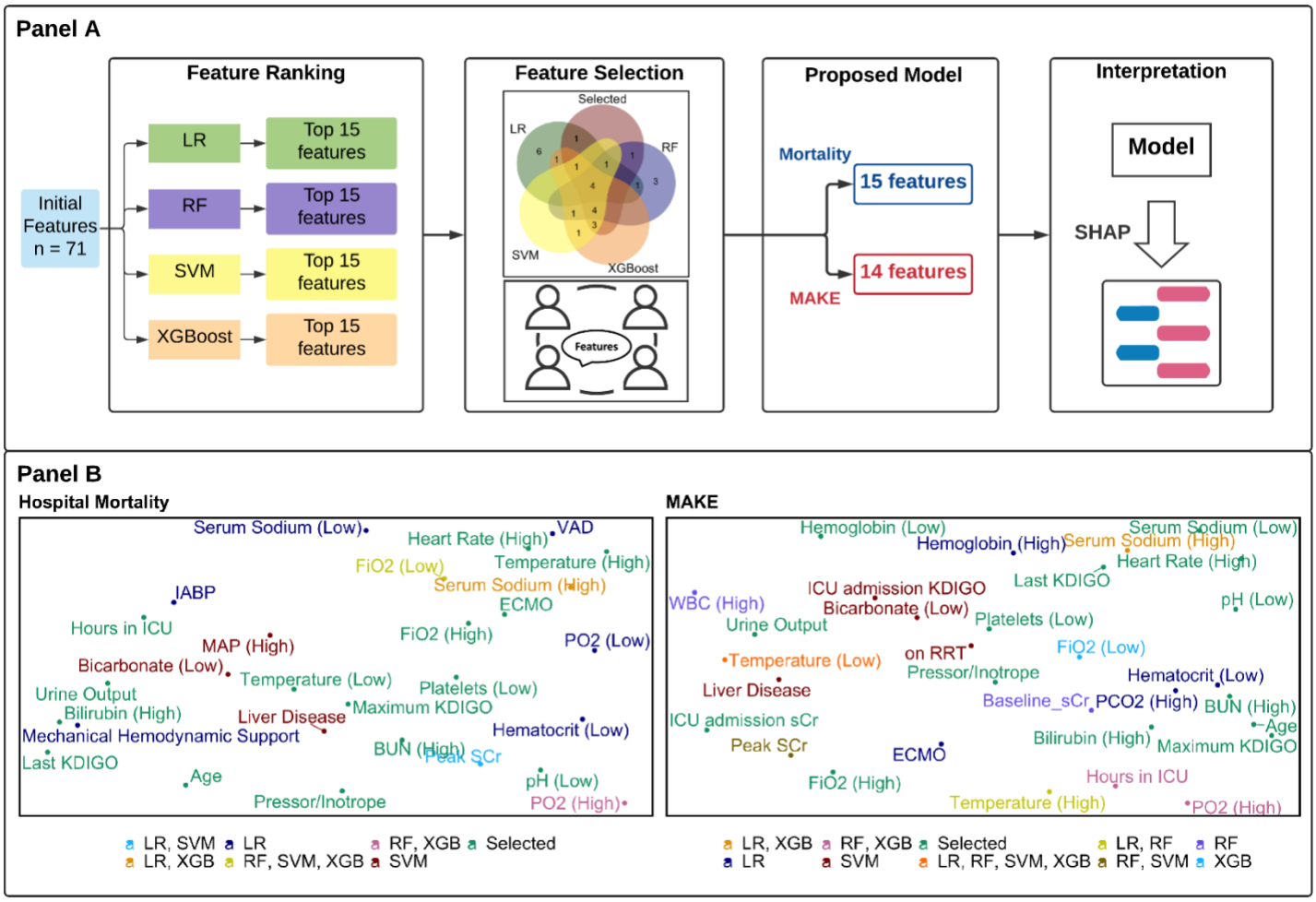

Figure S2. Case studies of SHAP framework with real feature data according to AKI severity and mortality status. The base value is the mean predicted risk probability. f(x) is the predicted probability of the outcome. Red color (moves probability to the right/higher risk) and blue color (moves probability to the left/lower risk) represent how each feature impact the predicted probability of the outcome.

Figure S3. Case studies of SHAP framework with real feature data according to AKI severity and MAKE outcome. The base value is the mean predicted risk probability. f(x) is the predicted probability of the outcome. Red color (moves probability to the right/higher risk) and blue color (moves probability to the left/lower risk) represent how each feature impact the predicted probability of the outcome.

Table S1. Definitions and data management procedures of all validated clinical features considered for the development of the clinical models

Feature	Definition	Units	UKY constraints	UTSW constraints	UKY Missing Data	UTSW Missing Data
ICU admission sCr	First sCr after ICU admission	mg/dL	-	-	0 (0.00%)	0 (0.00%)
Age	Age at admission	Years	-	-	0 (0.00%)	0 (0.00%)
Anemia	If Male: - Lowest Hematocrit < 39% or - Lowest Hemoglobin < 18 g/dL If Female: - Lowest Hematocrit < 36% or - Lowest Hemoglobin < 12 g/dL	boolean	-	-	24 (0.33%)	27 (1.21%)
Baseline sCr	a. The outpatient sCr closest to 7 days before hospital admission up to 1 year. b. If no outpatient sCr (a.), then use the inpatient sCr value closet to 7 days before hospital admission up to 1 year.	mg/dL	-	-	5348 (72.72%)	1124 (50.34%)
Bicarbonate (Low)	Lowest Value ICU D0-D3	mmol/L	Remove: <5, >50	Remove: <5, >50	32 (0.44%)	7 (0.31%)
Bicarbonate (High)	Highest Value ICU D0-D3	mmol/L	-	Remove: <5, >50	3 (0.04%)	7 (0.31%)
Bilirubin (High)	Highest Value ICU D0-D3	mg/dL	-	-	2085 (28.35%)	762 (34.12%)
BMI	Weight / (Height)^2 at Admission	kg/m^2	-	-	3428 (46.61%)	1460 (65.38%)
BUN	Highest Value ICU D0-D3	mg/dL	Remove: <5	Remove: <5	3 (0.04%)	9 (0.40%)
FiO2 (Low)	Lowest Value ICU D0-D3	%	Remove: <21, >100	Remove: <21, >100	2096 (28.5%)	529 (23.69%)
FiO2 (High)	Highest Value ICU D0-D3	%	Remove: <21, >100	Remove: <21, >100	1810 (24.61%)	525 (23.51%)
Fluid Overload	(Total Fluid Input - Total Fluid Output) *100/ Weight ICU D0-D3	(L – L) /(kg) %	-	-	2863 (38.93%)	523 (23.42%)

Gender	Male/Female at admission	1 = Male 0 = Female	-	-	0 (0.00%)	0 (0.00%)
Heart Rate (Low)	Lowest Value ICU D0-D3	bpm	Remove: <25	Remove: <25	190 (2.58%)	17 (0.76%)
Heart Rate (High)	Highest Value ICU D0-D3	bpm	Remove: <25	Remove: <25	6 (0.08%)	17 (0.76%)
Hematocrit (Low)	Lo0west Value ICU D0-D3	%	-	-	23 (0.31%)	25 (1.12%)
Hematocrit (High)	Highest Value ICU D0-D3	%	-	-	23 (0.31%)	25 (1.12%)
Hemoglobin (Low)	Lowest Value ICU D0-D3	g/dL	-	-	23 (0.31%)	20 (0.90%)
Hemoglobin (High)	Highest Value ICU D0-D3	g/dL	-	-	23 (0.31%)	20 (0.90%)
ECMO	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
IABP	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
Mechanical Ventilation	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
VAD	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
MAP (Low)	Lowest Value ICU D0-D3	mmHg	Remove: <0, Bottom 5th Percentile	Remove: Bottom 5th Percentile, Top 5th Percentile	434 (5.90%)	108 (4.84%)
MAP (High)	Highest Value ICU D0-D3	mmHg	Remove: <0, Top 5th Percentile	Remove: Bottom 5th Percentile, Top 5th Percentile	379 (5.15%)	106 (4.75%)
Admission KDIGO Score	KDIGO score at ICU admission	KDIGO	-	-	0 (0.00%)	0 (0.00%)
Nephrotoxin: ACEI, ARB, aminoglycoside, NSAIDs	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
Pressor/inotrope: dopamine, dobutamine, milrinone, epinephrine, norepinephrine, phenylephrine, vasopressin	Use in ICU D0-D3	boolean	-	-	0 (0.00%)	81 (3.63%)

pCO2 (Low)	Lowest Value ICU D0-D3	mmHg	Remove: <0, >125	Remove: >125	1401 (19.05%)	1738 (77.83%)
pCO2 (High)	Highest Value ICU D0-D3	mmHg	Remove: <0, >125	Remove: >125	1409 (19.16%)	1738 (77.83%)
Peak sCr	Highest Value ICU D0-D3	mg/dL	-	-	0 (0.00%)	0 (0.00%)
pH (Low)	Lowest Value ICU D0-D3	-	-	-	1400 (19.04%)	1737 (77.79%)
pH (High)	Highest Value ICU D0-D3	-	-	-	1400 (19.04%)	1737 (77.79%)
Platelets	Lowest Value ICU D0-D3	k/uL	-	-	34 (0.46%)	32 (1.43%)
pO2 (Low)	Lowest Value ICU D0-D3	mmHg	-	-	1400 (19.04%)	1788 (80.07%)
pO2 (High)	Highest Value ICU D0-D3	mmHg	-	-	1400 (19.04%)	1788 (80.07%)
Potassium (Low)	Lowest Value ICU D0-D3	mmol/L	Remove: Top 5th Percentile	-	418 (5.68%)	6 (0.27%)
Potassium (High)	Highest Value ICU D0-D3	mmol/L	Remove: Top 5th Percentile	-	376 (5.11%)	6 (0.27%)
Race	Race at admission	0=White, 1=Black, 2=Other	-	-	0 (0.00%)	0 (0.00%)
Respiration (Low)	Lowest Value ICU D0-D3	rpm	Remove: <5, >70	Remove: <5, >70	1098 (14.93%)	25 (1.12%)
Respiration (High)	Highest Value ICU D0-D3	rpm	Remove: <5, >70	Remove: <5, >70	172 (2.34%)	20 (0.9%)
Septic	Sepsis diagnosis before/at admission	boolean	-	-	0 (0.00%)	0 (0.00%)
Serum Sodium (Low)	Lowest Value ICU D0-D3	mmol/L	-	-	3 (0.04%)	6 (0.27%)
Serum Sodium (High)	Highest Value ICU D0-D3	mmol/L	-	-	3 (0.04%)	6 (0.27%)
Temperature (Low)	Lowest Value ICU D0-D3	°C	Remove: <30, >45	Remove: <30, >45	79 (1.07%)	17 (0.76%)
Temperature (High)	Highest Value ICU D0-D3	°C	Remove: <30, >45	Remove: <30, >45	19 (0.26%)	17 (0.76%)
Urine Output	Total urine output ICU D0-D3 / measurement time	ml/hr	Remove: Top 5th Percentile	Remove: Top 2.5th Percentile	858 (11.67%)	105 (4.7%)

Urine Flow	Total urine output ICU D0-D3 / weight / measurement time	ml/kg/hr	-	-	3226 (43.87%)	253 (11.33%)
WBC (Low)	Lowest Value ICU D0-D3	k/uL	Remove: Top 5th Percentile	Remove: Bottom 2.5th Percentile, Top 5th Percentile	408 (5.55%)	145 (6.49%)
WBC (High)	Highest Value ICU D0-D3	k/uL	Remove: Top 5th Percentile	Remove: Bottom 2.5th Percentile, Top 5th Percentile	409 (5.56%)	160 (7.17%)
Height	At admission/Average	meters	Remove: Bottom 5th Percentile, Top 5th Percentile	Remove: Bottom 5th Percentile, Top 5th Percentile	3384 (46.02%)	1453 (65.07%)
Weight	At admission	kg	Remove: <30, >200	Remove: <30, >200	2862 (38.92%)	173 (7.75%)
Hours in ICU	Hours in ICU D0-D3	hours	-	-	0 (0.00%)	0 (0.00%)
Mechanical Hemodynamic Support	Use of VAD, IABP, or ECMO in ICU D0-D3	boolean	-	-	0 (0.00%)	0 (0.00%)
Unplanned Admission	Patient did not have planned surgery/treatment	boolean	-	-	0 (0.00%)	0 (0.00%)
Maximum KDIGO Score	Maximum KDIGO score in ICU D0-D3	KDIGO	-	-	0 (0.00%)	0 (0.00%)
RRT Administration	No RRT - HD Only - CRRT (w/ or w/out HD) in ICU D0-D3	0=None, 1= HD Only, 2= CRRT (w/ or w/out HD)	-	-	0 (0.00%)	0 (0.00%)
Last KDIGO	Last KDIGO score in ICU D0-D3	KDIGO	-	-	0 (0.00%)	0 (0.00%)
Congestive Heart Failure	**ICD9**: 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4 - 425.9, 428.x **ICD10**: I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5 - I42.9, I43.x, I50.x, P29.0	boolean	-	-	0 (0.00%)	0 (0.00%)
Peripheral Vascular Disease	**ICD9**: 093.0, 437.3, 440.x, 441.x, 443.1 - 443.9, 447.1, 557.1, 557.9, V43.4	boolean	-	-	0 (0.00%)	0 (0.00%)

	ICD10: I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9					
Hypertension (Uncomplicated)	**ICD9**: 401.x **ICD10**: I10.	boolean	-	-	0 (0.00%)	0 (0.00%)
Hypertension (Complicated)	**ICD9**: 402.x - 405.x **ICD10**: I11.x - I13.x, I15.x	boolean	-	-	0 (0.00%)	0 (0.00%)
Chronic Pulmonary Disease	**ICD9**: 416.8, 416.9, 490.x - 505.x, 506.4, 508.1, 508.8 **ICD10**: I27.8, I27.9, J40.x - J47.x, J60.x - J67.x, J68.4, J70.1, J70.3	boolean	-	-	0 (0.00%)	0 (0.00%)
Diabetes (Without Chronic Complication)	**ICD9**: 250.0 - 250.3 **ICD10**: E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9, E13.0, E13.1, E13.9, E14.0, E14.1, E14.9	boolean	-	-	0 (0.00%)	0 (0.00%)
Diabetes (With Chronic Complication)	**ICD9**: 250.4 - 250.9 **ICD10**: E10.2 - E10.8, E11.2 - E11.8, E12.2 - E12.8, E13.2 - E13.8, E14.2 - E14.8	boolean	-	-	0 (0.00%)	0 (0.00%)
Liver Disease	**ICD9**: 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 456.0 - 456.2, 570.x, 571.x, 572.2 - 572.8, 573.3, 573.4, 573.8, 573.9, V42.7 **ICD10**: B18.x, I85.x, I86.4, I98.2, K70.x, K71.1, K71.3 - K71.5, K71.7, K72.x - K74.x, K76.0, K76.2 - K76.9, Z94.4	boolean	-	-	0 (0.00%)	0 (0.00%)
Peptic Ulcer Disease	**ICD9**: 531.7, 531.9, 532.7, 532.9, 533.7, 533.9, 534.7, 534.9 **ICD10**: K25.7, K25.9, K26.7, K26.9, K27.7, K27.9, K28.7, K28.9	boolean	-	-	0 (0.00%)	0 (0.00%)
Aids/HIV	**ICD9**: 042.x - 044.x **ICD10**: B20.x - B22.x, B24.x	boolean	-	-	0 (0.00%)	0 (0.00%)
Metastatic Solid Tumor	**ICD9**: 196.x - 199.x **ICD10**: C77.x - C80.x	boolean	-	-	0 (0.00%)	0 (0.00%)

Rheumatic Disease	**ICD9**: 446.x, 701.0, 710.0 - 710.4, 710.8, 710.9, 711.2, 714.x, 719.3, 720.x, 725.x, 728.5, 728.89, 729.30 **ICD10**: L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0 - M31.3, M32.x - M35.x, M45.x, M46.1, M46.8, M46.9	boolean	-	-	0 (0.00%)	0 (0.00%)
Depression	**ICD9**: 296.2, 296.3, 296.5, 300.4, 309.x, 311 **ICD10**: F20.4, F31.3 - F31.5, F32.x, F33.x, F34.1, F41.2, F43.2	boolean	-	-	0 (0.00%)	0 (0.00%)

Abbreviations: ACEI (angiotensin-converting enzyme inhibitors), ARB (angiotensin II receptor blockers), BMI (body mass index), bpm (beats per minute), BUN (blood urea nitrogen), CRRT (continuous renal replacement therapy), D0-D3 (day 0 through day 3 of ICU admission), ECMO (extracorporeal membrane oxygenation), HD (hemodialysis), IABP (intra-aortic balloon pump), ICD (international statistical classification of diseases and related health problems), ICU (intensive care unit), KDIGO (kidney disease improving global outcomes), MAP (mean arterial pressure), NSAIDs (nonsteroidal anti-inflammatory drugs), RRT (renal replacement therapy), sCr (serum creatinine), VAD (ventricular assist device), WBC (white blood cells).

Table S2. Top 15 clinical features ranked by each machine learning algorithm for the prediction of A) hospital mortality and B) MAKE. Features are ordered by the absolute value of beta-coefficient or importance score. Features that are bolded are the final 15 ones selected after interpretation and explainability procedures.

LR		Random Forest		SVM		XGBoost	
Feature	**Beta-Coef**	**Feature**	**Score**	**Feature**	**Score**	**Feature**	**Score**
A. Hospital mortality							
Peak sCr	-4.57	**Urine Output**	100.00	**Last KDIGO**	100.00	**Pressor/inotrope**	100.00
Serum Sodium (High)	4.19	**Pressor/inotrope**	71.71	**Urine Output**	92.14	**Urine Output**	84.12
ECMO	3.70	**FiO2 (High)**	62.98	**Pressor/inotrope**	82.07	**FiO2 (High)**	56.39
IABP	3.05	**Hours in ICU**	60.99	**Maximum KDIGO**	72.91	**Age**	47.81
VAD	-2.89	**Temperature (Low)**	59.25	**Platelets (Low)**	71.76	**Last KDIGO**	44.07
Platelets (Low)	-2.84	**Platelets (Low)**	58.33	**FiO2 (High)**	71.47	**Hours in ICU**	43.63
Bilirubin (High)	2.81	**Age**	55.91	**Temperature (Low)**	70.42	FiO2 (Low)	42.24
Serum Sodium (Low)	-2.63	**BUN (High)**	52.59	**BUN (High)**	66.23	**Temperature (Low)**	42.09
Temperature (High)	2.44	**Heart Rate (High)**	47.48	**Bilirubin (High)**	65.69	**Platelets (Low)**	39.54
Mechanical Hemodynamic Support	-2.38	**Last KDIGO**	45.46	Liver Disease	64.19	**BUN (High)**	37.54
Hematocrit (Low)	2.33	**pH (Low)**	44.22	**Heart Rate (High)**	62.23	**Heart Rate (High)**	32.05
PO2 (Low)	2.33	**Temperature (High)**	44.18	Bicarbonate (Low)	61.60	**Temperature (High)**	30.77
Temperature (Low)	-2.33	FiO2 (Low)	44.05	FiO2 (Low)	61.56	PO2 (High)	30.05
Heart Rate (High)	2.30	PO2 (High)	44.03	Peak sCr	56.63	**pH (Low)**	24.79
BUN (High)	2.29	**Bilirubin (High)**	40.20	MAP (High)	56.57	Serum Sodium (High)	24.05
B. MAKE							
Serum Sodium (High)	3.30	**Last KDIGO**	100.00	**Last KDIGO**	100.00	**Last KDIGO**	100.00
Hematocrit (Low)	2.98	**Urine Output**	75.20	**Maximum KDIGO**	79.58	**Urine Output**	38.19
Bilirubin (High)	2.81	**BUN (High)**	53.93	**Urine Output**	72.25	**Age**	24.50
Hemoglobin (Low)	-2.45	**Age**	50.46	**BUN (High)**	71.39	**BUN (High)**	17.76
Serum Sodium (Low)	-2.29	**Platelets (Low)**	43.15	Peak sCr	66.73	**FiO2 (High)**	17.47
Last KDIGO	2.28	Hours in ICU	42.24	**Pressor/inotrope**	51.91	**Platelets (Low)**	14.63
ICU admission sCr	-2.15	Temperature (Low)	38.60	Temperature (Low)	48.93	Hours in ICU	14.05
Hemoglobin (High)	-2.13	Peak sCr	34.53	On RRT	48.75	**Pressor/inotrope**	13.92
Age	1.89	**Heart Rate (High)**	33.03	**Hemoglobin (Low)**	45.61	Temperature (Low)	13.54
Temperature (Low)	-1.87	Temperature (High)	31.88	ICU admission KDIGO	45.32	PO2 (High)	10.03
BUN (High)	1.81	**FiO2 (High)**	31.77	**Platelets (Low)**	44.08	**Heart Rate (High)**	9.60
Heart Rate (High)	1.75	WBC_D1_HIGH	31.17	Bicarbonate (Low)	43.80	FiO2 (Low)	9.13
ECMO	1.72	PO2 (High)	30.68	Liver Disease	42.70	**pH (Low)**	9.04
PCO2 (High)	1.49	Baseline sCr	30.66	**ICU admission sCr**	42.49	**Bilirubin (High)**	8.93
Temperature (High)	1.44	**ICU admission sCr**	30.08	**FiO2 (High)**	42.13	Serum Sodium (High)	8.57

Abbreviations: BUN (blood urea nitrogen), ECMO (extracorporeal membrane oxygenation), IABP (intra-aortic balloon pump), ICU (intensive care unit), KDIGO (Kidney Disease Improving Global Outcomes), LR (logistic regression), MAKE (major adverse kidney events), MAP (mean arterial pressure), RRT (renal replacement therapy), sCr (serum creatinine), SVM (support vector machine), VAD (ventricular assist device), WBC (white blood cells).

Table S3. Machine learning algorithms of feature selection for the clinical models of A) hospital mortality and B) MAKE supporting its applicability and reproducibility

	UKY (Derivation)				UTSW (Validation)			
	LR	**RF**	**SVM**	**XGBoost**	**LR**	**RF**	**SVM**	**XGBoost**
A. Hospital Mortality								
AUC	0.77(0.77-0.77)	0.79 (0.79-0.80)	0.77 (0.77-0.77)	0.78 (0.78-0.78)	0.77 (0.77-0.78)	0.74 (0.73-0.74)	0.78 (0.77-0.79)	0.70 (0.68-0.72)
Diff vs. ref. (SOFA)[#]	0.06	0.11	0.06	0.07	0.06	0.07	0.07	-0.01
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.370
Accuracy	0.72 (0.72-0.72)	0.71 (0.71-0.71)	0.72 (0.72-0.72)	0.71 (0.71-0.71)	0.64 (0.62-0.66)	0.65 (0.64-0.66)	0.64 (0.62-0.66)	0.62 (0.60-0.65)
Precision	0.41 (0.41-0.42)	0.41 (0.40-0.42)	0.41 (0.41-0.42)	0.41 (0.40-0.41)	0.19 (0.18-0.19)	0.18 (0.17-0.18)	0.19 (0.18-0.20)	0.16 (0.15-0.17)
Sensitivity	0.67 (0.66-0.68)	0.72 (0.72-0.73)	0.67 (0.66-0.67)	0.68 (0.68-0.69)	0.77 (0.74-0.79)	0.69 (0.67-0.71)	0.79 (0.76-0.81)	0.67 (0.64-0.69)
Specificity	0.73 (0.73-0.74)	0.71 (0.70-0.71)	0.74 (0.73-0.74)	0.72 (0.71-0.72)	0.63 (0.60-0.65)	0.64 (0.63-0.65)	0.62 (0.59-0.65)	0.62 (0.59-0.65)
F1	0.51 (0.51-0.52)	0.52 (0.52-0.53)	0.51 (0.51-0.52)	0.51 (0.50-0.51)	0.30 (0.29-0.31)	0.28 (0.27-0.29)	0.30 (0.29-0.31)	0.26 (0.25-0.28)
PPV	0.41 (0.41-0.42)	0.41 (0.40-0.42)	0.41 (0.41-0.42)	0.41 (0.40-0.41)	0.19 (0.18-0.19)	0.18 (0.17-0.18)	0.19 (0.18-0.20)	0.16 (0.15-0.17)
NPV	0.89 (0.89-0.89)	0.90 (0.90-0.90)	0.89 (0.89-0.89)	0.89 (0.89-0.89)	0.96 (0.96-0.96)	0.95 (0.95-0.95)	0.96 (0.96-0.97)	0.94 (0.94-0.95)
B. MAKE								
AUC	0.77 (0.76-0.77)	0.78 (0.78-0.78)	0.77 (0.76-0.77)	0.77 (0.77-0.77)	0.73 (0.73-0.73)	0.73 (0.72-0.74)	0.74 (0.74-0.74)	0.72 (0.71-0.72)
Diff vs. ref. (max KDIGO)[#]	0.11	0.13	0.11	0.11	0.06	0.07	0.07	0.05
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Accuracy	0.71 (0.71-0.72)	0.72 (0.71-0.72)	0.71 (0.71-0.72)	0.71 (0.71-0.72)	0.71 (0.70-0.72)	0.67 (0.66-0.69)	0.72 (0.70-0.73)	0.65 (0.63-0.68)
Precision	0.55 (0.54-0.56)	0.55 (0.54-0.56)	0.55 (0.54-0.55)	0.55 (0.54-0.55)	0.45 (0.44-0.47)	0.42 (0.40-0.43)	0.46 (0.45-0.48)	0.40 (0.38-0.42)
Sensitivity	0.66 (0.65-0.67)	0.69 (0.69-0.70)	0.66 (0.65-0.66)	0.67 (0.66-0.67)	0.56 (0.53-0.59)	0.67 (0.64-0.69)	0.58 (0.55-0.62)	0.66 (0.62-0.71)
Specificity	0.74 (0.74-0.74)	0.73 (0.72-0.73)	0.74 (0.74-0.74)	0.73 (0.73-0.74)	0.76 (0.74-0.79)	0.68 (0.64-0.71)	0.76 (0.74-0.79)	0.65 (0.60-0.71)
F1	0.60 (0.59-0.61)	0.61 (0.61-0.62)	0.60 (0.59-0.60)	0.60 (0.59-0.60)	0.50 (0.49-0.51)	0.51 (0.50-0.52)	0.51 (0.51-0.52)	0.50 (0.49-0.51)
PPV	0.55 (0.54-0.56)	0.55 (0.54-0.56)	0.55 (0.54-0.55)	0.55 (0.54-0.55)	0.45 (0.44-0.47)	0.42 (0.40-0.43)	0.46 (0.45-0.48)	0.40 (0.38-0.42)
NPV	0.82 (0.82-0.82)	0.83 (0.83-0.83)	0.82 (0.82-0.82)	0.82 (0.82-0.82)	0.83 (0.83-0.84)	0.85 (0.85-0.86)	0.84 (0.83-0.85)	0.85 (0.84-0.86)

[#]The difference in AUC was computed between the clinical model and the reference model using the same machine learning method in each corresponding column. *Abbreviations: AUC (area under the curve), F1 (F1 score), KDIGO (Kidney Disease: Improving Global Outcomes), LR (logistic regression) MAKE (major adverse kidney events), NPV (negative predictive value), PPV (positive predictive value), RF (random forest), SOFA (sequential organ failure assessment score), SVM (Support Vector Machine), XGBoost (extreme gradient boosting), UKY (University of Kentucky), UTSW (University of Texas Southwestern).*

Table S4. MAKE outcome and its components in the 120 days following hospital discharge in both cohorts.

	UKY n = 7354	**UTSW n = 2233**
Hospital mortality, n (%)	1612 (21.9)	222 (9.9)
Hospital mortality + mortality up to 120 days in hospital survivors, n (%)	1959 (26.6)	369 (16.5)
On KRT within the last 48h of hospitalization*, n (%)	199 (2.7)	78 (3.5)
ESKD by USRDS after discharge*, n (%)	109 (1.5)	80 (3.6)
eGFR drop of 50%[#], n (%)	179 (2.4)	79 (3.5)
Total (MAKE) , n (%)	2382 (32.4)	574 (25.7)

*Patients considered KRT dependent can be included in these 2 categories
[#]Only for patients not considered KRT dependent

Abbreviations: eGFR (estimated glomerular filtration rate), ESKD (end-stage kidney disease), KRT (kidney replacement therapy), MAKE (major adverse kidney events), USRDS (United States Renal Data System).

Table S5. Final features included in the clinical model of hospital mortality in alphabetical order. Data are presented as n (percentage) or median (interquartile range).

	UKY (Derivation Cohort)			UTSW (Validation Cohort)		
Features	**Survived n = 5742**	**Died n = 1612**	**Mean Abs. SHAP Score**	**Survived n = 2011**	**Died n = 222**	**Mean Abs. SHAP Score**
Age	62.92 [51.21-73.50]	63.49 [52.92-73.81]	0.009	64.05 [53.87-73.75]	63.11 [53.41-73.08]	0.008
Bilirubin (High)	0.80 [0.50-1.60]	1.30 [0.60-3.10]	0.011	0.80 [0.50-1.80]	1.45 [0.70-3.62]	0.011
BUN (High)	37.00 [25.00-55.00]	47.00 [31.00-66.00]	0.018	30.00 [21.00-46.00]	44.00 [27.00-68.00]	0.020
ECMO	42 (0.73)	59 (3.66)	0.001	5 (0.25)	7 (3.15)	0.001
FiO2 (High)	60 [50 -100]	100 [60 -100]	0.045	45 [27-60]	75 [40-100]	0.040
Heart Rate (High)	116 [101-133]	125 [109-141]	0.007	109 [96-125]	122 [107-136]	0.006
Hours in ICU	75.95 [58.28-82.87]	79.02 [72.77-86.35]	0.012	75.32 [51.22-81.08]	80.53 [76.3-86.46]	0.011
Last KDIGO Stage 0 Stage 1 Stage 2 Stage 3	 2296 (39.99) 1710 (29.78) 784 (13.65) 952 (16.58)	 345 (21.40) 379 (23.51) 301 (18.67) 587 (36.41)	0.010	 814 (40.48) 669 (33.27) 235 (11.69) 293 (14.57)	 58 (26.13) 51 (22.97) 30 (13.51) 83 (37.39)	0.011
Maximum KDIGO Stage 1 Stage 2 Stage 3	 2984 (51.97) 1401 (24.40) 1357 (23.63)	 580 (35.98) 385 (23.88) 647 (40.14)	0.0003	 1201 (59.72) 414 (20.59) 396 (19.69)	 90 (40.54) 43 (19.37) 89 (40.09)	0.0002
pH (Low)	7.29 [7.22-7.36]	7.25 [7.15-7.35]	0.008	7.33 [7.26-7.39]	7.32 [7.26-7.38]	0.007
Platelets (Low)	154.00 [103.00-214.00]	118.00 [60.00-188.00]	0.021	148.00 [97.00-207.00]	113.00 [64.00-185.75]	0.017
Temperature (High)	37.78 [37.28-38.39]	37.89 [37.28-38.67]	0.005	37.39 [37.00-37.94]	37.39 [36.94-37.94]	0.004
Temperature (Low)	36.28 [35.72-36.50]	35.89 [35.17-36.39]	0.016	36.17 [35.89-36.50]	36.06 [35.67-36.39]	0.013
Urine Output	74.77 [46.13-116.23]	49.53 [21.32-86.43]	0.051	61.96 [41.27-92.33]	46.05 [20.60-69.28]	0.042
Pressor/inotrope	909 (15.83)	659 (40.88)	0.066	258 (13.36)	69 (31.22)	0.064

Abbreviations: BUN (blood urea nitrogen), ECMO (extracorporeal membrane oxygenation), FiO_2 (fraction of inspired oxygen), ICU (intensive care unit), KDIGO (Kidney Disease: Improving Global Outcomes), SHAP (shapley additive explanations), UKY (University of Kentucky), UTSW (University of Texas Southwestern)

Table S6. Reclassification of hospital mortality prediction comparing the proposed clinical model vs. SOFA and APACHE-II models.

			Clinical Model		
		SOFA model	0.0 - 0.5	0.5 - 1.0	% Reclassified
Derivation cohort (UKY)	Survived (n = 5742)	0.0 - 0.5	3148	517	14
		0.5 - 1.0	912	1165	44
	Died (n = 1612)	0.0 - 0.5	288	233	45
		0.5 - 1.0	153	938	14
Validation cohort (UTSW)	Survived (n = 2011)	0.0 - 0.5	1129	371	25
		0.5 - 1.0	180	331	35
	Died (n = 222)	0.0 - 0.5	47	52	53
		0.5 - 1.0	20	103	16
			Clinical Model		
		APACHE-II model	0.0 - 0.5	0.5 - 1.0	% Reclassified
Derivation cohort (UKY)	Survived (n = 5742)	0.0 - 0.5	3125	611	16
		0.5 - 1.0	935	1071	47
	Died (n = 1612)	0.0 - 0.5	275	319	54
		0.5 - 1.0	166	852	16
Validation cohort (UTSW)	Survived (n = 2011)	0.0 - 0.5	844	215	20
		0.5 - 1.0	465	487	49
	Died (n = 222)	0.0 - 0.5	32	34	52
		0.5 - 1.0	35	121	22

Table S7. Final features included in the clinical model of MAKE in alphabetical order. Data are presented as n (percentage) or median (interquartile range).

	UKY (Derivation Cohort)			UTSW (Validation Cohort)		
Features	**No MAKE n = 4972**	**MAKE n = 2382**	**Mean Abs. SHAP Score**	**No MAKE n = 1659**	**MAKE n = 574**	**Mean Abs. SHAP Score**
Age	62.56 [50.89-73.28]	63.98 [53.17-74.13]	0.017	64.16 [53.95-73.97]	63.36 [53.47-72.62]	0.016
Bilirubin (High)	0.80 [0.50-1.50]	1.10 [0.60-2.70]	0.012	0.80 [0.50-1.60]	1.20 [0.60-3.20]	0.012
BUN (High)	35.00 [25.00-52.00]	48.00 [32.00-69.00]	0.024	28.00 [20.00-42.00]	41.00 [28.00-66.00]	0.025
FiO2 (High)	60 [50-100]	100 [60-100]	0.045	40 [27-60]	50 [30-100]	0.041
Heart Rate (High)	116 [101-133]	121 [105-139]	0.005	109 [96-125]	114 [98-130.75]	0.005
Hemoglobin (Low)	9.40 [7.80-11.20]	8.50 [7.20-10.40]	0.010	9.40 [8.10-11.10]	8.50 [7.30-10.20]	0.008
ICU admission sCr	1.51 [1.11-2.15]	1.81 [1.27-2.70]	0.004	1.37 [0.97-1.98]	1.77 [1.15-2.90]	0.003
Last KDIGO Stage 0 Stage 1 Stage 2 Stage 3	 2170 (43.64) 1552 (31.21) 651 (13.09) 599 (12.05)	 471 (19.77) 537 (22.54) 434 (18.22) 940 (39.46)	0.110	 742 (44.73) 575 (34.66) 184 (11.09) 158 (9.52)	 130 (22.65) 145 (25.26) 81 (14.11) 218 (37.98)	0.112
Maximum KDIGO Stage 1 Stage 2 Stage 3	 2782 (55.95) 1228 (24.70) 962 (19.35)	 782 (32.83) 558 (23.43) 1042 (43.74)	0.001	 1074 (64.74) 343 (20.68) 242 (14.59)	 217 (37.80) 114 (19.86) 243 (42.33)	0.001
pH (Low)	7.30 [7.22-7.36]	7.26 [7.16-7.36]	0.007	7.33 [7.27-7.39]	7.31 [7.23-7.40]	0.006
Platelets (Low)	154.00 [105.00-214.00]	128.00 [68.00-197.00]	0.021	151.00 [102.00-208.00]	124.00 [64.00-194.00]	0.018
Serum Sodium (Low)	137.00 [134.00-140.00]	137.00 [134.00-140.00]	0.004	136.00 [133.00-139.00]	136.00 [132.00-140.00]	0.003
Urine Output	77.88 [50.04-119.97]	51.39 [22.41-88.63]	0.050	64.68 [43.72-94.18]	48.54 [21.17-75.82]	0.040
Pressor/inotrope	721 (14.50)	847 (35.56)	0.028	203 (12.79)	124 (21.95)	0.028

Abbreviations: BUN (blood urea nitrogen), ECMO (extracorporeal membrane oxygenation), FiO_2 (fraction of inspired oxygen), ICU (intensive care unit), KDIGO (Kidney Disease: Improving Global Outcomes), SHAP (shapley additive explanations), UKY (University of Kentucky), UTSW (University of Texas Southwestern)

Table S8. Reclassification of MAKE prediction comparing the proposed clinical model vs. maximum AKI KDIGO model.

			Clinical Model		
		AKI KDIGO	0.0 - 0.5	0.5 - 1.0	% Reclassified
Derivation cohort (UKY)	No MAKE (n = 4972)	0.0 - 0.5	2592	430	14
		0.5 - 1.0	1056	894	54
	MAKE (n = 2382)	0.0 - 0.5	479	410	46
		0.5 - 1.0	242	1251	16
Validation cohort (UTSW)	No MAKE (n = 1659)	0.0 - 0.5	888	186	17
		0.5 - 1.0	281	304	48
	MAKE (n = 574)	0.0 - 0.5	125	92	42
		0.5 - 1.0	63	294	18

Table S9. Reclassification of MAKE prediction comparing the proposed clinical model vs. maximum AKI KDIGO model in the subset of survivors up to 120 days after hospital discharge.

			Clinical Model		
		AKI KDIGO	0.0 - 0.5	0.5 - 1.0	% Reclassified
Derivation cohort (UKY)	No MAKE (n = 4972)	0.0 - 0.5	3722	288	7
		0.5 - 1.0	264	698	27
	MAKE (n = 423)	0.0 - 0.5	98	36	27
		0.5 - 1.0	5	284	2
Validation cohort (UTSW)	No MAKE (n = 1659)	0.0 - 0.5	1395	22	2
		0.5 - 1.0	72	170	30
	MAKE (n = 205)	0.0 - 0.5	80	7	8
		0.5 - 1.0	5	113	4

Table S10. Predictive performance of models for hospital mortality and MAKE prediction stratified by CKD patients (Panel A: CKD defined by baseline eGFR < or ≥60; Panel B: CKD defined by ICD 9/10 codes).

	Model for Hospital Mortality				**Model for MAKE**			
Panel A.	**Baseline eGFR <60**		**Baseline eGFR ≥60**		**Baseline eGFR <60**		**Baseline eGFR ≥60**	
	UKY Death N (%) 491 (22.32)	**UKY Death N (%) 491 (22.32)**	**UKY Death N (%) 1121 (21.75)**	**UTSW Death N (%) 131 (9.66)**	**UKY MAKE N (%) 223 (36.92)**	**UKY MAKE N (%) 223 (36.92)**	**UKY MAKE N (%) 2159 (31.99)**	**UTSW MAKE N (%) 450 (25.08)**
AUC	0.81(0.79-0.82)	0.74(0.73-0.75)	0.79(0.79-0.79)	0.73(0.73-0.74)	0.79(0.78-0.80)	0.70(0.68-0.71)	0.78(0.78-0.78)	0.74(0.73-0.75)
Accuracy	0.70(0.69-0.71)	0.61(0.59-0.63)	0.71(0.71-0.72)	0.66(0.65-0.67)	0.72(0.71-0.72)	0.63(0.61-0.65)	0.72(0.71-0.72)	0.69(0.67-0.70)
Precision	0.43(0.41-0.45)	0.18(0.17-0.19)	0.41(0.40-0.41)	0.17(0.17-0.18)	0.59(0.58-0.60)	0.40(0.39-0.42)	0.55(0.54-0.55)	0.42(0.41-0.44)
Sensitivity	0.80(0.77-0.82)	0.75(0.72-0.79)	0.71(0.71-0.72)	0.67(0.65-0.69)	0.73(0.71-0.74)	0.68(0.65-0.70)	0.69(0.69-0.70)	0.66(0.64-0.69)
Specificity	0.67(0.66-0.68)	0.59(0.57-0.61)	0.71(0.71-0.72)	0.65(0.64-0.67)	0.71(0.70-0.72)	0.61(0.57-0.64)	0.73(0.72-0.73)	0.69(0.66-0.72)
F1	0.55(0.53-0.57)	0.29(0.28-0.30)	0.52(0.51-0.52)	0.28(0.27-0.28)	0.65(0.64-0.66)	0.51(0.49-0.52)	0.61(0.60-0.61)	0.51(0.50-0.52)
Panel B.	**CKD by ICD codes**		**No CKD by ICD codes**		**CKD by ICD codes**		**No CKD by ICD codes**	
	UKY Death N (%) 491 (22.32)	**UKY Death N (%) 491 (22.32)**	**UKY Death N (%) 1121 (21.75)**	**UTSW Death N (%) 131 (9.66)**	**UKY MAKE N (%) 892 (40.55)**	**UTSW MAKE N (%) 285 (32.5)**	**UKY MAKE N (%) 1490 (28.91)**	**UTSW MAKE N (%) 289 (21.31)**
AUC	0.76(0.75-0.76)	0.76(0.75-0.76)	0.81(0.80-0.81)	0.76(0.75-0.77)	0.75(0.74-0.75)	0.69(0.68-0.70)	0.79(0.79-0.79)	0.75(0.74-0.76)
Accuracy	0.66(0.65-0.67)	0.66(0.65-0.67)	0.73(0.73-0.74)	0.67(0.66-0.68)	0.66(0.65-0.67)	0.62(0.61-0.63)	0.74(0.74-0.74)	0.71(0.69-0.73)
Precision	0.37(0.36-0.38)	0.37(0.36-0.38)	0.43(0.42-0.44)	0.19(0.18-0.19)	0.56(0.55-0.57)	0.45(0.43-0.46)	0.54(0.54-0.55)	0.39(0.37-0.41)
Sensitivity	0.73(0.72-0.74)	0.73(0.72-0.74)	0.72(0.71-0.72)	0.70(0.68-0.72)	0.76(0.75-0.76)	0.68(0.65-0.71)	0.66(0.65-0.66)	0.65(0.62-0.67)
Specificity	0.64(0.63-0.65)	0.64(0.63-0.65)	0.74(0.73-0.74)	0.67(0.66-0.68)	0.59(0.58-0.60)	0.59(0.56-0.62)	0.78(0.77-0.78)	0.72(0.69-0.76)
F1	0.49(0.48-0.50)	0.49(0.48-0.50)	0.54(0.53-0.54)	0.29(0.28-0.30)	0.64(0.64-0.65)	0.54(0.53-0.55)	0.59(0.59-0.60)	0.49(0.48-0.50)