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Abstract Topic : Acute Kidney Injury

Identification of Acute Kidney Injury Subtypes Using Deep Learning-Based Clustering of Serum Creatinine Trajectories and Clinical Features in Critically Ill Patients

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Objectives : This study aimed to classify intensive care unit (ICU) patients who developed acute kidney injury (AKI) into clusters based on serum creatinine trajectories and clinical characteristics, and to assess differences in outcomes across clusters.

Methods : In this retrospective cohort study using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, ICU patients who developed AKI (defined per KDIGO criteria) were included. Patients with end-stage kidney disease or prior kidney replacement therapy (KRT) were excluded. We collected creatinine measurements (7 days prior, 4 days after AKI onset), demographics, vital signs, comorbidities, nephrotoxin and vasopressor use, sepsis, cardiac surgery history, and laboratory results. Missing data were imputed using multiple imputation and linear interpolation. Clusters were generated via deep learning-based autoencoders and Deep Embedded K-Means clustering. The optimal number of clusters was selected using the Davies-Bouldin index. Clinical outcomes, including mortality and KRT initiation at 7, 14, and 30 days post-AKI, were compared across clusters.

Results : A total of 30,096 ICU patients with AKI were included, and ten clusters were identified. Baseline creatinine differed significantly among clusters ($p < 0.001$), highest in cluster 6 (2.90 ± 2.62 mg/dL) and lowest in cluster 2 (1.43 ± 1.10 mg/dL). Nephrotoxic medication use was highest in cluster 7 (46.8%) and lowest in cluster 8 (15.1%). Sepsis incidence was highest in cluster 5 (85.4%) and lowest in cluster 1 (14.1%). Regarding creatinine trajectories, clusters 5 and 7 exhibited abrupt elevations, while other clusters showed gradual increases. Clinical outcomes varied significantly across clusters (all $p < 0.001$). The 7-day mortality rate was highest in cluster 3 (2.44%), followed by cluster 6 (0.53%), while the 7-day KRT initiation rate was highest in cluster 7 (25.00%), followed by cluster 8 (3.45%).

Conclusions : Deep learning-based clustering identified clinically distinct AKI subtypes, which may facilitate future AKI risk stratification, biomarker discovery, and mechanistic research.

table.png



Table 1. Baseline characteristics of clusters

variable	Total population (N = 30096)	Cluster 1 (N = 10254)	Cluster 2 (N = 4332)	Cluster 3 (N = 9710)	Cluster 4 (N = 2624)	Cluster 5 (N = 89)	Cluster 6 (N = 1366)	Cluster 7 (N = 124)	Cluster 8 (N = 1198)	Cluster 9 (N = 178)	Cluster 10 (N = 221)	p-value
Male	16080 (53.4%)	4717 (46.00%)	2605 (60.13%)	5794 (59.67%)	1148 (43.75%)	46 (51.69%)	873 (63.91%)	79 (63.71%)	623 (52.00%)	95 (53.37%)	100 (45.25%)	<0.001
Age (years)	64.45 ± 16.33	64.60 ± 16.58	63.21 ± 16.58	66.35 ± 15.38	58.89 ± 17.19	54.54 ± 15.06	67.04 ± 14.72	56.60 ± 17.54	64.41 ± 16.54	62.58 ± 15.97	58.99 ± 17.25	<0.001
Weight (Kg)	82.46 ± 14.96	81.23 ± 14.96	84.33 ± 18.37	82.68 ± 16.56	80.93 ± 14.85	85.60 ± 21.83	85.70 ± 22.26	84.08 ± 21.34	83.81 ± 19.35	82.75 ± 17.95	82.24 ± 20.63	<0.001
SBP (mmHg)	88.40 ± 12.31	90.34 ± 10.82	84.70 ± 14.23	88.08 ± 11.87	90.78 ± 11.23	79.29 ± 23.08	83.42 ± 13.93	79.83 ± 21.61	89.89 ± 12.32	87.64 ± 13.18	89.00 ± 12.39	<0.001
DBP (mmHg)	45.09 ± 8.39	46.16 ± 7.70	43.86 ± 9.70	44.52 ± 7.95	46.96 ± 7.93	42.17 ± 15.51	41.09 ± 8.63	42.37 ± 15.04	45.66 ± 8.54	45.71 ± 8.05	46.59 ± 9.53	<0.001
Baseline creatinine (mg/dL)	1.61 ± 1.31	1.57 ± 1.21	1.43 ± 1.10	1.60 ± 1.16	1.44 ± 1.17	1.47 ± 1.40	2.90 ± 2.62	1.73 ± 1.42	1.58 ± 1.21	1.44 ± 1.20	1.50 ± 1.17	<0.001
pH	7.37 ± 0.07	7.37 ± 0.06	7.36 ± 0.08	7.37 ± 0.06	7.37 ± 0.07	7.31 ± 0.11	7.34 ± 0.08	7.30 ± 0.11	7.37 ± 0.06	7.36 ± 0.07	7.37 ± 0.06	<0.001
Albumin (g/dL)	3.33 ± 0.58	3.44 ± 0.56	3.16 ± 0.58	3.31 ± 0.56	3.27 ± 0.60	2.88 ± 0.72	3.16 ± 0.62	2.89 ± 0.61	3.42 ± 0.53	3.30 ± 0.50	3.26 ± 0.59	<0.001
Lactate (mg/dL)	2.04 ± 1.68	1.76 ± 1.30	2.98 ± 2.35	1.85 ± 1.32	1.85 ± 1.48	6.42 ± 4.83	2.32 ± 2.02	5.45 ± 4.43	1.92 ± 1.33	2.34 ± 1.50	2.11 ± 1.44	<0.001
Total bilirubin (mg/dL)	1.66 ± 3.52	1.02 ± 1.96	2.39 ± 3.69	1.73 ± 3.27	0.96 ± 2.37	4.05 ± 4.11	4.93 ± 9.38	3.25 ± 3.99	1.39 ± 2.25	1.84 ± 2.63	1.14 ± 1.69	<0.001
ALT (U/L)	117.65 ± 488.34	42.05 ± 128.33	347.38 ± 385.30	36.88 ± 33.10	53.10 ± 66.47	5750.82 ± 3947.92	36.58 ± 32.36	3113.80 ± 2166.36	80.86 ± 133.34	232.03 ± 556.70	96.14 ± 134.60	<0.001
AST (U/L)	182.55 ± 793.53	51.01 ± 67.42	533.85 ± 519.56	53.99 ± 52.13	69.41 ± 109.39	11786.75 ± 4317.67	51.51 ± 51.55	5018.25 ± 1184.48	109.22 ± 119.85	269.80 ± 263.22	142.51 ± 201.75	<0.001
aPTT (sec)	37.81 ± 18.69	34.84 ± 12.11	39.62 ± 20.20	34.81 ± 9.91	35.28 ± 13.09	46.19 ± 26.46	80.68 ± 43.64	39.51 ± 15.85	37.00 ± 15.83	37.07 ± 15.23	37.70 ± 18.73	<0.001
PT INR	1.53 ± 0.83	1.41 ± 0.63	1.81 ± 1.12	1.43 ± 0.59	1.43 ± 0.99	3.78 ± 2.72	1.93 ± 1.23	2.55 ± 1.40	1.48 ± 0.69	1.55 ± 0.67	1.62 ± 1.04	<0.001
Calcium (mg/dL)	8.33 ± 1.70	8.68 ± 1.14	7.29 ± 2.84	8.29 ± 1.52	8.67 ± 1.24	7.65 ± 1.75	8.50 ± 1.20	7.45 ± 2.01	8.54 ± 1.25	7.98 ± 2.16	8.58 ± 1.16	<0.001
Platelet (x10³/μL)	220.82 ± 117.91	269.15 ± 47.47	167.19 ± 65.22	134.19 ± 45.35	482.71 ± 126.11	137.54 ± 86.54	139.57 ± 65.33	126.62 ± 73.23	214.26 ± 39.71	201.42 ± 76.21	366.56 ± 37.93	<0.001
WBC (x10³/μL)	11.09 ± 8.96	10.97 ± 7.40	12.16 ± 8.69	9.62 ± 7.17	14.06 ± 8.05	14.88 ± 7.36	11.01 ± 7.74	13.77 ± 7.93	12.41 ± 20.10	11.24 ± 6.00	15.57 ± 31.34	<0.001
Hemoglobin (g/dL)	10.66 ± 2.24	10.97 ± 2.25	10.90 ± 2.24	10.31 ± 2.14	10.54 ± 2.26	10.46 ± 2.19	9.74 ± 2.12	10.80 ± 2.19	11.06 ± 2.31	11.02 ± 2.31	10.53 ± 2.27	<0.001
Anion gap (mmol/L)	15.30 ± 4.26	15.20 ± 3.90	16.41 ± 4.83	14.19 ± 3.66	16.21 ± 4.54	23.40 ± 6.60	17.58 ± 5.03	21.02 ± 6.86	15.22 ± 3.78	15.72 ± 4.40	16.48 ± 4.08	<0.001
Chloride (mmol/L)	101.37 ± 6.21	100.77 ± 6.02	102.11 ± 6.08	102.46 ± 5.97	99.23 ± 6.47	100.30 ± 6.49	100.63 ± 7.46	101.45 ± 6.56	101.00 ± 5.87	101.88 ± 5.89	99.27 ± 6.17	<0.001
Sodium (mmol/L)	137.42 ± 5.09	137.46 ± 4.95	137.73 ± 5.03	137.69 ± 5.02	136.14 ± 5.07	138.16 ± 5.78	136.71 ± 6.53	137.94 ± 5.28	137.49 ± 4.62	137.58 ± 5.08	136.16 ± 4.81	<0.001
Bicarbonate (mmol/L)	23.39 ± 5.06	24.12 ± 4.90	22.13 ± 5.02	23.53 ± 4.83	23.63 ± 5.26	17.03 ± 5.18	21.05 ± 5.78	18.19 ± 4.97	23.91 ± 4.85	22.98 ± 4.62	23.04 ± 4.62	<0.001
Potassium (mmol/L)	4.41 ± 0.76	4.39 ± 0.75	4.52 ± 0.80	4.33 ± 0.68	4.49 ± 0.84	4.68 ± 1.02	4.52 ± 0.85	4.58 ± 0.90	4.39 ± 0.72	4.51 ± 0.82	4.50 ± 0.87	<0.001
BUN (mg/dL)	34.40 ± 23.01	32.44 ± 20.98	32.78 ± 20.80	33.62 ± 18.61	28.79 ± 20.96	38.42 ± 20.44	71.06 ± 39.75	39.34 ± 22.84	33.81 ± 21.51	31.47 ± 21.18	32.52 ± 26.82	<0.001
Norepinephrine (%)	2876 (9.6%)	553 (5.39%)	726 (16.76%)	926 (9.54%)	163 (6.21%)	47 (52.81%)	287 (21.01%)	66 (53.23%)	69 (5.76%)	19 (10.67%)	20 (9.05%)	<0.001
Dopamine (%)	437 (1.5%)	101 (0.98%)	136 (3.14%)	101 (1.04%)	20 (0.76%)	8 (8.99%)	45 (3.29%)	7 (5.65%)	12 (1.00%)	3 (1.69%)	4 (1.81%)	<0.001
Vasopressin (%)	1201 (4.0%)	177 (1.73%)	349 (8.06%)	391 (4.03%)	63 (2.40%)	30 (33.71%)	119 (8.71%)	38 (30.65%)	19 (1.59%)	8 (4.49%)	7 (3.17%)	<0.001
Epinephrine (%)	749 (2.5%)	63 (0.61%)	284 (6.56%)	301 (3.10%)	14 (0.53%)	11 (12.36%)	30 (2.20%)	23 (18.55%)	12 (1.00%)	7 (3.93%)	4 (1.81%)	<0.001
Nephrotoxin medication (%)	6376 (21.2%)	1740 (16.97%)	1068 (24.65%)	2126 (21.89%)	678 (25.84%)	38 (42.70%)	390 (28.55%)	58 (46.77%)	181 (15.11%)	38 (21.35%)	59 (26.70%)	<0.001
Chronic pulmonary disease (%)	7574 (25.2%)	2742 (26.74%)	1021 (23.57%)	2346 (24.16%)	651 (24.81%)	15 (16.85%)	347 (25.40%)	34 (27.42%)	320 (26.71%)	37 (20.79%)	61 (27.60%)	<0.001
Chronic kidney disease (%)	9655 (32.1%)	3202 (31.23%)	1156 (26.69%)	3562 (36.68%)	500 (19.05%)	16 (17.98%)	693 (50.73%)	17 (13.71%)	401 (33.47%)	47 (26.40%)	61 (27.60%)	<0.001
Hypertension (%)	14618 (48.6%)	5209 (50.80%)	2194 (50.65%)	4548 (46.84%)	1262 (48.09%)	27 (30.34%)	534 (39.09%)	57 (45.97%)	603 (50.33%)	89 (50.00%)	95 (42.99%)	<0.001
Cardiac surgery (%)	1901 (6.3%)	184 (1.79%)	658 (15.19%)	963 (9.92%)	14 (0.53%)	0 (0.00%)	14 (1.02%)	6 (4.84%)	43 (3.59%)	18 (10.11%)	1 (0.45%)	<0.001
Myocardial infarct (%)	4596 (15.3%)	1427 (13.92%)	701 (16.18%)	1578 (16.25%)	255 (9.72%)	21 (23.60%)	334 (24.45%)	24 (19.35%)	205 (17.11%)	28 (15.73%)	23 (10.41%)	<0.001
Congestive heart failure (%)	10464 (34.8%)	3586 (34.97%)	1438 (33.19%)	3480 (35.84%)	627 (23.89%)	31 (34.83%)	691 (50.59%)	41 (33.06%)	459 (38.31%)	53 (29.78%)	58 (26.24%)	<0.001
Cerebrovascular disease (%)	2845 (9.5%)	1016 (9.91%)	386 (8.91%)	982 (10.11%)	172 (6.55%)	6 (6.74%)	125 (9.15%)	10 (8.06%)	124 (10.35%)	17 (9.55%)	7 (3.17%)	<0.001
Chronic liver disease (%)	4396 (14.6%)	762 (7.43%)	734 (16.94%)	2021 (20.81%)	181 (6.90%)	52 (58.43%)	431 (31.55%)	73 (58.87%)	103 (8.60%)	18 (10.11%)	21 (9.50%)	<0.001
Diabetes (%)	11423 (38.0%)	4124 (40.22%)	1514 (34.95%)	3632 (37.40%)	868 (33.08%)	23 (25.84%)	605 (44.29%)	28 (22.58%)	489 (40.82%)	53 (29.78%)	87 (39.37%)	<0.001
Cancer (%)	4774 (15.9%)	1478 (14.41%)	625 (14.43%)	1711 (17.62%)	532 (20.27%)	10 (11.24%)	192 (14.06%)	21 (16.94%)	153 (12.77%)	25 (14.04%)	27 (12.22%)	<0.001
Sepsis (%)	6704 (22.3%)	1447 (14.11%)	1498 (34.58%)	2364 (24.35%)	426 (16.23%)	76 (85.39%)	516 (37.77%)	92 (74.19%)	203 (16.94%)	44 (24.72%)	38 (17.19%)	<0.001

SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; aPTT, activated partial thromboplastin time; PT INR, prothrombin time international normalized ratio; WBC, white blood cell; BUN, blood urea nitrogen.



Figure 1. Davies-Bouldin index

Figure 2. t-SNE

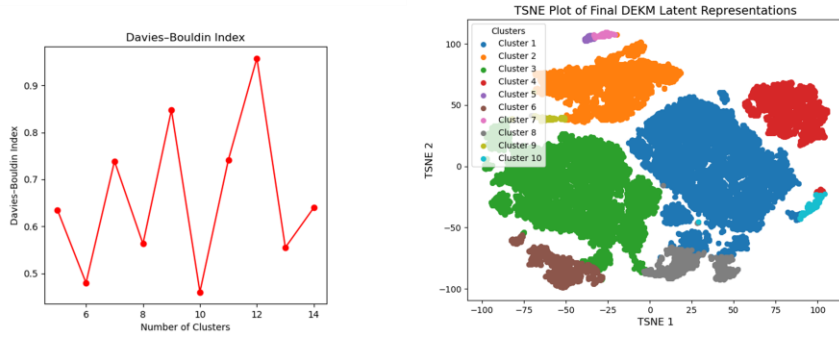


Figure 3. Creatinine trajectory

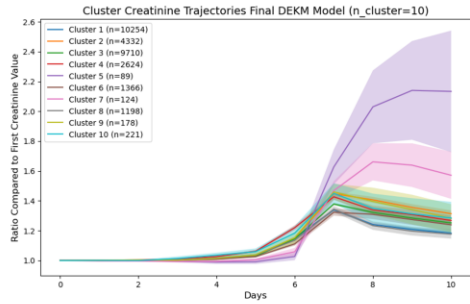


Figure 4. Outcomes

