

Supplementary Figures and Tables:

Figure Legends:

Figure S1: Incremental AUC by adding 1 more day of post-anticoagulant D-dimer measurements among a subset of 687 patients that have 7 day observation time. After 3 days, the incremental AUC is marginal.

Figure S2: Adjusted ORs estimates and 95% CI for model including post-anticoagulant fibrinogen levels in subset of 668 patients. Post-anticoagulant D-Dimer groups remain the most critical predictors of in-hospital mortality.

Figure S1:

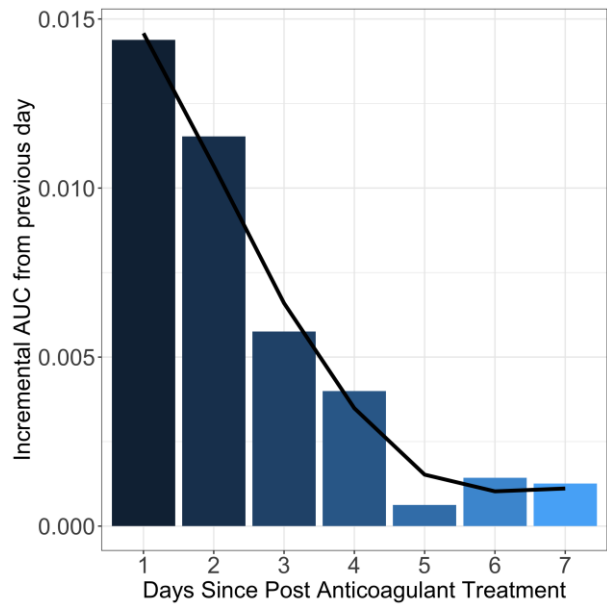


Figure S2:

Variable	OR	95% CI
Post-A/C D-dimer HI vs. LD	20.86	(6.87,63.31)
Post-A/C D-dimer LI vs. LD	7.8	(2.28,26.69)
Post-A/C D-dimer HD vs. LD	7.01	(2.3,21.31)
ARDS (Yes vs. No)	2.46	(1.29,4.71)
Age (years)	1.03	(1.01,1.05)
Monocyte (%)	0.89	(0.82,0.96)

Table S1: Characteristics of Hospitalized COVID-19 Patients Stratified by Survival			
Characteristic	Discharged from Hospital	Deceased in Hospital	P-value
N	1365	470	
Age in years - median [IQR]	65 [54, 75]	73 [65, 83]	<0.001*
Male sex — no. (%)	805 (59.0)	262 (55.7)	0.242
Race and ethnic group — no. (%)			0.374
Non-Hispanic white	275 (20.1)	111 (23.6)	
Non-Hispanic black	277 (20.3)	83 (17.7)	
Hispanic	404 (29.6)	138 (29.4)	
Other	236 (17.3)	73 (15.5)	
Missing data	173 (12.7)	65 (13.8)	
Smoking status — no. (%)			0.714
Never smoker	688 (50.4)	229 (48.7)	
Ever smoker	384 (28.1)	132 (28.1)	
Missing data	293 (21.5)	109 (23.2)	
Baseline diagnoses — no. (%)			
Asthma	88 (6.4)	26 (5.5)	0.55
Chronic obstructive pulmonary disease	62 (4.5)	30 (6.4)	0.146
Hypertension	489 (35.8)	211 (44.9)	0.001*
Obstructive sleep apnea	31 (2.3)	8 (1.7)	0.581
Obesity	115 (8.4)	38 (8.1)	0.894
Diabetes	348 (25.5)	117 (24.9)	0.844
Chronic kidney disease	161 (11.8)	68 (14.5)	0.152
HIV	24 (1.8)	7 (1.5)	0.855
Cancer	110 (8.1)	45 (9.6)	0.356
Coronary artery disease	162 (11.9)	84 (17.9)	0.001
Atrial fibrillation	84 (6.2)	50 (10.6)	0.002

Heart failure	86 (6.3)	35 (7.4)	0.45
Chronic viral hepatitis	21 (1.5)	2 (0.4)	0.103
Alcoholic nonalcoholic liver disease	28 (2.1)	8 (1.7)	0.781
Acute respiratory distress syndrome	107 (7.8)	110 (23.4)	<0.001*
Acute kidney injury	260 (19.0)	205 (43.6)	<0.001*
Cerebral infarction	61 (4.5)	26 (5.5)	0.418
Intracerebral hemorrhage	5 (0.4)	2 (0.4)	1
BMI (kg/m²) - median [IQR]	27.55 [23.88, 32.12]	27.46 [24.32, 32.48]	0.331
Initial vital signs — median [IQR]			
Systolic blood pressure maximum — mm Hg	143 [129, 159]	144 [129, 161]	0.531
Diastolic blood pressure maximum — mm Hg	83 [76, 92]	81 [73, 91]	0.017
Heart rate maximum — beats/min	101.00 [90.75, 114.00]	103.00 [91.00, 120.75]	0.009
Respiratory rate maximum — breaths/min	22 [20, 28]	24 [20, 30]	<0.001*
Temperature max — fahrenheit	99.80 [98.60, 101.30]	99.60 [98.60, 101.10]	0.064
Oxygen saturation minimum — %	93 [90, 95]	90 [84, 94]	<0.001*
Days from encounter to first therapeutic dose of anticoagulant — median [IQR]	0.55 [0.20, 1.68]	0.67 [0.24, 2.13]	0.017
Laboratory tests — median [IQR]			
Baseline D-dimer (ug/mL)	1.37 [0.79, 2.46]	1.76 [1.08, 2.92]	<0.001*

Platelet (x10E3/uL)	221.00 [167.00, 293.00]	187.00 [147.00, 244.00]	<0.001*
Mean platelet volume mpv (FL)	8.40 [7.70, 9.20]	8.70 [7.90, 9.53]	0.002
Red blood cell (RBC) count (x10E6/uL)	4.27 [3.79, 4.76]	4.36 [3.77, 4.75]	0.564
While blood cell (WBC) count (x10E3/uL)	7.60 [5.50, 10.40]	8.14 [5.90, 12.28]	0.011
Lymphocyte % (%)	13.05 [8.30, 18.58]	11.00 [7.25, 16.95]	0.003
Lymphocyte no. (x10E3/uL)	1.00 [0.70, 1.30]	0.90 [0.60, 1.30]	0.024
Neutrophil % (%)	78.60 [70.45, 84.77]	81.90 [73.40, 87.10]	<0.001*
Neutrophil no. (x10E3/uL)	5.90 [3.90, 8.71]	6.65 [4.50, 10.53]	0.002
Monocyte % (%)	6.40 [4.30, 9.10]	5.10 [3.30, 8.70]	<0.001*
Monocyte no. (x10E3/uL)	0.50 [0.30, 0.70]	0.40 [0.30, 0.70]	0.012
Basophil % (%)	0.20 [0.10, 0.40]	0.10 [0.00, 0.30]	<0.001*
Basophil no. (x10e3/uL)	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.104
Eosinophil % (%)	0.20 [0.00, 0.70]	0.10 [0.10, 0.30]	0.018
Eosinophil no. (x10E3/uL)	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.002
Mean corpuscular hemoglobin (MCH)	29.90 [28.30,	29.90	0.806

(pg)	31.10]	[28.10, 31.40]	
Mean corpuscular hemoglobin concentration (MCHC) (g/dL)	32.90 [32.10, 33.60]	32.65 [31.80, 33.40]	0.011
Mean corpuscular volume (MCV) (fL)	90.40 [86.50, 93.80]	91.15 [86.82, 94.90]	0.074
Serum creatinine (mg/dL)	0.95 [0.73, 1.41]	1.20 [0.82, 2.00]	<0.001*
C-reactive protein (mg/L)	113.50 [53.70, 194.30]	159.10 [90.82, 235.70]	<0.001*
Estimated glomerular filtration rate (EGFR) (ml/min/1.73m ²)	54.00 [30.15, 77.00]	41.28 [26.00, 58.33]	<0.001*
Blood urea nitrogen (BUN) (mg/dL)	18.00 [12.00, 31.00]	26.00 [15.25, 47.75]	<0.001*
Alanine aminotransferase (ALT) (u/L)	30.00 [19.00, 50.00]	30.00 [20.25, 50.75]	0.885
aspartate aminotransferase (AST) (U/L)	40.00 [27.00, 63.50]	48.00 [33.00, 71.75]	<0.001*
Total bilirubin (mg/dL)	0.60 [0.40, 0.80]	0.50 [0.40, 0.80]	0.356
Glucose (mg/dL)	116.50 [97.00, 164.75]	133.00 [105.00, 186.50]	<0.001*
Lactate dehydrogenase (LDH) (U/L)	412.00 [312.00, 528.50]	516.50 [381.25, 660.75]	<0.001*
Hemoglobin (g/dL)	12.70 [11.10, 13.90]	12.90 [11.10, 14.10]	0.448
Ferritin (ng/mL)	697.00 [330.00, 1512.00]	1038.00 [480.00,]	<0.001*

		2092.00]	
Calcium (mg/dL)	8.30 [7.90, 8.70]	8.20 [7.70, 8.60]	0.001
Albumin (g/dL)	3.00 [2.70, 3.40]	2.90 [2.60, 3.20]	0.001
Sodium (MEQ/L)	138.00 [135.00, 140.00]	137.50 [134.00, 144.00]	0.102
Potassium (mmol/L)	4.20 [3.70, 4.60]	4.30 [3.83, 4.88]	0.002
Chloride (mEq/L)	103.00 [99.00, 106.00]	104.00 [100.00, 108.00]	<0.001*
Anion gap (mEq/L)	11.90 [10.00, 14.00]	12.20 [10.20, 15.00]	0.002
Post A/C D-dimer values			
Mean D-dimer (ug/ml)	1.69 [0.86, 3.41]	3.71 [1.98, 8.05]	<0.001*
Trend D-dimer (ug/ml per day)	-0.05 [-0.21, 0.04]	0.09 [-0.12, 0.60]	<0.001*

Table S2: Characteristics of Hospitalized COVID-19 Patients Stratified by post-anticoagulant D-dimer groups

Characteristic	Patients with high and increasing D-dimer	Patients with high and decreasing D-dimer	Patients with low and increasing D-dimer	Patients with low and decreasing D-dimer	P-value for Independence	P-value for high vs low groups	P-value for Increasing vs decreasing in high group	P-value for Increasing vs decreasing in low group
N	430	508	337	560				
In-hospital mortality — no. (%)	212 (49.3)	137 (27.0)	70 (20.8)	51 (9.1)				
Age in years - median [IQR]	70 [61, 80]	70.00 [61.00, 79.00]	63.00 [53.00, 74.00]	64.00 [54.00, 74.25]	<0.001	<0.001	0.293	0.609
Male sex — no. (%)	253 (58.8)	311 (61.2)	204 (60.5)	299 (53.4)	0.045	0.087	0.499	0.044
Race and ethnic group — no. (%)						0.303	0.882	0.122
Non-Hispanic white	89 (20.7)	103 (20.3)	67 (19.9)	127 (22.7)				
Non-Hispanic black	89 (20.7)	113 (22.2)	74 (22.0)	84 (15.0)				
Hispanic	126 (29.3)	143 (28.1)	100 (29.7)	173 (30.9)				
Other	66 (15.3)	86 (16.9)	56 (16.6)	101 (18.0)				
Missing data	60 (14.0)	63 (12.4)	40 (11.9)	75 (13.4)				
Smoking status — no. (%)						0.832	0.472	0.79

Never smoker	208 (48.4)	264 (52.0)	171 (50.7)	274 (48.9)				
Ever smoker	120 (27.9)	138 (27.2)	97 (28.8)	161 (28.7)				
Missing data	102 (23.7)	106 (20.9)	69 (20.5)	125 (22.3)				
No of baseline comorbidities — no. (%)					<0.001	<0.001	0.456	0.355
0	88 (20.5)	121 (23.8)	121 (35.9)	215 (38.4)				
1-2	193 (44.9)	215 (42.3)	117 (34.7)	205 (36.6)				
3+	149 (34.7)	172 (33.9)	99 (29.4)	140 (25)				
Baseline diagnoses — no. (%)								
Asthma	20 (4.7)	23 (4.5)	30 (8.9)	41 (7.3)	0.022	0.004	1	0.471
Chronic obstructive pulmonary disease	28 (6.5)	18 (3.5)	22 (6.5)	24 (4.3)	0.087	0.91	0.052	0.187
Hypertension	179 (41.6)	211 (41.5)	114 (33.8)	196 (35.0)	0.021	0.002	1	0.776
Obstructive sleep apnea	10 (2.3)	7 (1.4)	7 (2.1)	15 (2.7)	0.517	0.43	0.402	0.733
Obesity	37 (8.6)	30 (5.9)	36 (10.7)	50 (8.9)	0.084	0.07	0.141	0.455
Diabetes	112 (26.0)	140 (27.6)	79 (23.4)	134 (23.9)	0.446	0.138	0.655	0.932

Chronic kidney disease	62 (14.4)	79 (15.6)	36 (10.7)	52 (9.3)	0.007	0.001	0.695	0.572
HIV	6 (1.4)	12 (2.4)	4 (1.2)	9 (1.6)	0.543	0.549	0.403	0.825
Cancer	32 (7.4)	48 (9.4)	26 (7.7)	49 (8.8)	0.677	0.964	0.327	0.676
Coronary artery disease	58 (13.5)	73 (14.4)	48 (14.2)	67 (12.0)	0.656	0.515	0.769	0.376
Atrial fibrillation	35 (8.1)	33 (6.5)	29 (8.6)	37 (6.6)	0.536	1	0.4	0.328
Heart failure	33 (7.7)	27 (5.3)	26 (7.7)	35 (6.2)	0.398	0.799	0.181	0.479
Chronic viral hepatitis	3 (0.7)	7 (1.4)	4 (1.2)	9 (1.6)	0.634	0.598	0.489	0.825
Alcoholic nonalcoholic liver disease	6 (1.4)	8 (1.6)	10 (3.0)	12 (2.1)	0.395	0.189	1	0.582
Acute respiratory distress syndrome	94 (21.9)	73 (14.4)	24 (7.1)	26 (4.6)	<0.001	<0.001	0.004	0.157
Acute kidney injury	167 (38.8)	167 (32.9)	58 (17.2)	73 (13.0)	<0.001	<0.001	0.067	0.106
Cerebral infarction	17 (4.0)	31 (6.1)	18 (5.3)	21 (3.8)	0.245	0.506	0.18	0.336
Intracerebral hemorrhage	2 (0.5)	1 (0.2)	2 (0.6)	2 (0.4)	0.815	0.953	0.885	1
BMI (kg/m²) - median [IQR]	27.46 [23.86, 32.79]	26.46 [23.04, 31.06]	28.13 [24.48, 32.53]	27.90 [24.58, 32.54]	<0.001	0.001	0.003	0.621
Initial vital signs — median [IQR]								
Systolic blood pressure maximum — mm Hg	146.00 [131.25, 163.75]	145.00 [131.00, 163.00]	140.00 [127.00, 156.00]	141.00 [127.00, 156.00]	<0.001	<0.001	0.748	0.944

Diastolic blood pressure maximum — mm Hg	82.50 [74.00, 92.00]	84.00 [76.00, 93.00]	82.00 [75.00, 90.00]	82.00 [74.00, 90.00]	0.021	0.01	0.135	0.516
Heart rate maximum — beats/min	102.00 [89.00, 118.00]	104.00 [92.00, 117.00]	102.00 [91.00, 114.00]	100.00 [90.00, 113.00]	0.063	0.022	0.236	0.437
Respiratory rate maximum — breaths/min	22.00 [20.00, 30.00]	22.00 [20.00, 30.00]	21.00 [20.00, 26.00]	21.50 [20.00, 26.00]	<0.001	<0.001	0.796	0.393
Temperature max — fahrenheit	99.70 [98.60, 101.20]	99.50 [98.60, 100.80]	100.00 [98.80, 101.70]	99.90 [98.70, 101.30]	<0.001	<0.001	0.054	0.132
Oxygen saturation minimum — %	91.00 [87.00, 94.00]	92.00 [87.00, 95.00]	93.00 [90.00, 95.00]	93.00 [90.00, 95.00]	<0.001	<0.001	0.163	0.059
Time from encounter to first therapeutic dose of anticoagulant — median [IQR]	0.71 [0.24, 2.57]	0.68 [0.22, 1.96]	0.54 [0.21, 1.71]	0.49 [0.18, 1.41]	0.001	<0.001	0.426	0.163
Initial laboratory tests — median [IQR]								
D-dimer (ug/mL FEU)	2.10 [1.30, 3.23]	3.35 [2.05, 7.14]	0.87 [0.54, 1.28]	1.11 [0.72, 1.58]	<0.001	<0.001	<0.001	<0.001
Platelet (x10E3/uL)	203.00 [163.00, 282.00]	226.00 [163.00, 290.50]	194.00 [150.00, 256.00]	216.00 [159.00, 285.50]	0.038	0.119	0.191	0.036
Mean platelet volume mpv (fL)	8.50 [7.80, 9.40]	8.60 [7.70, 9.50]	8.40 [7.70, 9.20]	8.40 [7.70, 9.20]	0.613	0.195	0.724	0.9

RBC count (x10E6/uL)	4.25 [3.69, 4.72]	4.13 [3.56, 4.69]	4.39 [3.98, 4.79]	4.33 [3.96, 4.80]	<0.001	<0.001	0.247	0.623
WBC count (x10E3/uL)	8.20 [5.90, 12.20]	8.85 [6.20, 11.88]	6.60 [4.84, 8.80]	7.15 [5.20, 10.10]	<0.001	<0.001	0.257	0.115
Lymphocyte % (%)	11.80 [7.50, 17.20]	9.90 [6.55, 16.80]	14.10 [9.60, 20.10]	13.95 [9.12, 20.65]	<0.001	<0.001	0.049	0.908
Lymphocyte no. (x10E3/uL)	0.90 [0.70, 1.30]	0.90 [0.60, 1.30]	0.90 [0.70, 1.30]	0.90 [0.70, 1.30]	0.425	0.108	0.715	0.785
Neutrophil % (%)	80.80 [72.62, 86.80]	81.85 [74.30, 87.00]	77.00 [69.60, 83.50]	77.10 [68.93, 84.18]	<0.001	<0.001	0.241	0.788
Neutrophil no. (x10E3/uL)	6.50 [4.25, 10.15]	7.35 [4.90, 10.45]	5.06 [3.50, 7.40]	5.40 [3.70, 7.80]	<0.001	<0.001	0.062	0.184
Monocyte no. (x10E3/uL)	0.50 [0.30, 0.70]	0.50 [0.30, 0.70]	0.50 [0.30, 0.70]	0.40 [0.30, 0.60]	0.045	0.04	0.67	0.048
Monocyte % (%)	6.05 [3.68, 9.23]	5.60 [4.00, 8.20]	6.60 [4.80, 9.60]	6.30 [4.00, 9.07]	0.011	0.01	0.225	0.114
Basophil number (x10e3/uL)	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.192	0.253	0.078	0.797
Basophil percent (%)	0.10 [0.10, 0.30]	0.20 [0.10, 0.40]	0.20 [0.10, 0.40]	0.20 [0.10, 0.40]	0.006	0.001	0.147	0.861
Eosinophil no. (x10E3/uL)	0.00 [0.00, 0.00]	0.00 [0.00, 0.10]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.04	0.044	0.061	0.439
Eosinophil % (%)	0.20 [0.10, 0.40]	0.20 [0.00, 0.70]	0.10 [0.00, 0.50]	0.20 [0.00, 0.50]	0.198	0.132	0.123	0.646
MCH (pg)	29.80 [27.80, 30.20]	30.20 [28.30, 29.50]	29.50 [28.10, 29.90]	29.90 [28.40, 29.80]	0.263	0.816	0.225	0.111

	31.10]	31.20]	30.90]	31.10]				
MCHC (g/dL)	32.60 [32.00, 33.40]	32.70 [31.70, 33.50]	33.00 [32.10, 33.60]	33.00 [32.30, 33.60]	0.002	<0.001	0.694	0.677
MCV (FL)	90.40 [86.60, 94.70]	91.30 [86.95, 95.40]	89.80 [86.40, 92.40]	90.70 [86.85, 93.93]	0.018	0.027	0.2	0.056
Serum creatinine (mg/dL)	1.11 [0.83, 2.00]	1.14 [0.81, 2.02]	0.89 [0.70, 1.21]	0.87 [0.71, 1.20]	<0.001	<0.001	0.966	0.706
C-reactive protein (mg/L)	137.30 [79.03, 226.30]	167.82 [81.00, 235.15]	96.70 [50.52, 159.38]	108.35 [48.55, 190.49]	<0.001	<0.001	0.17	0.35
Estimated glomerular filtration rate (EGFR) (ml/min/1.73m ²)	45.00 [24.75, 62.00]	46.00 [20.34, 64.00]	58.19 [32.75, 91.00]	56.14 [39.09, 76.50]	<0.001	<0.001	0.996	0.73
Blood urea nitrogen (BUN) (mg/dL)	23.00 [14.00, 43.00]	24.00 [15.00, 45.00]	16.00 [11.00, 26.00]	16.00 [11.00, 26.00]	<0.001	<0.001	0.343	0.904
Alanine aminotransferase (ALT) (u/L)	31.00 [19.00, 51.00]	30.00 [20.00, 50.00]	27.00 [19.00, 48.00]	32.00 [19.00, 50.00]	0.615	0.852	0.918	0.187
aspartate aminotransferase (AST) (U/L)	43.00 [30.00, 70.00]	43.00 [29.00, 69.50]	39.00 [27.00, 58.00]	42.00 [28.00, 63.00]	0.276	0.066	0.95	0.474
Total bilirubin (mg/dL)	0.60 [0.40, 0.80]	0.60 [0.40, 0.83]	0.50 [0.40, 0.80]	0.50 [0.40, 0.80]	0.076	0.015	0.352	0.641
Anion gap (mEq/L)	12.00 [10.00, 14.50]	12.50 [10.00, 15.00]	11.70 [10.00, 13.55]	11.30 [9.60, 13.00]	<0.001	<0.001	0.395	0.077

Albumin (g/dL)	3.00 [2.60, 3.30]	2.80 [2.50, 3.20]	3.10 [2.90, 3.50]	3.10 [2.80, 3.40]	<0.001	<0.001	0.009	0.093
Calcium (mg/dL)	8.30 [7.90, 8.70]	8.20 [7.70, 8.70]	8.20 [7.90, 8.70]	8.30 [8.00, 8.70]	0.011	0.013	0.067	0.183
Chloride (mEq/L)	104.00 [100.00, 107.00]	103.00 [99.00, 108.00]	103.00 [99.00, 106.00]	103.00 [99.00, 107.00]	0.007	0.001	0.413	0.59
Ferritin (ng/mL)	888.00 [399.50, 2137.50]	909.50 [476.25, 1947.75]	697.00 [308.00, 1768.00]	638.50 [299.50, 1239.50]	<0.001	<0.001	0.805	0.546
Glucose (mg/dL)	130.00 [100.00, 181.50]	128.00 [99.25, 184.00]	114.00 [96.00, 157.00]	115.00 [97.00, 152.50]	<0.001	<0.001	0.938	0.704
Hemoglobin (g/dL)	12.35 [10.70, 14.00]	12.50 [10.55, 13.80]	12.90 [11.80, 14.10]	13.10 [11.80, 14.10]	<0.001	<0.001	0.611	0.59
Lactate dehydrogenase (LDH) (U/L)	491.00 [351.25, 626.00]	496.00 [366.25, 657.00]	379.00 [306.00, 487.00]	399.50 [304.75, 492.75]	<0.001	<0.001	0.279	0.445
Potassium (mmol/L)	4.20 [3.90, 4.70]	4.30 [3.80, 4.80]	4.10 [3.70, 4.50]	4.10 [3.70, 4.50]	<0.001	<0.001	0.357	0.421
Sodium (MEQ/L)	138.00 [135.00, 141.00]	137.00 [134.00, 142.75]	138.00 [135.00, 140.00]	138.00 [135.00, 140.00]	0.443	0.181	0.38	0.995

Table S3: Unimputed Analysis						
term	OR	OR_lower	OR_upper	p.value	auc_change	p_bonferroni
Post-A/C D-dimer HI (Ref: LD)	8.6	3.3	22.8	1.49143E-05	0.045	0.000164057
ARDS	3.3	1.5	7.4	0.002982326	0.029	0.03280559
Post-A/C D-dimer LI (Ref: LD)	3.3	1.1	9.4	0.027278089	0.014	0.300058977
Acute Kidney Injury	2.5	1.3	5.0	0.006749455	0.025	0.074244004
Post-A/C D-dimer HD (Ref: LD)	1.9	0.7	5.4	0.209672822	0.018	1
basophil_percent	1.7	0.7	4.0	0.214340486	0.005	1
Age	1.0	1.0	1.1	0.000761589	0.030	0.008377481
sodium	1.0	1.0	1.1	0.434094472	0.019	1
LDH	1.0	1.0	1.0	0.334443227	0.003	1
Platelet	1.0	1.0	1.0	0.000123421	0.046	0.001357635
O2 Sat Min	0.9	0.9	1.0	0.00014103	0.019	0.001551334