Development and Validation of a Real-time Prediction Model for Acute Kidney Injury in Hospitalized Patients - Supplementary Information

Table of contents

Table S1 Demographics for all cohorts stratified by AKI status

Characteristic	Derivation cohort n=47750			Site 1 (2020) n=17074			Site 2 n=39605		
	AKI n=1739	Non-AKI n=46011	P	AKI n=682	Non-AKI n=16392	P	AKI n=2681	Non-AKI n=36924	P
Age, y	63.3 ± 18.4	58.9 ± 16.2	<0.001	65.7 ± 16.8	59.4 ± 16.1	<0.001	64.8 ± 16.9	59.9 ± 17.1	<0.001
Female, n (%)	715 (41.1)	20130 (43.8)	0.03	280 (41.1)	7170 (43.7)	0.20	1064 (39.7)	13472 (36.5)	0.001
Internal Medicine admission, n (%)	754 (43.4)	18930 (41.1)	0.07	316 (46.3)	6532 (39.8)	0.001	1002 (37.4)	19981 (54.1)	<0.001
Surgical Ward admission, n (%)	783 (45.0)	25690 (55.8)	<0.001	305 (44.7)	9374 (57.2)	<0.001	922 (34.4)	15800 (42.8)	<0.001
ICU admission, n (%)	202 (11.6)	1391 (3.0)	<0.001	61 (8.9)	486 (3.0)	<0.001	757 (28.2)	1143 (3.1)	<0.001
Preexisting CKD	846 (48.6)	9927 (21.6)	<0.001	368 (54.0)	3577 (21.8)	<0.001	1127 (42.0)	8424 (22.8)	<0.001
Admission Laboratory parameters									
Scr, μmol/L	103.7 ± 60.9	81.7 ± 31.7	<0.001	116.6 ± 73.2	83.0 ± 32.1	<0.001	94.7 ± 61.4	78.3 ±36.9	<0.001
eGFR	72.6 ± 31.0	85.0 ± 22.1	<0.001	66.7 ± 32.4	83.7 ± 22.2	<0.001	78.6 ± 32.3	89.2 ± 24.8	<0.001
BUN, mmol/L	8.6 ± 5.7	6.0 ± 2.8	<0.001	9.3 ± 6.6	6.1 ± 3.0	<0.001	8.5 ± 5.8	6.3 ± 3.5	<0.001
White Blood Cells, 10^9/L	6.7 (5.1, 9.3)	6.1 (4.9, 7.6)	<0.001	6.9 (5.1, 9.1)	6.2 (5.1, 7.8)	<0.001	7.8 (5.4, 11.5)	6.4 (5.0, 8.7)	<0.001
Hemoglobin, g/L	113.7 ± 26.4	131.0 ± 20.3	<0.001	110.5 ± 26.2	129.8 ± 20.7	<0.001	113.4 ±29.4	124.9 ± 25.7	<0.001
Platelet, 10^9/L	189.0(137.0,248.0)	207.0(167.0,254.0)	<0.001	201.0(146.0,255.0)	217.0(176.0,264.0)	<0.001	165.0(112.0,222.0)	176.0(132.0,228.0)	<0.001
AST, IU/L	23.0 (17.0, 37.0)	21.0 (17.0, 27.0)	<0.001	23.0 (17.0, 34.3)	21.0 (17.0, 27.0)	<0.001	37.0(26.0,63.0)	29.0(22.0,41.0)	<0.001
Serum albumin, g/L	35.1 ± 7.0	40.0 ± 6.3	<0.001	34.4 ± 6.7	39.5 ± 6.3	<0.001	34.4 ±6.6	37.8 ± 5.6	<0.001
C-reactive protein, mg/L	13.3 (2.9, 53.5)	2.6 (1.0, 10.2)	<0.001	13.0 (2.2, 57.7)	2.4 (0.9, 8.6)	<0.001	14.1(3.3, 55.7)	6.3(1.6, 27.1)	<0.001
Urine protein, positive, n (%)	694 (39.9)	8519 (18.5)	<0.001	297 (43.5)	2969 (18.1)	<0.001	619 (23.1)	5107 (13.8)	<0.001
Operation during stay, n (%)	509 (29.3)	16557 (36.0)	<0.001	214 (31.4)	6528 (39.8)	<0.001	1034 (38.6)	14033(38.0)	0.6
Length of stay, d	21 (11, 33)	9 (6, 15)	<0.001	22 (12, 34)	8 (6, 14)	<0.001	16 (10, 27)	11 (7, 16)	<0.001
Inpatient mortality, n (%)	266 (15.3)	131 (0.3)	<0.001	119 (17.4)	62 (0.4)	<0.001	438 (16.3)	236 (0.6)	<0.001

Characteristic	Site 3 n=21239			Site 4 n=22603			Site 5 n=13605		
	AKI n=1941	Non-AKI n=19298	P	AKI n=829	Non-AKI n=21774	P	AKI n=849	Non-AKI n=12756	P
Age, y	61.2 ± 14.8	59.0± 14.4	<0.001	71.2 ± 13.5	66.5 ± 14.7	<0.001	66.5 ± 16.1	63.3 ± 15.9	<0.001
Female, n (%)	849 (43.7)	7607(39.4)	<0.001	360 (43.4)	7653 (35.1)	<0.001	350 (41.2)	4733 (37.1)	0.02
Internal Medicine admission, n (%)	635 (32.7)	9590 (49.7)	<0.001	489 (59.0)	13396 (61.5)	0.14	445 (52.4)	9222 (72.3)	<0.001
Surgical Ward admission, n (%)	736 (37.9)	8456 (43.8)	<0.001	207 (25.0)	8152 (37.4)	<0.001	299 (35.2)	3190 (25.0)	<0.001
ICU admission, n (%)	570 (29.4)	1252 (6.5)	<0.001	133 (16.0)	226 (1.0)	<0.001	105 (12.4)	344 (2.7)	<0.001
Preexisting CKD	1094 (56.4)	7238 (37.5)	<0.001	484 (58.4)	6910 (31.7)	<0.001	348 (41.0)	3286 (25.8)	<0.001
Admission Laboratory parameters									
Scr, μmol/L	110.7 ± 67.8	90.1± 43.5	<0.001	91.4 ± 58.3	77.5 ± 34.5	<0.001	92.2 ± 66.0	83.3 ± 42.8	<0.001
eGFR	70.4 ± 32.0	80.5 ± 25.4	<0.001	76.0 ± 33.0	85.1 ± 23.7	<0.001	80.6 ± 35.6	83.9 ± 26.1	0.009
BUN, mmol/L	9.5 ±6.9	6.8 ±4.3	<0.001	10.3 ± 7.3	6.7 ± 3.8	<0.001	9.0 ± 6.8	7.0 ± 4.1	<0.001
White Blood Cells, 10^9/L	9.6(6.7, 13.7)	8.3(6.1,11.7)	<0.001	8.7(6.1, 12.0)	6.9(5.4, 9.1)	<0.001	9.1 (6.4, 13.8)	7.2 (5.6, 9.9)	<0.001
Hemoglobin, g/L	111.9 ± 28.9	120.5 ± 24.0	<0.001	114.8 ± 27.2	126.7 ± 23.7	<0.001	122.7 ± 29.8	132.3 ± 26.0	<0.001
Platelet, 10^9/L	211.0(156.0, 272.0)	221.0(172.0, 275.0)	<0.001	194.0(142.0,245.5)	202.0(162.0,249.0)	<0.001	203.0(146.0,261.5)	212.0(165.0,266.0)	<0.001
AST, IU/L	26.0 (17.0, 57.0)	22.0 (16.0, 39.0)	<0.001	34.1 (22.9, 67.7)	24.1 (19.0, 34.9)	<0.001	26.3 (19.0, 46.0)	22.0 (17.1, 31.3)	<0.001
Serum albumin, g/L	36.6 ± 6.6	38.4 ± 5.6	<0.001	32.3 ± 6.9	35.9 ± 5.6	<0.001	33.6 ± 7.3	37.6 ± 6.7	<0.001
C-reactive protein, mg/L	14.2 (5.0, 30.2)	12.0 (2.8, 23.5)	<0.001	42.0 (13.1, 103.0)	14.1 (4.1, 55.0)	<0.001	55.0 (11.5, 116.7)	9.1 (1.8, 52.9)	<0.001
Urine protein, positive, n (%)	749 (38.6)	5026 (26.0)	<0.001	342 (41.3)	4781 (22.0)	<0.001	174 (20.5)	1490 (11.7)	<0.001
Operation during stay, n (%)	643 (33.1)	5760 (29.8)	0.003	124 (15.0)	3079 (14.1)	0.5	220 (25.9)	2136 (16.7)	<0.001
Length of stay, d	13 (8, 22.5)	10 (7, 16)	<0.001	15 (9, 24)	12 (9,16)	<0.001	20 (11.5, 36)	17 (12, 25)	<0.001
Inpatient mortality, n (%)	234 (12.1)	221 (1.1)	<0.001	297 (35.8)	512 (2.4)	<0.001	179 (21.1)	265 (2.1)	<0.001

Continuous variables were compared using Student’s t test or the Mann-Whitney U test as appropriate, categorical variables were compared using the $\chi 2$ test, with the level of significance set at $P < 0.05$ (2-tailed).

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; Scr, serum creatinine; BUN, blood urea nitrogen; AST, aspartate aminotransferase; Site 1, Peking University First Hospital; Site 2, Sichuan Provincial People's Hospital; Site 3, the Second Affiliated Hospital of Harbin Medical University; Site 4, Beijing Miyun District Hospital; Site 5, Peking University First Hospital Taiyuan Hospital

Table S2 Predictive performance for AKI and severe AKI in the Derivation Cohort.

	AKI			Severe AKI (AKI stage 2-3)		
	24h	48h	72h	24h	48h	72h
AUC	0.92(0.90-0.93)	0.91(0.90-0.92)	0.91(0.90-0.91)	0.95(0.94-0.97)	0.95(0.94-0.96)	0.94(0.94-0.95)
Accuracy (%)	89.9	88.3	86.6	96.0	94.7	93.8
Sensitivity (%)	78.4	78.2	78.4	78.2	78.3	78.0
Specificity (%)	90.5	89.2	87.6	96.6	95.9	95.4
PPV (%)	29.6	40.2	44.7	47.5	57.8	63.6
NPV (%)	97.0	95.0	93.4	98.3	96.7	95.2

Abbreviations: AKI, acute kidney injury; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value

Table S3 Definition for features included in the final models

A. Features in the prediction model of AKI:

Feature	Definition	Unit
Latest changing rate of Scr	The parameter is calculated using the difference between the latest two Scr values divided by the time interval (hour) between two measurements	μmol/L/h
Use of Diuretics	Use of Diuretics	-
Percentage of lymphocyte	Latest percentage of lymphocyte	%
Admission to ICU	Admission to ICU	-
Use of human albumin	Use of human albumin	-
Lowest Scr	Lowest Scr value since admission	μmol/L
NE percentage/albumin ratio	The ratio of latest neutrophils percentage to the latest albumin value	%/(g/L)
Scr	Latest value of Scr	μmol/L
Lowest BUN	Lowest BUN value since admission	mmol/L
Heart rate	Latest heart rate	/min
Cardiac troponin I	Latest value of cardiac troponin I	ng/ml
Highest NE percentage	Highest percentage of neutrophils since admission	%
BUN	Latest value of BUN	mmol/L
Procalcitonin	Latest value of procalcitonin	ng/ml
Baseline red blood cell count	Admission red blood cell count	10^{12}/L
Lowest D-dimer	Lowest value of D-dimer since admission	mg/L
Blood platelet count	Latest blood platelet count	10^{9}/L
Respiratory rate	Latest respiratory rate	/min
Lactic dehydrogenase	Latest value of lactic dehydrogenase	IU/L
Cardiovascular surgery	Receive cardiovascular surgery	-

B. Features in the prediction model of severe AKI:

Feature	Definition	Unit
Initial changing rate of Scr	The parameter is calculated using the difference between the latest and the initial Scr values since admission divided by the time interval (hour) between two measurements	μmol/L/h
BUN	Latest value of BUN	mmol/L
Percentage of lymphocyte	Latest percentage of lymphocyte	%
Use of Diuretics	Use of Diuretics	-
Latest changing rate of Scr	The parameter is calculated using the difference between the latest two Scr values divided by the time interval (hour) between two measurements.	μmol/L/h
Highest D-dimer	Highest D-dimer value since admission	mg/L
Highest BUN	Highest BUN value since admission	mmol/L
Procalcitonin	Latest value of procalcitonin	ng/ml
Heart rate	Latest heart rate	/min
Lowest Scr	Lowest Scr value since admission	μmol/L
Scr	Latest value of Scr	μmol/L
Admission to ICU	Admission to ICU	-
Baseline red blood cell count	Admission red blood cell count	10^{12}/L
White blood cell count	Latest white blood cell count	10^{9}/L
High-sensitive CRP/albumin ratio	Latest value of high-sensitive CRP divided by latest albumin value	(mg/L)/(g/L)
Blood platelet count	Latest blood platelet count	10^{9}/L
Lactic dehydrogenase	Latest value of lactic dehydrogenase	IU/L
Direct bilirubin	Latest value of direct bilirubin	μmol/L
High-sensitive CRP	Latest value of high-sensitive CRP	mg/L
Sodium	Latest value of sodium	mmol/L

Table S4 Performance in detecting AKI within 48 hours during hospitalization prior to the event using different probability cutoffs.

Probability cutoff	Patients, No.	Time to AKI	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Site 1						
0.2	16458	36(36-36)	97.9	3.3	3.7	97.7
0.25	10610	36(36-36)	96.1	38.9	5.6	99.6
0.3	5767	36(30-36)	94.1	68.4	10.1	99.7
0.35	3982	36(24-36)	92.0	79.2	14.4	99.6
0.4	3043	36(18-36)	90.5	84.9	18.5	99.6
0.45[#]	2298	36(12-36)	87.9	89.3	23.8	99.5
0.5	1769	30(12-36)	83.1	92.4	29.2	99.3
0.55	1315	24(12-36)	72.0	94.7	34.1	98.9
0.6	959	12(6-36)	61.9	96.5	40.1	98.5
0.65	609	12(6-25)	44.4	98.0	45.3	97.9
0.7	330	12(6-18)	26.2	99.0	49.4	97.2
Site 2						
0.2	39552	36(36-42)	98.2	0.0	6.7	7.7
0.25	39340	36(36-42)	97.7	0.5	6.7	76.9
0.3	37721	36(36-42)	96.7	4.9	6.9	95.3
0.35	32471	36(30-42)	94.3	18.9	7.8	97.9
0.4	24684	36(30-42)	91.9	39.8	10.0	98.5
0.45	18514	36(24-42)	89.4	56.3	12.9	98.7
0.5[#]	12892	36(18-42)	84.8	71.2	17.6	98.5

0.55	9290	30(18-36)	76.3	80.4	22.0	97.9
0.6	5920	30(12-36)	60.6	88.4	27.4	96.9
0.65	3257	24(12-36)	39.7	94.1	32.7	95.6
0.7	1238	18(12-36)	17.6	97.9	38.2	94.2
0.75	297	18(6-36)	4.9	99.6	44.4	93.5
Site 3						
0.2	21041	42(36-42)	95.3	0.6	8.8	54.0
0.25	19861	36(36-42)	92.3	6.4	9.0	89.1
0.3	16308	36(30-42)	88.4	24.4	10.5	95.4
0.35	12815	36(30-42)	84.6	42.1	12.8	96.5
0.4	10250	36(24-42)	79.8	54.9	15.1	96.4
0.45[#]	7870	36(18-42)	71.7	66.4	17.7	95.9
0.5	5856	30(18-42)	60.7	75.8	20.1	95.0
0.55	4011	30(18-42)	43.7	83.6	21.2	93.7
0.6	2408	30(18-42)	28.1	90.3	22.6	92.6
0.65	1215	24(18-39)	15.2	95.2	24.3	91.8
0.7	410	18(12-36)	5.8	98.5	27.3	91.2
0.75	94	12(10-30)	1.6	99.7	34.0	91.0
Site 4						
0.2	22563	42(36-42)	98.6	0.1	3.6	70.0
0.25	22097	42(36-42)	97.3	2.2	3.7	95.7
0.3	20813	42(36-42)	94.9	8.0	3.8	97.7
0.35	15865	42(36-42)	92.5	30.7	4.8	99.1
0.4	9048	42(36-42)	89.3	61.8	8.2	99.3
0.45[#]	6726	36(24-42)	81.5	72.2	10.1	99.0

0.5	4524	36(24-42)	70.2	81.9	12.9	98.6
0.55	2993	36(18-42)	57.5	88.4	15.9	98.2
0.6	1813	36(12-42)	44.4	93.4	20.3	97.8
0.65	944	30(12-36)	28.5	96.7	25.0	97.3
0.7	348	30(7-36)	13.8	98.9	32.8	96.8
0.75	102	18(6-36)	7.2	99.8	58.8	96.6
Site 5						
0.25	13578	36(36-36)	98.5	0.1	6.2	51.9
0.3	8997	36(30-36)	97.1	35.9	9.2	99.5
0.35	7306	36(24-36)	95.2	49.1	11.1	99.3
0.4	5928	36(24-36)	92.8	59.7	13.3	99.2
0.45	4754	36(18-36)	90.3	68.7	16.1	99.1
0.5	3656	36(12-36)	86.7	77.1	20.1	98.9
0.55[#]	2627	30(12-36)	80.1	84.7	25.9	98.5
0.6	1743	24(6-36)	68.3	90.9	33.3	97.7
0.65	993	12(6-36)	52.3	95.7	44.7	96.8
0.7	419	12(6-36)	29.7	98.7	60.1	95.5
0.75	138	12(6-31)	12.7	99.8	78.3	94.5

The optimal probability cutoffs selected by taking into account both sensitivity and specificity.

Site 1, Peking University First Hospital; Site 2, Sichuan Provincial People's Hospital; Site 3, the Second Affiliated Hospital of Harbin Medical University; Site 4, Beijing Miyun District Hospital; Site 5, Peking University First Hospital Taiyuan Hospital. AKI, acute kidney injury; PPV, positive predictive value; NPV, negative predictive value.

Table S5 Performance in detecting severe AKI within 48 hours during hospitalization prior to the event using different probability cutoffs

Probability cutoff	Patients, No.	Time to Severe AKI	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Site 1						
0.05	15156	36(36-42)	98.9	11.4	1.8	99.8
0.1	6424	36(36-36)	97.8	63.4	4.2	99.9
0.15	4034	36(36-36)	96.7	77.6	6.6	99.9
0.2	3060	36(36-36)	94.9	83.3	8.5	99.9
0.25	2388	36(36-36)	93.1	87.3	10.7	99.9
0.3	1928	36(36-36)	91.2	90.0	13.0	99.8
0.35	1560	36(30-36)	89.4	92.2	15.7	99.8
0.4	1269	36(18-36)	88.0	93.9	19.0	99.8
0.45[#]	1033	36(18-36)	83.9	95.2	22.3	99.7
0.5	834	36(12-36)	77.7	96.3	25.5	99.6
0.55	651	30(12-36)	71.5	97.3	30.1	99.5
0.6	481	18(12-36)	64.6	98.2	36.8	99.4
0.65	333	18(12-36)	52.2	98.9	42.9	99.2
Site 2						
0.05	39246	36(36-42)	99.7	0.9	3.0	98.9
0.1	35123	36(36-42)	98.3	11.6	3.3	99.6
0.15	31845	36(36-42)	97.5	20.1	3.6	99.6
0.2	30027	36(36-42)	96.7	24.8	3.8	99.6
0.25	15099	36(36-42)	95.8	63.7	7.5	99.8
0.3	12527	36(30-42)	94.2	70.3	8.9	99.7

0.35	10834	36(30-42)	93.1	74.7	10.2	99.7
0.4	8859	36(24-42)	92.2	79.8	12.3	99.7
0.45	7315	36(18-42)	89.8	83.7	14.5	99.6
0.5[#]	6082	36(18-42)	85.7	86.8	16.7	99.5
0.55	4881	30(18-42)	73.9	89.6	17.9	99.1
0.6	3821	24(12-42)	59.1	91.9	18.3	98.6
0.65	2877	18(12-36)	43.4	93.8	17.9	98.2
Site 3						
0.05	20991	42(36-42)	97.1	1.1	3.3	91.5
0.1	17058	42(36-42)	94.3	20.2	4.0	99.0
0.15	12458	42(36-42)	90.8	42.5	5.2	99.2
0.2	10101	42(36-42)	89.8	53.9	6.4	99.3
0.25	8032	42(30-42)	87.2	63.9	7.8	99.3
0.3	6430	36(30-42)	85.5	71.7	9.6	99.3
0.35[#]	5160	36(18-42)	81.2	77.7	11.3	99.2
0.4	4038	36(18-42)	74.5	82.9	13.3	98.9
0.45	3097	36(18-42)	64.7	87.2	15.0	98.6
0.5	2267	30(18-42)	51.5	90.8	16.3	98.2
0.55	1542	24(18-42)	38.5	93.8	18.0	97.8
0.6	980	24(18-42)	28.1	96.2	20.6	97.4
0.65	543	18(18-42)	18.1	98.0	23.9	97.2
Site 4						
0.05	22502	36(36-42)	99.5	0.4	1.8	98.0
0.1	15221	36(36-42)	97.8	33.2	2.6	99.9
0.15	10805	36(36-42)	95.6	53.1	3.6	99.8

0.2	7591	36(36-42)	92.8	67.5	5.0	99.8
0.25	5839	36(36-42)	90.4	75.3	6.3	99.8
0.3	4539	36(36-42)	89.1	81.2	8.0	99.8
0.35	3648	36(36-42)	85.2	85.1	9.5	99.7
0.4[#]	2937	36(36-42)	81.2	88.3	11.2	99.6
0.45	2311	36(30-36)	77.8	91.0	13.6	99.6
0.5	1727	36(25-36)	70.6	93.5	16.6	99.4
0.55	1233	36(18-36)	61.2	95.6	20.1	99.3
0.6	841	36(18-36)	49.6	97.1	23.9	99.1
0.65	478	36(12-36)	38.3	98.5	32.4	98.9
Site 5						
0.05	13183	36(36-42)	100.0	3.2	2.9	100.0
0.1	9360	36(36-42)	99.2	32.1	4.0	99.9
0.15	7365	36(36-42)	97.9	47.1	5.0	99.9
0.2	6227	36(36-42)	95.7	55.7	5.8	99.8
0.25	5115	36(36-42)	93.4	64.0	6.9	99.7
0.3	4227	36(36-42)	91.5	70.6	8.1	99.7
0.35	3455	36(36-42)	88.8	76.4	9.7	99.6
0.4	2791	36(30-42)	85.6	81.3	11.5	99.5
0.45[#]	2217	36(18-36)	83.0	85.6	14.1	99.4
0.5	1687	36(18-36)	76.6	89.4	17.1	99.3
0.55	1208	36(12-36)	69.4	92.8	21.6	99.1
0.6	771	36(12-36)	56.1	95.8	27.4	98.7
0.65	460	36(12-36)	45.2	97.8	37.0	98.4

The optimal probability cutoffs selected by taking into account both sensitivity and specificity.

Site 1, Peking University First Hospital; Site 2, Sichuan Provincial People's Hospital; Site 3, the Second Affiliated Hospital of Harbin Medical University; Site 4, Beijing Miyun District Hospital; Site 5, Peking University First Hospital Taiyuan Hospital. AKI, acute kidney injury; PPV, positive predictive value; NPV, negative predictive value.

Table S6 Comparison in performances of re-refitted models and refitted models for detecting AKI and severe AKI in Site 3

Probability cutoff	Re-refitted models				Refitted models			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
AKI								
0.45	80.8	82.6	31.9	97.7	78.7	66.4	19.1	96.9
Severe AKI								
0.35	86.0	84.3	16.1	99.4	83.2	77.7	11.6	99.2
AKI within 48 hours								
0.45	76.2	82.6	30.6	97.2	71.7	66.4	17.7	95.9
Severe AKI within 48 hours								
0.35	83.6	84.3	15.7	99.3	81.2	77.7	11.3	99.2

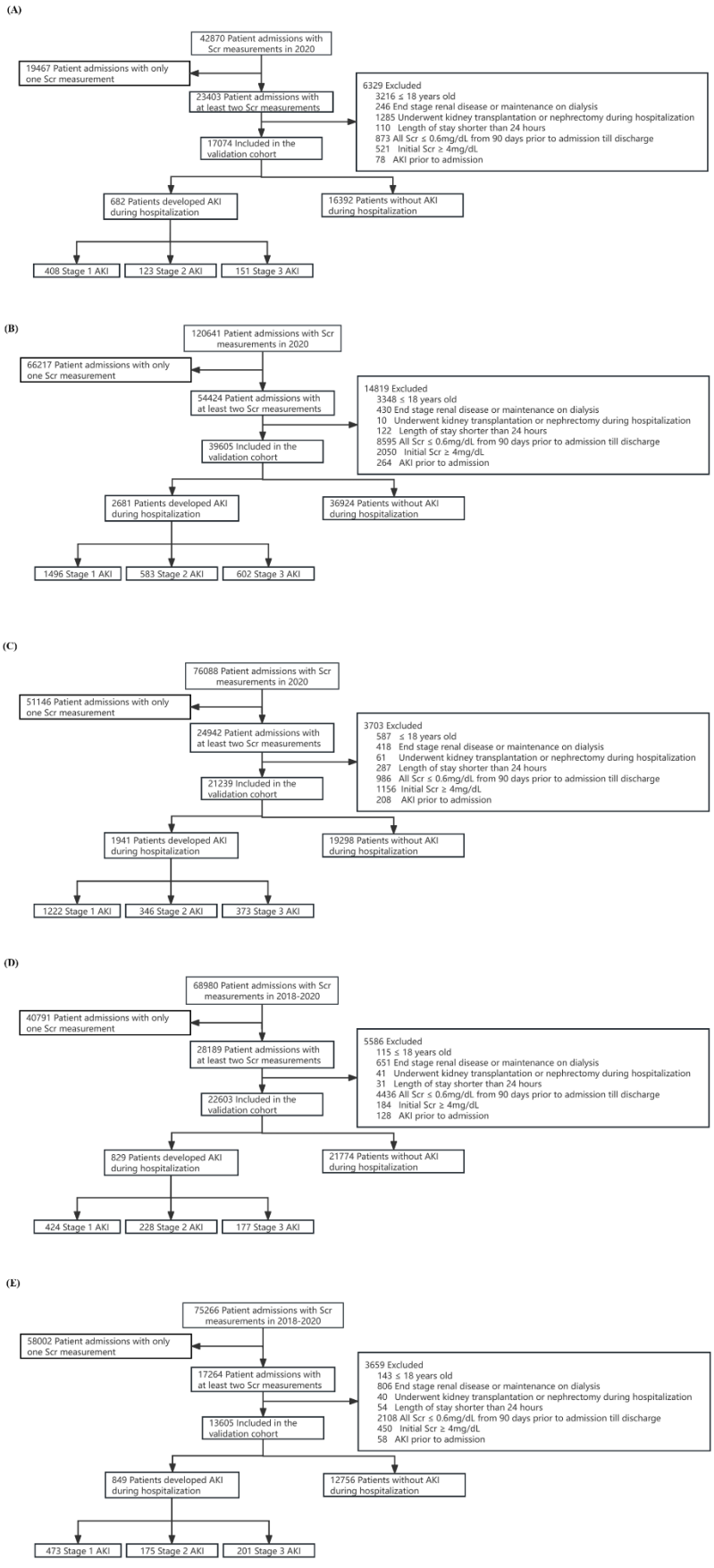
AKI, acute kidney injury; PPV, positive predictive value; NPV, negative predictive value.

Table S7 The predictive performance of the model for AKI within 48 hours using different combinations of feature selection method and model in the testing set of the Derivation Cohort and Internal Validation Cohort

Derivation Cohort				
Feature selection method+Model	AUC	Accuracy (%)	Sensitivity (%)	Specificity (%)
LightGBM + LR	0.853	75.9	80.0	75.5
LightGBM + LightGBM	0.919	87.6	80.0	88.3
LightGBM + RF	0.911	88.3	78.2	89.2
LightGBM + xGB	0.903	85.2	79.9	85.7
RF + LR	0.810	66.5	80.0	65.3
RF + LightGBM	0.910	86.7	80.0	87.3
RF + RF	0.899	86.8	78.5	87.5
RF + xGB	0.890	83.5	80.0	83.8
Internal Validation Cohort				
Feature selection method+Model	AUC	Accuracy (%)	Sensitivity (%)	Specificity (%)
LightGBM + LR	0.817	68.6	80.0	68.6
LightGBM + LightGBM	0.839	73.6	80.0	73.6
LightGBM + RF	0.850	78.5	77.4	78.5
LightGBM + xGB	0.805	63.5	80.0	63.4
RF + LR	0.805	68.8	80.0	68.7
RF + LightGBM	0.802	62.9	80.0	62.8
RF + RF	0.801	63.1	77.6	63.0
RF + xGB	0.733	48.3	80.0	48.1

Abbreviations: AKI, acute kidney injury; AUC, area under the curve; LR: Logistic Regression; LightGBM: Light Gradient Boosting Machine; RF: Random Forest; xGB: Exterme Gradient Boosting.

Figure S1 Flow diagram for five validation Cohort

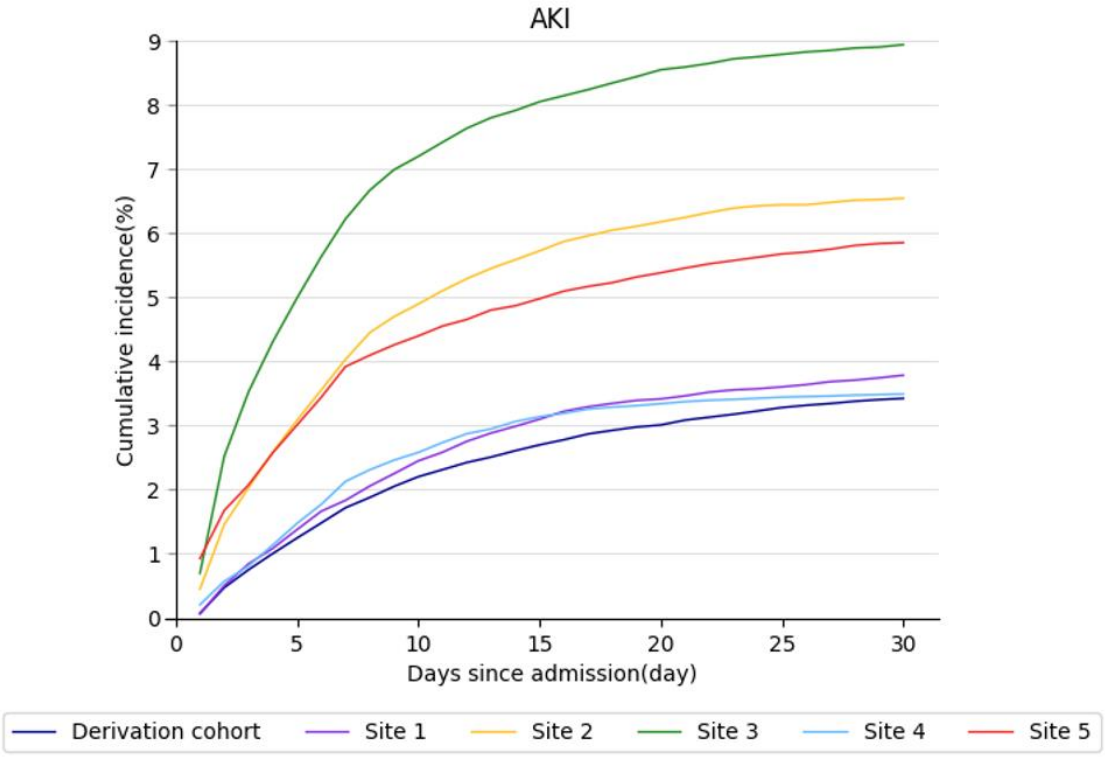


(A)Flow diagram for the Internal Validation in Site 1; (B)-(D) Flow diagram for the External Validation in Site 2-5

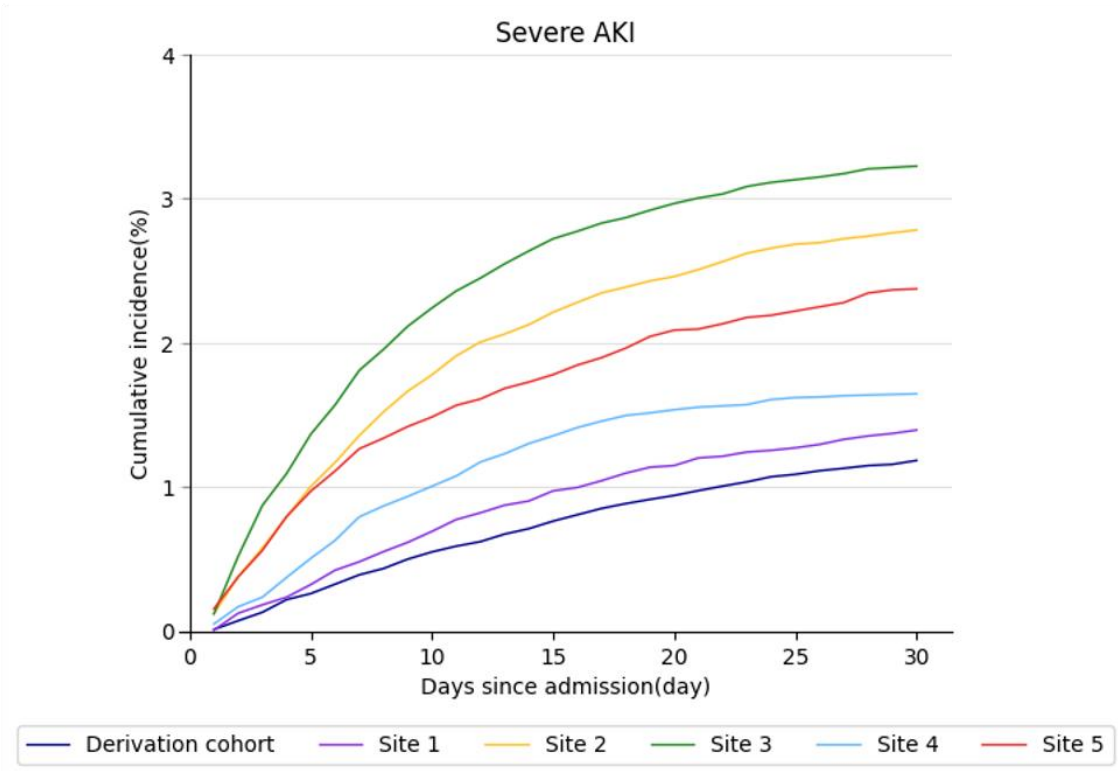
Site 1, Peking University First Hospital; Site 2, Sichuan Provincial People's Hospital; Site 3, the Second Affiliated Hospital of Harbin Medical University; Site 4, Beijing Miyun District Hospital; Site 5, Peking University First Hospital Taiyuan Hospital.

Figure S2 Cumulative incidence plot for AKI and severe AKI across six cohorts

(A)

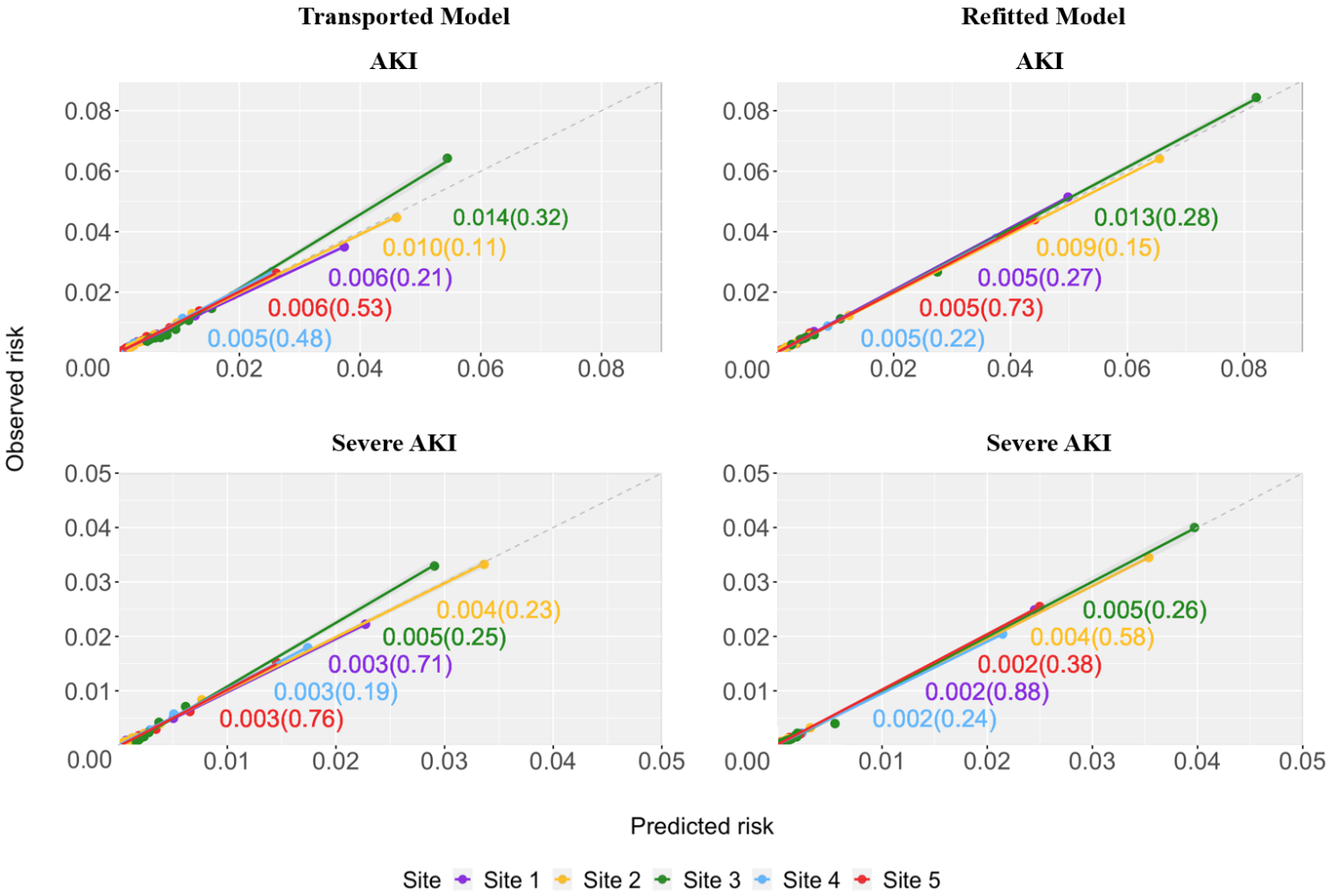


(B)



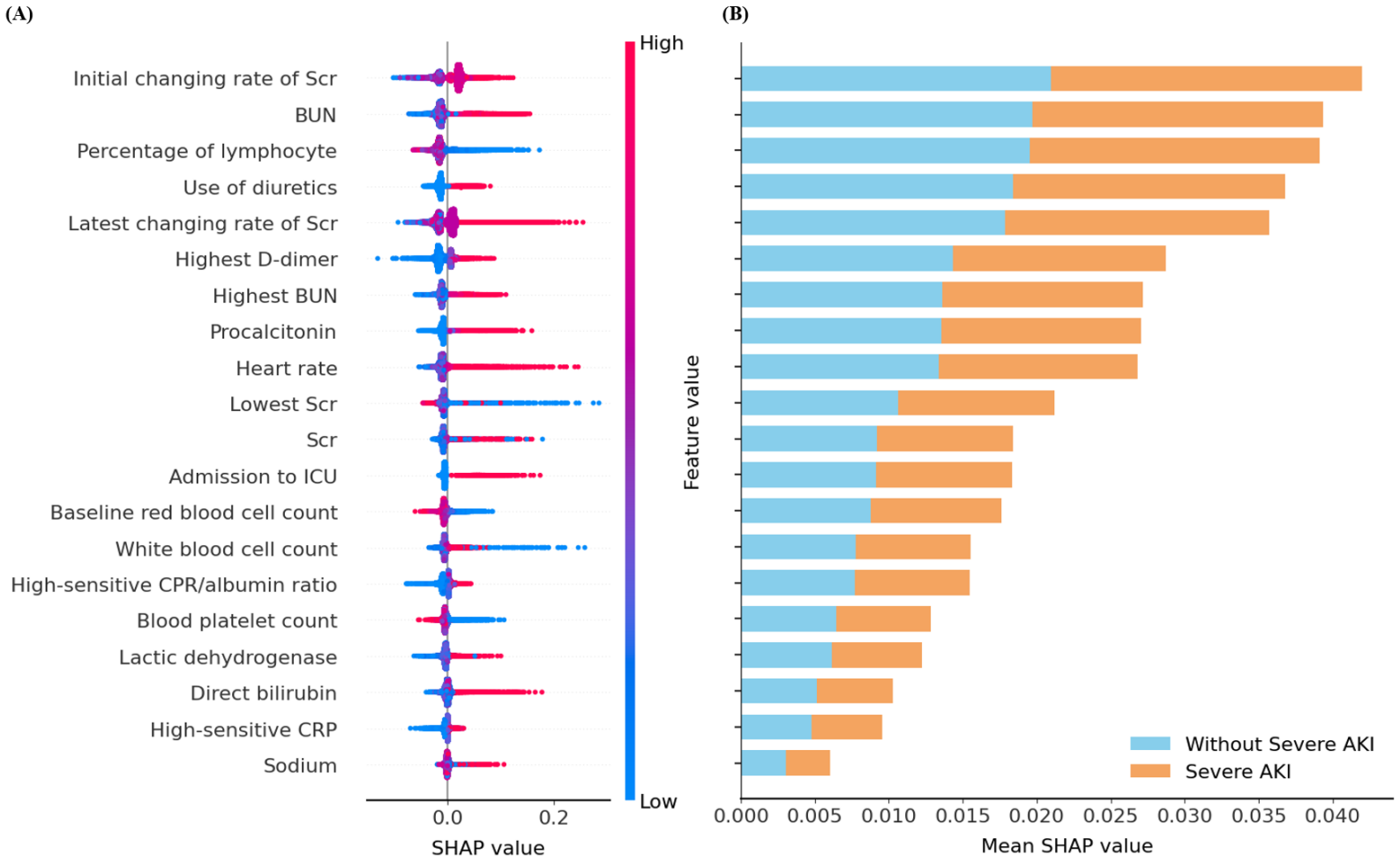
(A) Cumulative incidence plot for AKI across six cohorts; (B) Cumulative incidence plot for severe AKI across six cohorts.
Site 1, Peking University First Hospital; Site 2, Sichuan Provincial People's Hospital; Site 3, the Second Affiliated Hospital of Harbin Medical University; Site 4, Beijing Miyun District Hospital; Site 5, Peking University First Hospital Taiyuan Hospital.
Source data are provided as a Source Data file.

Figure S3 Calibration Plots for AKI and severe AKI within 48 hours in five Validation Cohorts



Calibration plots for transported models (left) and refitted models (right) predicting AKI and severe AKI within 48 hours using isotonic regression. Brier scores and *P* values (2-tailed) by Hosmer-Lemeshow test are also reported, represented as “Brier score (*P*)”. Shaded area represents 95% confidence band for each calibration line. Source data are provided as a Source Data file.

Figure S4 Model interpretability analysis of features included in the prediction model for severe AKI within 48 hours

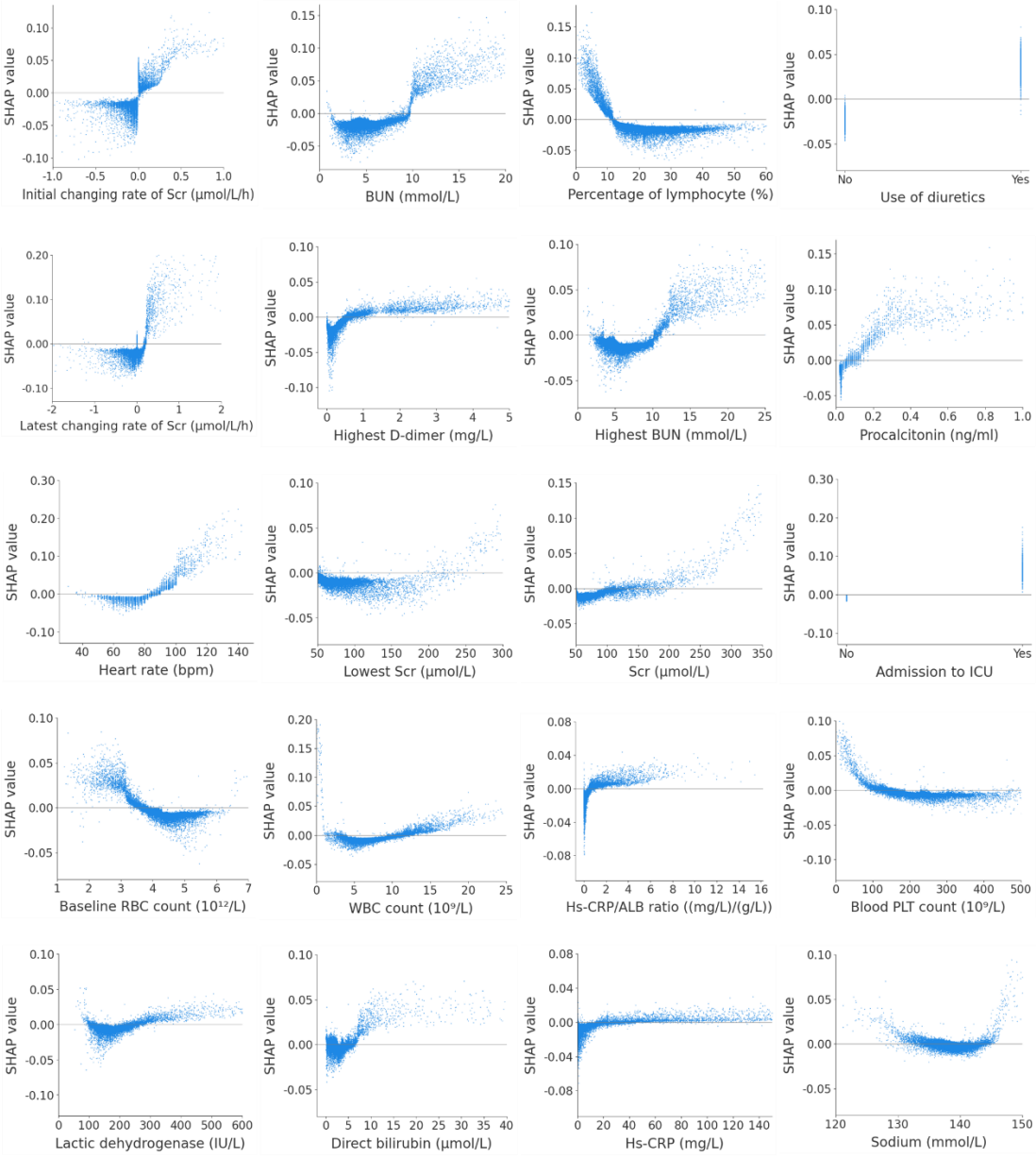


(A) SHAP summary plot of 20 features included in the prediction model for severe AKI. SHAP value represents the impact of each feature on model output, with SHAP values over zero representing an increased risk of severe AKI and higher SHAP value representing higher probability of severe AKI. Each sample in the internal validation dataset is represented as a dot per feature. Dots are colored according to feature values for each sample and accumulated vertically to depict density. (B) The mean absolute SHAP value summary plot, representing the average impact of each feature on the prediction of severe AKI.

Abbreviation: Scr, serum creatinine; BUN, blood urea nitrogen; ICU, intensive care unit; CRP, C-reactive protein; SHAP, Shapley Additive exPlanations.

Source data are provided as a Source Data file.

Figure S5 The SHAP dependence plot for features included in the prediction model for severe AKI within 48 hours

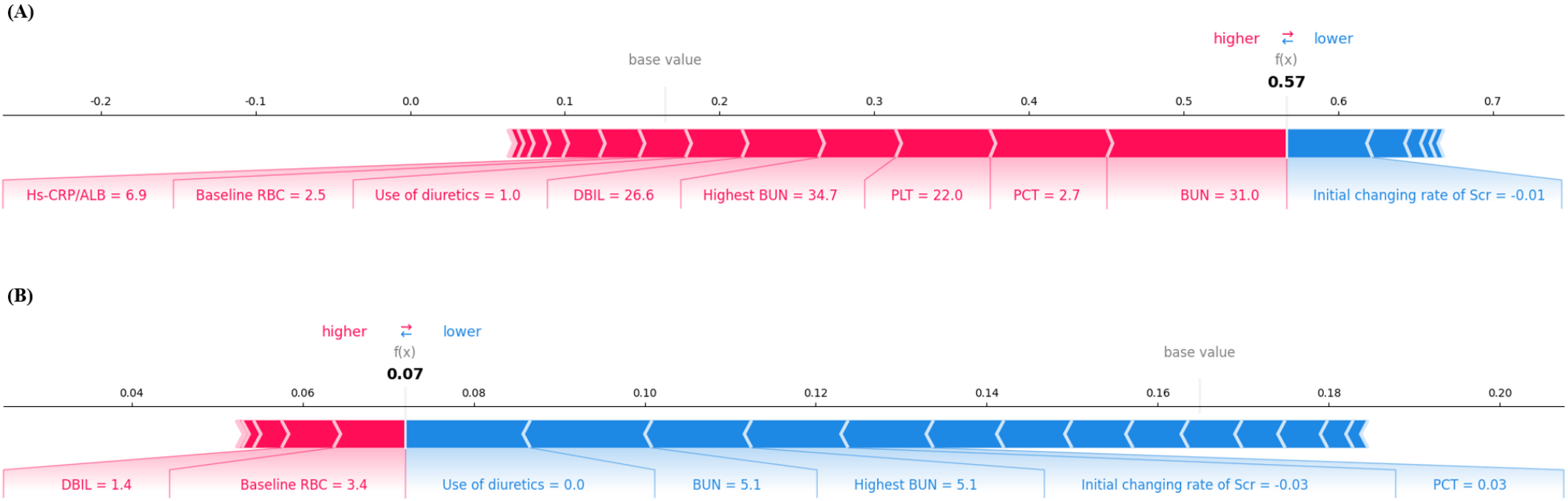


The plot shows the relationships and SHAP values. The y-axis indicates SHAP values of features, corresponding to feature values on the x-axis. The dataset was from timepoints in the predictive data timeframe, which was before the severe AKI identification for patients with severe AKI, and before hospital discharge for patients without severe AKI.

Abbreviation: Scr, serum creatinine; BUN, blood urea nitrogen; ICU, intensive care unit; RBC, red blood cell; WBC, white blood cell; Hs-CRP, high-sensitive C-reactive protein; ALB, albumin; PLT, platelet; SHAP, Shapley Additive exPlanations.

Source data are provided as a Source Data file.

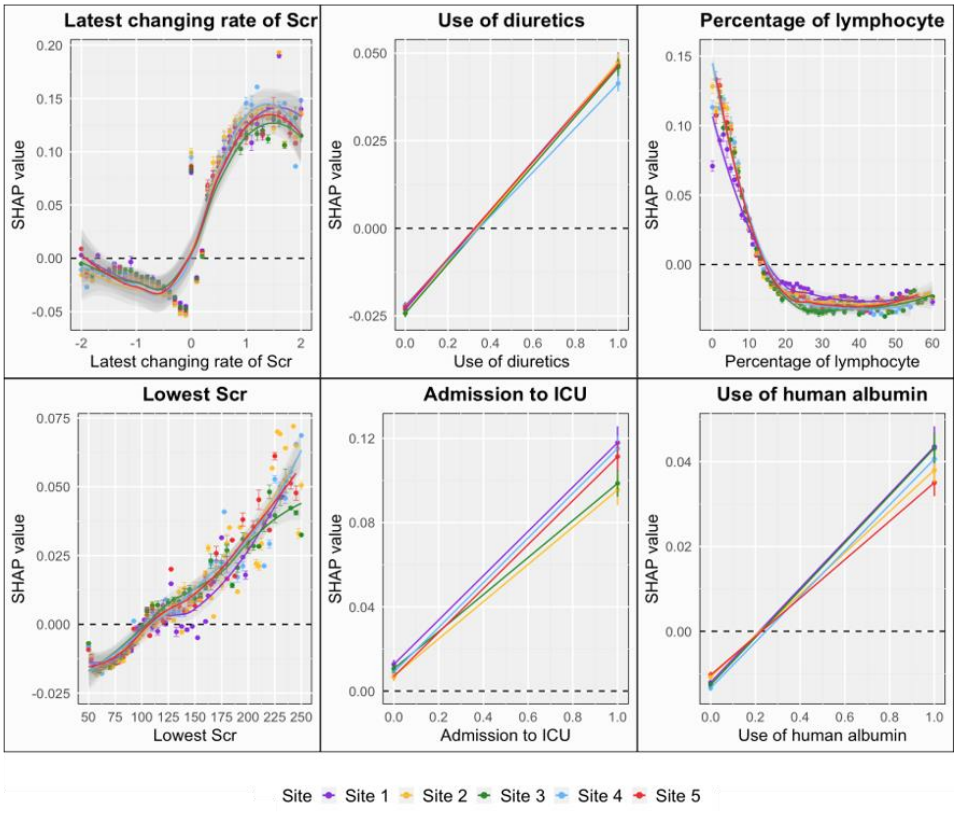
Figure S6 Force Plots showing feature contributions to model output in the prediction model for severe AKI within 48 hours



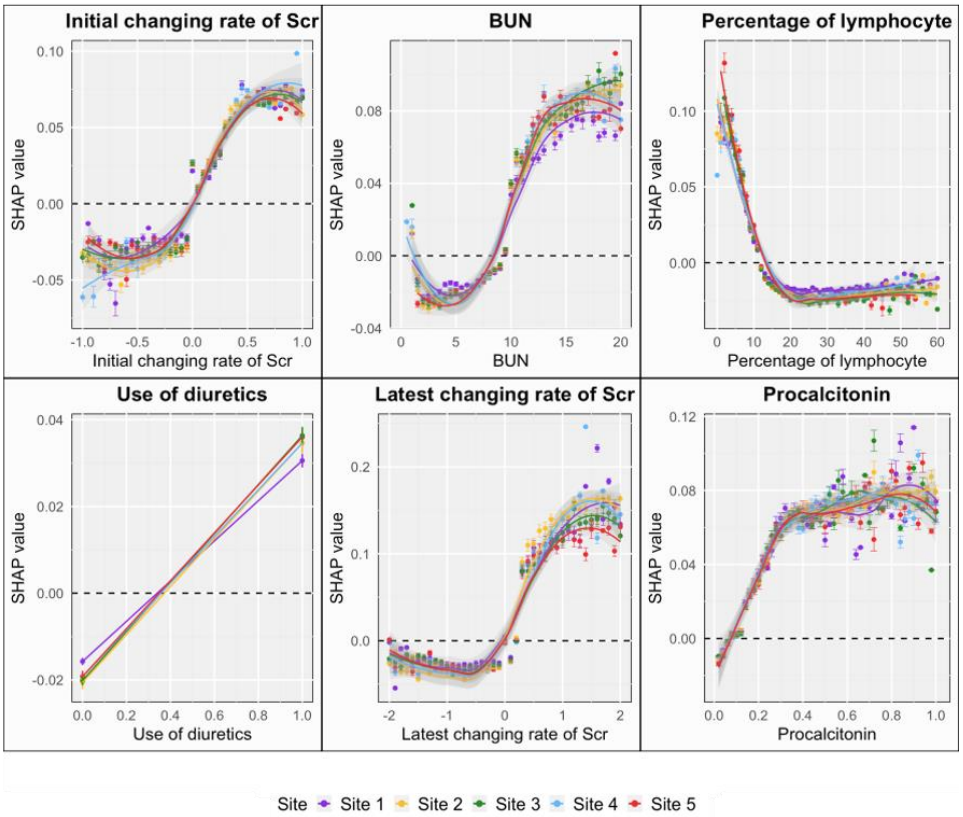
(A) Force plot of a patient with severe AKI, the model generated a predicted AKI probability of 57%. An elevated BUN and procalcitonin, low platelet count, elevated direct bilirubin, and use of diuretics are major features contributing to a higher predicted risk score.
(B) Force plot of a patient without severe AKI, the model generated a predicted AKI probability of 7%. Absence of diuretics, normal BUN, negative initial changing rate of Scr, and normal PCT are major features that drive toward a lower risk of severe AKI.
Abbreviation: Hs-CRP, high-sensitive C-reactive protein; RBC, red blood cell; DBIL, direct bilirubin; BUN, blood urea nitrogen; PLT, platelet; PCT, procalcitonin; Scr, serum creatinine.
Source data are provided as a Source Data file.

Figure S7 Marginal effect differences of top important features for predicting AKI and severe AKI within 48 hours

(A)



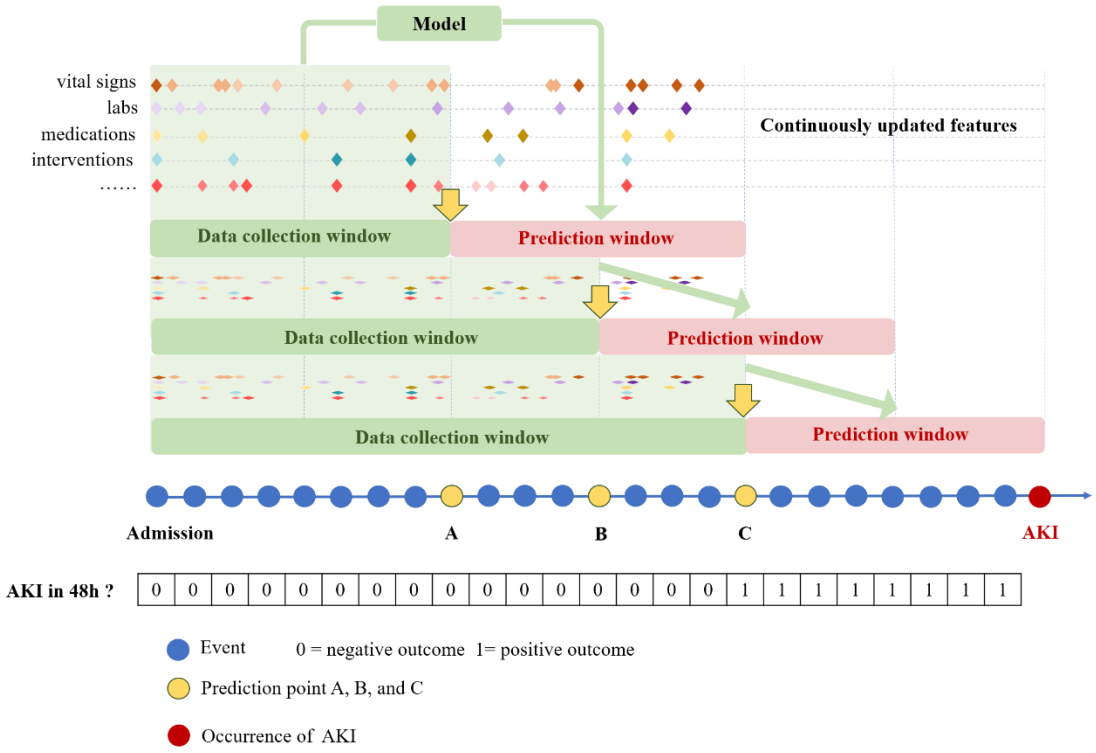
(B)



(A) Marginal effect differences of top important features for AKI within 48 hours; (B) Marginal effect differences of top important features for severe AKI within 48 hours

Marginal effects are measured by SHAP value of top important features in all validation sites. Taken certain values within a bootstrapped sample, each dot represents the corresponding average SHAP value for a variable value. Each colored vertical short line depicts a 95% confidence interval based on 100 bootstrapped samples. Shaded area represents 95% confidence band for each line.
Abbreviation: Scr, serum creatinine; ICU, intensive care unit; BUN, blood urea nitrogen.
Source data are provided as a Source Data file.

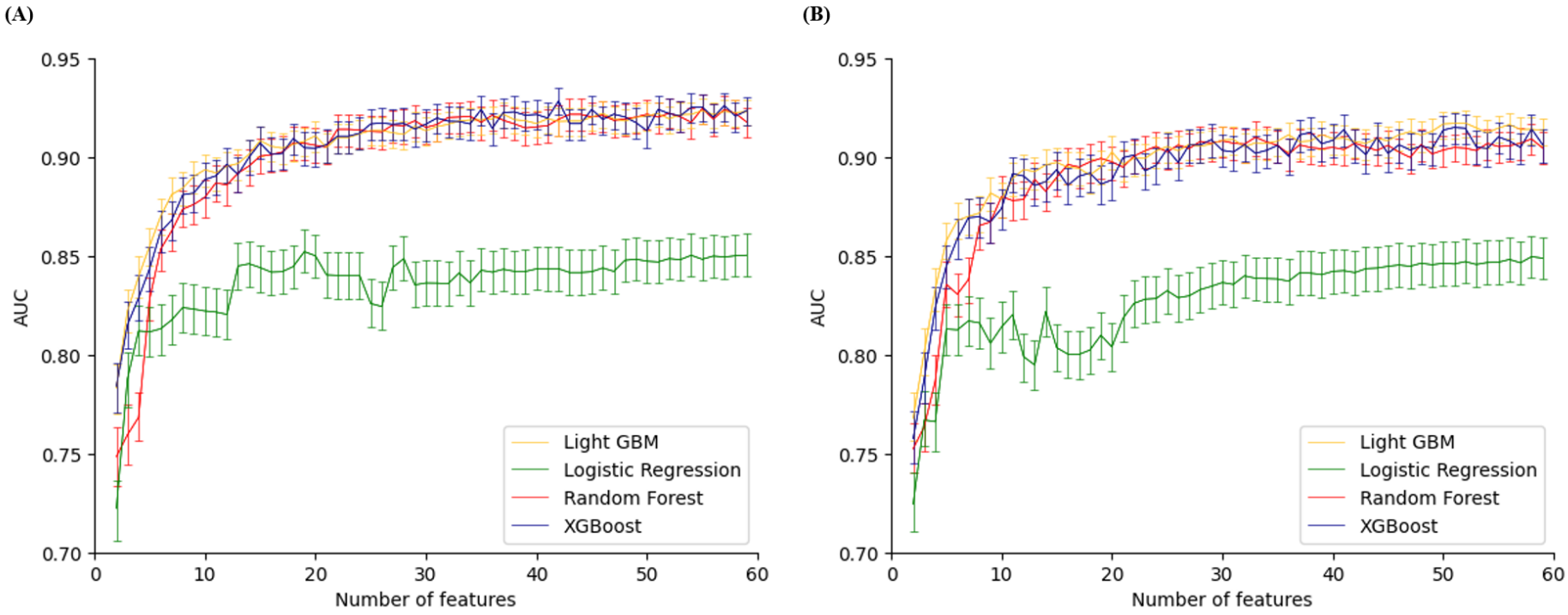
Figure S8 Illustration of Discrete-time survival analysis



Predictions are generated every 6 hours since admission, corresponding to the blue circles that denote each prediction point. Data from EHR system was updated at each prediction point and inputted into the model to predict the development of AKI within the following 48 hours on a continuous basis. With time goes on and features updated every six hours, the predictive model continuously generate new AKI predictions at regular intervals, providing ongoing prediction over the entire hospitalization. Highlighted by yellow circles, three sample prediction points (prediction point A, B, and C) exemplify dynamic predictions. At each prediction point, data from admission to the prediction point were collected, including baseline features, updated latest features, and updated feature trends. Taken the above data as input, the model will return a prediction result for AKI within the following 48 hours for each prediction point. As illustrated in the form, the results remained negative (prediction point A and

B) from admission until prediction point C. The prediction models for AKI within 24 and 72 hours shared similar pattern

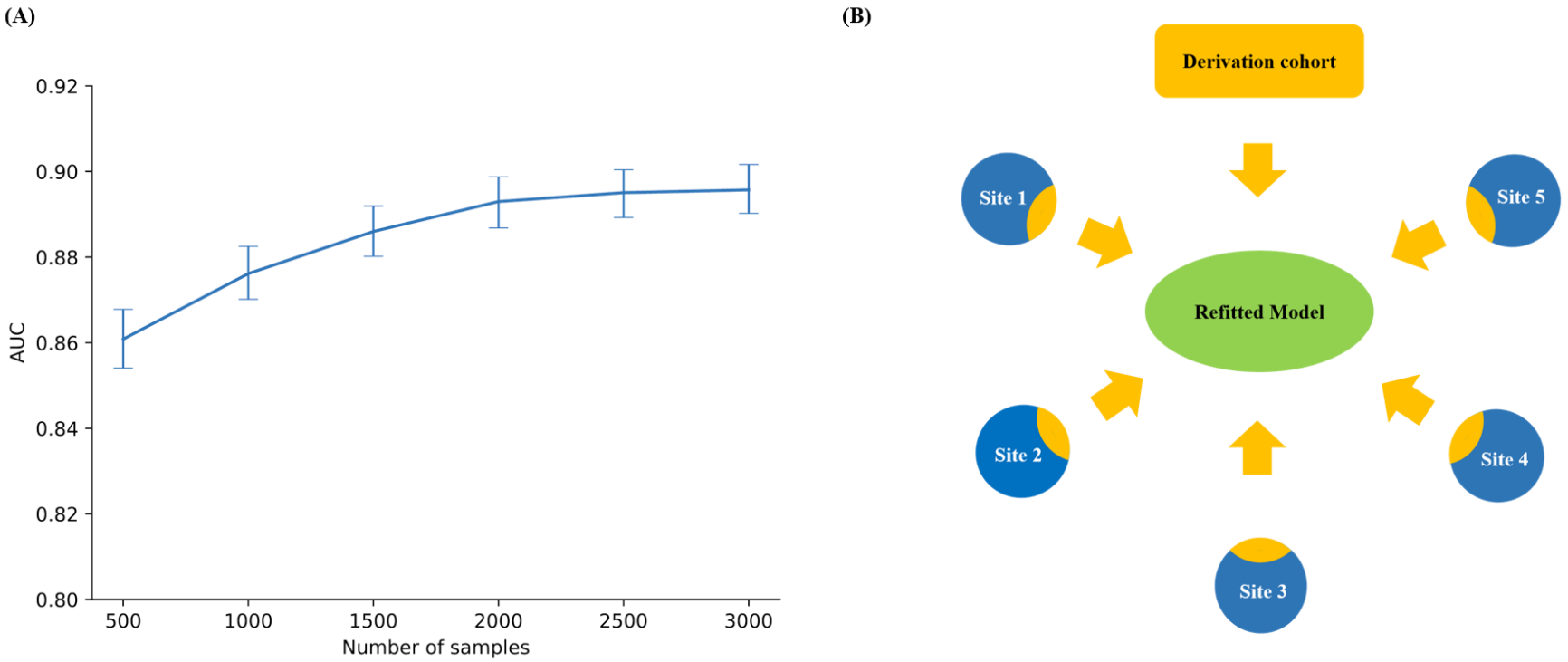
Figure S9 Selecting optimal number of features for the model



(A) Light GBM feature selection method combined with four models; (B) Random Forest feature selection method combined with four models

The plot shows the AUC of the models with increasing number of features for the prediction of AKI within 48 hours in testing set of derivation cohort using different combinations. Limited AUC improvement was observed when incorporating more than 20 features in model building for both feature selection methods. Error bars represent 95% confidence intervals. Source data are provided as a Source Data file.

Figure S10 Construction of refitted models



(A) Selecting optimal number of samples from each site for model refitting; (B) Illustration of Refitted Model

(A) The plot illustrates the AUC of the refitted model in internal validation as the sample size from each site increases. Limited AUC improvement was observed when incorporating more than 2500 samples from each site into the training dataset in model refitting. Error bars represent 95% confidence intervals. (B) The plot illustrates the development of the refitted model. Data for 2500 samples (20 features required in the original model, represented by orange area of circles) from each validation site was

extracted randomly, and incorporated into the training dataset of the derivation cohort for the training of refitted model. Then, the refitted model was validated in all validation sites (blue area of circles). Source data are provided as a Source Data file.

Item S Supplementary methods

Item S1 Details in data preprocessing

While conducting feature selection, we established a threshold of 50% for missing data proportion to exclude features with high levels of missingness, except for several specific features that were usually selectively prescribed by physicians under disease conditions with high relevance to AKI. These specific features included procalcitonin, blood culture, serum myoglobin, fecal occult blood, ANCA, and Coombs test. In the cases with missing data of these features, we made imputations with normal values (negative for binary features, average or median within normal range for continuous features), assuming that patients with no test prescriptions had been assessed by the physicians and regarded as having low risks of developing these disease conditions.

The cutoffs for excluding extreme values include: height 100-230cm; weight 20-250kg; heart rate 0-200/min; respiratory rate 0-150/min; systolic blood pressure 0-270mmHg, diastolic blood pressure 0-270mmHg, systolic blood pressure > diastolic blood pressure; other vital signs≥0; hemoglobin > 25g/L, serum potassium≥0 and <19, other laboratory test values≥0.

Item S2 Details in model building

Different feature selection strategies were compared to achieve the most satisfying performance using the minimum number of features. The combinations of two features selection methods (LightGBM and Random Forest) and four models (LightGBM, Logistic regression, Random Forest, and XGBoost) were compared for model

performance, sequential feature selection algorithm was used to determine the optimal number of features. By iteratively evaluating the AUC of the model based on increasing number of features, we found limited AUC improvement by including more than 20 features for most combinations, thus 20 was chosen as the optimal number of features. **(Figure S9)** The combination of LightGBM feature selection method and Random Forest (RF) model was chosen based on its performance in internal validation. **(Table S7)**

LightGBM could discover the correlation between features and AKI episode, especially the non-linear correlation, following a gradient-boosting framework to rank each feature. In addition, LightGBM could handle large dataset fast using a histogram-based algorithm to find the best-split point. By model training on the derivation cohort, the RF model learns the patterns and correlations between features and AKI episode, which could be used for accurate prediction. Bootstrap sampling approach was used to construct multiple training subsets during the implementation of RF model. Decision trees were employed to obtain prediction results for each subset, which are subsequently aggregated through majority voting, leading to the final prediction of AKI.

Item S3 Details in the development of refitted models

The performances of the models were evaluated both by directly transportation of the model to the validation cohorts (Transported model) and refitting the model using data from validation sites (Refitted model). By iteratively evaluating the AUC of the refitted model in internal validation based on increasing number of samples from each validation cohort incorporated into the training dataset, we found limited AUC

improvement by incorporating more than 2500 samples from each validation cohort into the training dataset. Therefore, 2500 was chosen as the optimal number of samples from each site in model refitting. **(Figure S10)**