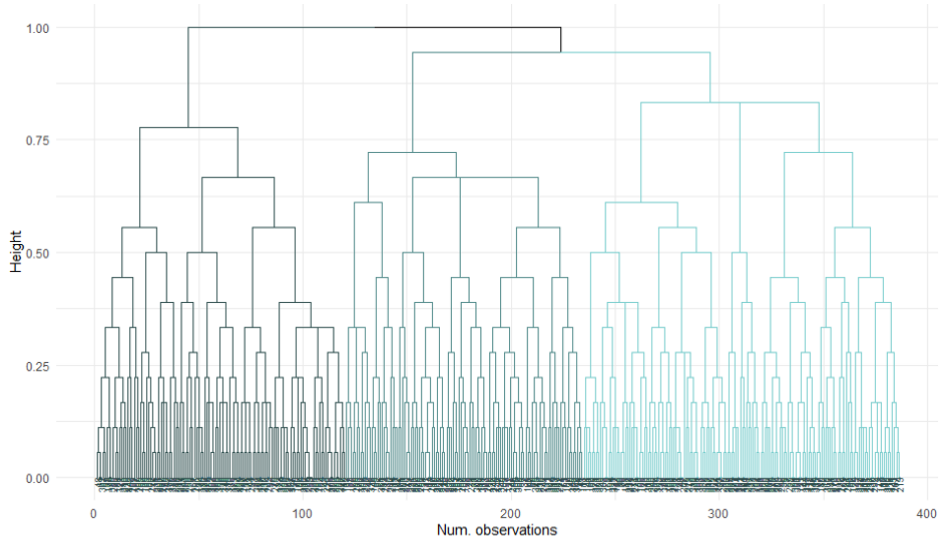
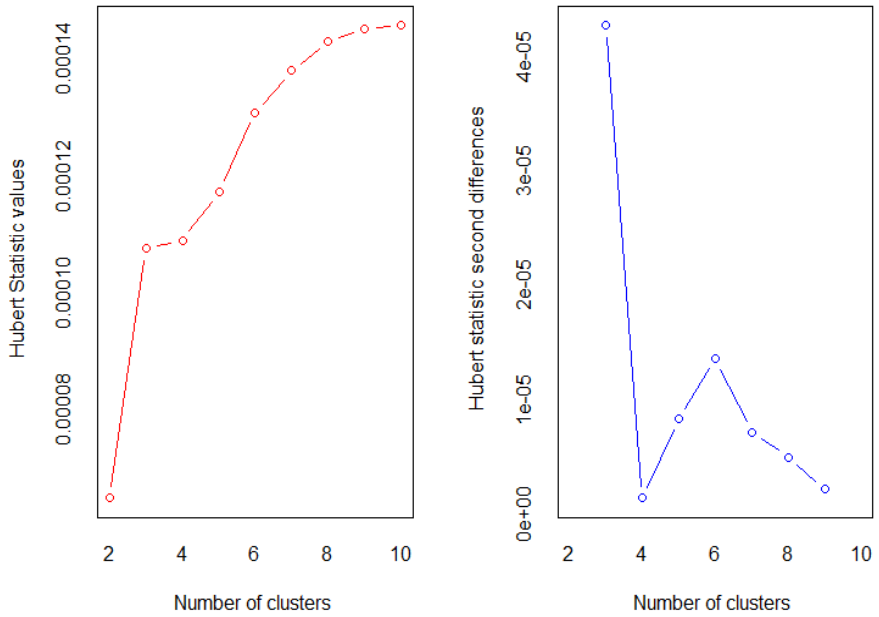
Supplemental Material

Supplemental Figure I: Machine learning cluster analysis methods showing a) dendrogram plotting each observation and b) Hubert index for optimal number of clusters

a)



b)



Supplemental Table II: Cluster analysis variable outputs with defined quartile boundaries

Biomarker: CRP, (mg/l)					
Quartile:	0%	25%	50%	75%	100%
Value:	0.5	4.3	10.5	18.7	100.00
Biomarker: D-dimer, (mg/ml)					
Quartile:	0%	25%	50%	75%	100%
Value:	0.22	0.91	1.84	4.0	20.0
Biomarker: LDH, (U/l)					
Quartile:	0%	25%	50%	75%	100%
Value:	10.0	294.0	402.0	546.3	9772.0
Biomarker: **PTT (seconds)**					
Quartile:	0%	25%	50%	75%	100%
Value:	19.0	29.7	32.9	37.1	200.0
Biomarker: WBC, (k-per-mm^3)					
Quartile:	0%	25%	50%	75%	100%
Value:	0.20	5.8	7.7	10.6	202.7

Supplemental Table II: Complete reporting of baseline demographics, clinical variables, biomarkers and outcomes each stratified by cluster

	Overall	Cluster 1	Cluster 2	Cluster 3	Cluster 4	p
N	2908	522	1178	532	676	
Demographics						
Age (mean (SD))	64.22 (15.65)	65.19 (14.34)	63.97 (15.89)	67.68 (14.48)	61.20 (16.48)	<0.001
Age Categorical, n (%)						<0.001
[00 to 55]	761 (26.2)	120 (23.0)	307 (26.1)	94 (17.7)	240 (35.5)	
(55 to 65]	700 (24.1)	133 (25.5)	293 (24.9)	126 (23.7)	148 (21.9)	
(65 to 75]	683 (23.5)	134 (25.7)	271 (23.0)	144 (27.1)	134 (19.8)	
75+)	764 (26.3)	135 (25.9)	307 (26.1)	168 (31.6)	154 (22.8)	
Female sex, n (%)	1297 (44.6)	193 (37.0)	496 (42.1)	237 (44.5)	371 (54.9)	<0.001
Race, n (%)						<0.001
Asian	74 (2.5)	13 (2.5)	38 (3.2)	13 (2.4)	10 (1.5)	
Black	1063 (36.6)	182 (34.9)	398 (33.8)	230 (43.2)	253 (37.4)	
Hispanic	1090 (37.5)	206 (39.5)	476 (40.4)	151 (28.4)	257 (38.0)	
Other	445 (15.3)	87 (16.7)	163 (13.8)	95 (17.9)	100 (14.8)	
White	236 (8.1)	34 (6.5)	103 (8.7)	43 (8.1)	56 (8.3)	
Comorbidities						
Hypertension, n (%)	1178 (40.5)	174 (33.3)	480 (40.7)	207 (38.9)	317 (46.9)	<0.001
Diabetes, n (%)	1085 (37.3)	215 (41.2)	410 (34.8)	213 (40.0)	247 (36.5)	0.039
Myocardial infarction, n (%)	194 (6.7)	41 (7.9)	77 (6.5)	32 (6.0)	44 (6.5)	0.658
Heart Failure, n (%)	494 (17.0)	141 (27.0)	174 (14.8)	82 (15.4)	97 (14.3)	<0.001
Cerebrovascular disease, n (%)	381 (13.1)	84 (16.1)	148 (12.6)	72 (13.5)	77 (11.4)	0.101
Dementia, n (%)	315 (10.8)	46 (8.8)	135 (11.5)	72 (13.5)	62 (9.2)	0.035
COPD, n (%)	38 (1.3)	7 (1.3)	16 (1.4)	2 (0.4)	13 (1.9)	0.133
Renal disease, n (%)	720 (24.8)	175 (33.5)	271 (23.0)	133 (25.0)	141 (20.9)	<0.001
Clinical Variables						
Temperature (mean (SD))	37.28 (2.01)	37.55 (1.08)	37.31 (1.86)	37.05 (2.56)	37.21 (2.30)	<0.001
Oxygen saturation (mean (SD))	92.19 (8.42)	92.69 (7.10)	91.32 (8.81)	90.27 (11.01)	94.86 (4.83)	<0.001
Systolic Blood Pressure (mean (SD))	133.19 (25.82)	134.64 (26.28)	132.42 (25.95)	131.78 (27.95)	134.51 (23.33)	0.112
Anticoagulants (n,%)	2565 (88.2)	455 (87.2)	1038 (88.1)	460 (86.5)	612 (90.5)	0.132
Antiplatelets (n,%)	769 (26.4)	155 (29.7)	279 (23.7)	146 (27.4)	189 (28.0)	0.036
Steroids (n,%)	700 (24.1)	151 (28.9)	300 (25.5)	134 (25.2)	115 (17.0)	<0.001
COVID-19 medications, n (%)	2126 (73.1)	432 (82.8)	836 (71.0)	398 (74.8)	460 (68.0)	<0.001
Biomarkers						
CRP, mg/L (mean (SD))	13.12 (11.37)	15.72 (11.10)	15.80 (11.76)	14.91 (11.95)	5.02 (4.70)	<0.001
D-dimer, mcg/ml FEU (mean (SD))	4.33 (5.79)	3.11 (4.54)	3.47 (4.91)	10.31 (7.06)	2.05 (3.35)	<0.001
PTT, sec. (mean (SD))	35.43 (14.30)	44.21 (20.78)	35.51 (14.69)	32.79 (9.54)	30.61 (3.38)	<0.001
LDH, U/L (mean (SD))	475.49 (377.4)	419.71 (210.8)	489.93 (284.8)	707.97 (672.4)	310.45 (96.0)	<0.001
WBC, k-per-mm^3 (mean (SD))	8.99 (6.99)	6.02 (1.90)	11.36 (7.99)	10.83 (8.99)	5.70 (1.69)	<0.001
CRP quartiles, n (%)						<0.001
Q1	665 (22.9)	72 (13.8)	184 (15.6)	69 (13.0)	340 (50.3)	
Q2	716 (24.6)	116 (22.2)	219 (18.6)	132 (24.8)	249 (36.8)	
Q3	759 (26.1)	125 (23.9)	368 (31.2)	194 (36.5)	72 (10.7)	
Q4	768 (26.4)	209 (40.0)	407 (34.6)	137 (25.8)	15 (2.2)	
D-dimer quartiles, n (%)						<0.001
Q1	670 (23.0)	149 (28.5)	203 (17.2)	0 (0.0)	318 (47.0)	

Q2	736 (25.3)	163 (31.2)	393 (33.4)	13 (2.4)	167 (24.7)	
Q3	739 (25.4)	115 (22.0)	394 (33.4)	107 (20.1)	123 (18.2)	
Q4	763 (26.2)	95 (18.2)	188 (16.0)	412 (77.4)	68 (10.1)	
PTT quartiles, n (%)						<0.001
Q1	707 (24.3)	0 (0.0)	236 (20.0)	212 (39.8)	259 (38.3)	
Q2	718 (24.7)	14 (2.7)	316 (26.8)	133 (25.0)	255 (37.7)	
Q3	745 (25.6)	139 (26.6)	347 (29.5)	99 (18.6)	160 (23.7)	
Q4	738 (25.4)	369 (70.7)	279 (23.7)	88 (16.5)	2 (0.3)	
LDH quartiles, n (%)						<0.001
Q1	622 (21.4)	104 (19.9)	217 (18.4)	20 (3.8)	281 (41.6)	
Q2	710 (24.4)	158 (30.3)	226 (19.2)	62 (11.7)	264 (39.1)	
Q3	780 (26.8)	180 (34.5)	355 (30.1)	118 (22.2)	127 (18.8)	
Q4	796 (27.4)	80 (15.3)	380 (32.3)	332 (62.4)	4 (0.6)	
WBC quartiles, n (%)						<0.001
Q1	672 (23.1)	230 (44.1)	43 (3.7)	52 (9.8)	347 (51.3)	
Q2	696 (23.9)	185 (35.4)	151 (12.8)	112 (21.1)	248 (36.7)	
Q3	763 (26.2)	107 (20.5)	431 (36.6)	144 (27.1)	81 (12.0)	
Q4	777 (26.7)	0 (0.0)	553 (46.9)	224 (42.1)	0 (0.0)	
Outcomes						
Inpatient mortality, n (%)	729 (25.1)	150 (28.7)	301 (25.6)	217 (40.8)	61 (9.0)	<0.001
Composite thrombotic events, n (%)[Ŧ]	124 (4.3)	20 (3.8)	50 (4.2)	43 (8.1)	11 (1.6)	<0.001
Acute ischemic Stroke, n (%)	48 (1.7)	4 (0.8)	14 (1.2)	19 (3.6)	11 (1.6)	0.001
Large vessel occlusion, n (%)	17 (0.6)	1 (0.2)	5 (0.4)	9 (1.7)	2 (0.3)	0.003
Present on arrival, n (%)	27 (56.2)	0 (0.0)	7 (50.0)	9 (47.4)	11 (100.0)	0.002
Stroke severity, n (%)						0.004
None	2862 (98.5)	518 (99.2)	1165 (98.9)	514 (96.8)	665 (98.4)	
coma/intubated	8 (0.3)	2 (0.4)	3 (0.3)	3 (0.6)	0 (0.0)	
Minor	12 (0.4)	0 (0.0)	2 (0.2)	4 (0.8)	6 (0.9)	
Moderate	16 (0.6)	2 (0.4)	7 (0.6)	4 (0.8)	3 (0.4)	
Severe	9 (0.3)	0 (0.0)	1 (0.1)	6 (1.1)	2 (0.3)	
Ischemic stroke subtype, n (%)						<0.001
Atherosclerotic	6 (0.2)	1 (0.2)	1 (0.1)	1 (0.2)	3 (0.4)	
Cardioembolic	13 (0.4)	1 (0.2)	9 (0.8)	3 (0.6)	0 (0.0)	
Cryptogenic	25 (0.9)	1 (0.2)	4 (0.3)	14 (2.6)	6 (0.9)	
Lacunar	3 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.3)	
Other	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	
None	2860 (98.3)	518 (99.2)	1164 (98.8)	513 (96.4)	665 (98.4)	

COPD: chronic obstructive pulmonary disease. CRP: C-reactive protein. PTT: partial thromboplastin time. LDH: lactate dehydrogenase. WBC: white blood cells**.** [Ŧ] Not including acute ischemic stroke.

Stroke severity was defined using the National Institutes of Health Stroke Scale (NIHSS) with 0-4 rated as mild, 5-15 moderate, and >16 severe. **Anticoagulants** include full dose enoxaparin, intravenous heparin or any direct oral anticoagulant at any dose. **COVID-19 medications** include azithromycin and/or hydroxychloroquine. Remdesivir was not standard of care during the duration of the study and therefore not included. **Steroid therap**y included prednisone and methylprednisolone as defined by hospital protocol. **Composite thrombotic events** were confirmed by manual chart review and imaging (except for myocardial infarction) and include ischemic myocardial infarction (type 1 or 2), pulmonary embolism, deep vein thrombosis and acute limb thrombosis.

Supplemental Table III: Demographic, clinical and biomarker features of patients hospitalized with acute ischemic stroke and COVID-19 in three healthcare systems in NYC comprising the validation cohort.

	Cryptogenic	Cardioembolic	LAA/lacunar	p-value
Total n	71	61	26	
Demographics				
Age <60, n (%)	32 (45.1%)	22 (36.1%)	15 (57.7%)	0.17
Sex (women), n (%)	28 (39.4%)	24 (39.3%)	10 (38.5%)	0.99
Comorbidities				
Hypertension, n (%)	39 (54.9%)	41 (67.2%)	20 (76.9%)	0.099
Diabetes Mellitus II, n (%)	21 (29.6%)	32 (52.5%)	12 (46.2%)	0.025
Coronary artery disease, n (%)	4 (5.6%)	13 (21.3%)	5 (19.2%)	0.024
Heart Failure, n (%)	3 (4.2%)	14 (23.0%)	4 (15.4%)	0.0064
Atrial fibrillation, n (%)	1 (1.4%)	34 (55.7%)	4 (15.4%)	<0.0001
Prior stroke or TIA, n (%)	4 (5.6%)	16 (26.2%)	10 (38.5%)	0.0002
Clinical				
D-dimer >10mcg/ml FEU or >10,000ng/ml DDU, n/total (%) *n missing (%)*	33 (50.8%) *6 (9.2%)*	17 (32.7%) *9 (14.8%)*	1 (4.5%) *4 (15.4%)*	0.0064
NIHSS >10, n (%) *n missing (%)*	38 (54.3%) *1 (1.4%)*	32 (54.2%) *2 (3.3%)*	5 (19.2%)	0.0049
LVO, n (%) *n missing (%)*	20 (33.3%) *11 (15.5%)*	20 (33.3%) *1 (1.6%)*	3 (11.5%)	0.087
Mortality, n (%)	26 (36.6%)	26 (42.6%)	7 (26.9%)	0.37

LAA: large artery atherosclerosis. NIHSS: National Institutes of Health stroke scale. LVO: large vessel occlusion.

Supplemental Table IV: Adjusted outcomes by individual biomarkers

outcome	*control_reference*	*treatment_reference*	*RR*	*std.dev*	*pvalue*	*ci.lb*	*ci.ub*
mortality	Q1 [n=646; Y=51]	Q2 [n=705; Y=124]	0.06	0.02	0.001	0.03	0.10
mortality	Q1 [n=646; Y=51]	Q2 [n=705; Y=124]	1.70	0.17	0.001	1.23	2.37
mortality	Q1 [n=646; Y=51]	Q2 [n=705; Y=124]	0.16	0.01	0.000	0.13	0.18
mortality	Q1 [n=646; Y=51]	Q2 [n=705; Y=124]	0.09	0.01	0.000	0.07	0.12
mortality	Q1 [n=646; Y=51]	Q3 [n=747; Y=230]	0.18	0.03	0.000	0.13	0.23
mortality	Q1 [n=646; Y=51]	Q3 [n=747; Y=230]	2.74	0.20	0.000	1.86	4.05
mortality	Q1 [n=646; Y=51]	Q3 [n=747; Y=230]	0.28	0.02	0.000	0.24	0.32
mortality	Q1 [n=646; Y=51]	Q3 [n=747; Y=230]	0.10	0.02	0.000	0.06	0.14
mortality	Q1 [n=646; Y=51]	Q4 [n=757; Y=316]	0.27	0.03	0.000	0.21	0.33
mortality	Q1 [n=646; Y=51]	Q4 [n=757; Y=316]	3.63	0.21	0.000	2.39	5.52
mortality	Q1 [n=646; Y=51]	Q4 [n=757; Y=316]	0.37	0.02	0.000	0.33	0.42
mortality	Q1 [n=646; Y=51]	Q4 [n=757; Y=316]	0.10	0.02	0.000	0.06	0.14
mortality	Q1 [n=650; Y=68]	Q2 [n=722; Y=130]	0.02	0.02	0.344	-0.02	0.06
mortality	Q1 [n=650; Y=68]	Q2 [n=722; Y=130]	1.14	0.14	0.352	0.87	1.50
mortality	Q1 [n=650; Y=68]	Q2 [n=722; Y=130]	0.16	0.01	0.000	0.13	0.18
mortality	Q1 [n=650; Y=68]	Q2 [n=722; Y=130]	0.14	0.02	0.000	0.11	0.17
mortality	Q1 [n=650; Y=68]	Q3 [n=727; Y=189]	0.07	0.02	0.002	0.03	0.11
mortality	Q1 [n=650; Y=68]	Q3 [n=727; Y=189]	1.46	0.13	0.004	1.13	1.89
mortality	Q1 [n=650; Y=68]	Q3 [n=727; Y=189]	0.22	0.01	0.000	0.19	0.25
mortality	Q1 [n=650; Y=68]	Q3 [n=727; Y=189]	0.15	0.02	0.000	0.12	0.19
mortality	Q1 [n=650; Y=68]	Q4 [n=756; Y=334]	0.22	0.03	0.000	0.16	0.27
mortality	Q1 [n=650; Y=68]	Q4 [n=756; Y=334]	2.27	0.13	0.000	1.77	2.91
mortality	Q1 [n=650; Y=68]	Q4 [n=756; Y=334]	0.39	0.02	0.000	0.36	0.43
mortality	Q1 [n=650; Y=68]	Q4 [n=756; Y=334]	0.17	0.02	0.000	0.13	0.21
mortality	Q1 [n=695; Y=151]	Q2 [n=705; Y=157]	0.01	0.02	0.806	-0.04	0.05
mortality	Q1 [n=695; Y=151]	Q2 [n=705; Y=157]	1.02	0.10	0.806	0.84	1.25
mortality	Q1 [n=695; Y=151]	Q2 [n=705; Y=157]	0.22	0.02	0.000	0.19	0.25
mortality	Q1 [n=695; Y=151]	Q2 [n=705; Y=157]	0.22	0.02	0.000	0.19	0.25
mortality	Q1 [n=695; Y=151]	Q3 [n=732; Y=189]	0.03	0.02	0.159	-0.01	0.08
mortality	Q1 [n=695; Y=151]	Q3 [n=732; Y=189]	1.14	0.09	0.162	0.95	1.38
mortality	Q1 [n=695; Y=151]	Q3 [n=732; Y=189]	0.26	0.02	0.000	0.23	0.29
mortality	Q1 [n=695; Y=151]	Q3 [n=732; Y=189]	0.23	0.02	0.000	0.20	0.26
mortality	Q1 [n=695; Y=151]	Q4 [n=723; Y=224]	0.04	0.02	0.070	0.00	0.09
mortality	Q1 [n=695; Y=151]	Q4 [n=723; Y=224]	1.18	0.09	0.074	0.98	1.42
mortality	Q1 [n=695; Y=151]	Q4 [n=723; Y=224]	0.29	0.02	0.000	0.25	0.32
mortality	Q1 [n=695; Y=151]	Q4 [n=723; Y=224]	0.24	0.02	0.000	0.21	0.28
mortality	Q1 [n=606; Y=65]	Q2 [n=691; Y=116]	0.01	0.02	0.654	-0.04	0.06
mortality	Q1 [n=606; Y=65]	Q2 [n=691; Y=116]	1.07	0.16	0.658	0.79	1.47
mortality	Q1 [n=606; Y=65]	Q2 [n=691; Y=116]	0.15	0.01	0.000	0.13	0.18
mortality	Q1 [n=606; Y=65]	Q2 [n=691; Y=116]	0.14	0.02	0.000	0.11	0.18
mortality	Q1 [n=606; Y=65]	Q3 [n=771; Y=183]	0.06	0.04	0.164	-0.02	0.14
mortality	Q1 [n=606; Y=65]	Q3 [n=771; Y=183]	1.34	0.24	0.217	0.84	2.15
mortality	Q1 [n=606; Y=65]	Q3 [n=771; Y=183]	0.23	0.02	0.000	0.20	0.26
mortality	Q1 [n=606; Y=65]	Q3 [n=771; Y=183]	0.17	0.04	0.000	0.09	0.24
mortality	Q1 [n=606; Y=65]	Q4 [n=787; Y=357]	0.24	0.06	0.000	0.12	0.36
mortality	Q1 [n=606; Y=65]	Q4 [n=787; Y=357]	2.18	0.29	0.007	1.24	3.85

mortality	Q1 [n=606; Y=65]	Q4 [n=787; Y=357]	0.45	0.02	0.000	0.41	0.49
mortality	Q1 [n=606; Y=65]	Q4 [n=787; Y=357]	0.21	0.06	0.000	0.09	0.32
mortality	Q1 [n=659; Y=140]	Q2 [n=686; Y=147]	-0.01	0.02	0.646	-0.05	0.03
mortality	Q1 [n=659; Y=140]	Q2 [n=686; Y=147]	0.95	0.10	0.646	0.78	1.17
mortality	Q1 [n=659; Y=140]	Q2 [n=686; Y=147]	0.21	0.02	0.000	0.18	0.24
mortality	Q1 [n=659; Y=140]	Q2 [n=686; Y=147]	0.22	0.02	0.000	0.19	0.25
mortality	Q1 [n=659; Y=140]	Q3 [n=748; Y=190]	0.04	0.02	0.096	-0.01	0.08
mortality	Q1 [n=659; Y=140]	Q3 [n=748; Y=190]	1.18	0.10	0.099	0.97	1.43
mortality	Q1 [n=659; Y=140]	Q3 [n=748; Y=190]	0.25	0.02	0.000	0.22	0.28
mortality	Q1 [n=659; Y=140]	Q3 [n=748; Y=190]	0.21	0.02	0.000	0.18	0.25
mortality	Q1 [n=659; Y=140]	Q4 [n=762; Y=244]	0.07	0.03	0.013	0.01	0.12
mortality	Q1 [n=659; Y=140]	Q4 [n=762; Y=244]	1.28	0.10	0.016	1.05	1.56
mortality	Q1 [n=659; Y=140]	Q4 [n=762; Y=244]	0.30	0.02	0.000	0.27	0.34
mortality	Q1 [n=659; Y=140]	Q4 [n=762; Y=244]	0.24	0.02	0.000	0.20	0.28
stroke	Q1 [n=646; Y=17]	Q2 [n=705; Y=6]	-0.01	0.01	0.089	-0.03	0.00
stroke	Q1 [n=646; Y=17]	Q2 [n=705; Y=6]	0.43	0.50	0.094	0.16	1.15
stroke	Q1 [n=646; Y=17]	Q2 [n=705; Y=6]	0.01	0.00	0.017	0.00	0.02
stroke	Q1 [n=646; Y=17]	Q2 [n=705; Y=6]	0.02	0.01	0.000	0.01	0.04
stroke	Q1 [n=646; Y=17]	Q3 [n=747; Y=14]	0.00	0.01	0.950	-0.02	0.03
stroke	Q1 [n=646; Y=17]	Q3 [n=747; Y=14]	1.03	0.50	0.950	0.39	2.75
stroke	Q1 [n=646; Y=17]	Q3 [n=747; Y=14]	0.03	0.01	0.011	0.01	0.05
stroke	Q1 [n=646; Y=17]	Q3 [n=747; Y=14]	0.03	0.01	0.003	0.01	0.04
stroke	Q1 [n=646; Y=17]	Q4 [n=757; Y=10]	-0.01	0.01	0.225	-0.04	0.01
stroke	Q1 [n=646; Y=17]	Q4 [n=757; Y=10]	0.50	0.54	0.201	0.17	1.45
stroke	Q1 [n=646; Y=17]	Q4 [n=757; Y=10]	0.01	0.01	0.013	0.00	0.03
stroke	Q1 [n=646; Y=17]	Q4 [n=757; Y=10]	0.03	0.01	0.005	0.01	0.05
stroke	Q1 [n=650; Y=3]	Q2 [n=722; Y=7]	0.01	0.00	0.217	0.00	0.01
stroke	Q1 [n=650; Y=3]	Q2 [n=722; Y=7]	2.31	0.70	0.235	0.58	9.15
stroke	Q1 [n=650; Y=3]	Q2 [n=722; Y=7]	0.01	0.00	0.009	0.00	0.02
stroke	Q1 [n=650; Y=3]	Q2 [n=722; Y=7]	0.00	0.00	0.094	0.00	0.01
stroke	Q1 [n=650; Y=3]	Q3 [n=727; Y=12]	0.01	0.01	0.036	0.00	0.02
stroke	Q1 [n=650; Y=3]	Q3 [n=727; Y=12]	3.51	0.66	0.058	0.96	12.91
stroke	Q1 [n=650; Y=3]	Q3 [n=727; Y=12]	0.02	0.01	0.001	0.01	0.03
stroke	Q1 [n=650; Y=3]	Q3 [n=727; Y=12]	0.00	0.00	0.093	0.00	0.01
stroke	Q1 [n=650; Y=3]	Q4 [n=756; Y=25]	0.03	0.01	0.000	0.02	0.05
stroke	Q1 [n=650; Y=3]	Q4 [n=756; Y=25]	8.02	0.75	0.005	1.86	34.61
stroke	Q1 [n=650; Y=3]	Q4 [n=756; Y=25]	0.04	0.01	0.000	0.02	0.05
stroke	Q1 [n=650; Y=3]	Q4 [n=756; Y=25]	0.00	0.00	0.163	0.00	0.01
stroke	Q1 [n=695; Y=15]	Q2 [n=705; Y=12]	0.00	0.01	0.565	-0.02	0.01
stroke	Q1 [n=695; Y=15]	Q2 [n=705; Y=12]	0.80	0.38	0.566	0.38	1.70
stroke	Q1 [n=695; Y=15]	Q2 [n=705; Y=12]	0.02	0.00	0.000	0.01	0.03
stroke	Q1 [n=695; Y=15]	Q2 [n=705; Y=12]	0.02	0.01	0.000	0.01	0.03
stroke	Q1 [n=695; Y=15]	Q3 [n=732; Y=10]	-0.01	0.01	0.354	-0.02	0.01
stroke	Q1 [n=695; Y=15]	Q3 [n=732; Y=10]	0.68	0.41	0.355	0.30	1.53
stroke	Q1 [n=695; Y=15]	Q3 [n=732; Y=10]	0.01	0.00	0.002	0.01	0.02
stroke	Q1 [n=695; Y=15]	Q3 [n=732; Y=10]	0.02	0.01	0.000	0.01	0.03
stroke	Q1 [n=695; Y=15]	Q4 [n=723; Y=10]	-0.01	0.01	0.462	-0.02	0.01
stroke	Q1 [n=695; Y=15]	Q4 [n=723; Y=10]	0.72	0.45	0.460	0.30	1.73

stroke	Q1 [n=695; Y=15]	Q4 [n=723; Y=10]	0.01	0.00	0.003	0.00	0.02
stroke	Q1 [n=695; Y=15]	Q4 [n=723; Y=10]	0.02	0.01	0.001	0.01	0.03
stroke	Q1 [n=606; Y=13]	Q2 [n=691; Y=11]	0.00	0.01	0.666	-0.02	0.01
stroke	Q1 [n=606; Y=13]	Q2 [n=691; Y=11]	0.83	0.42	0.665	0.36	1.90
stroke	Q1 [n=606; Y=13]	Q2 [n=691; Y=11]	0.02	0.01	0.001	0.01	0.03
stroke	Q1 [n=606; Y=13]	Q2 [n=691; Y=11]	0.02	0.01	0.001	0.01	0.03
stroke	Q1 [n=606; Y=13]	Q3 [n=771; Y=10]	-0.01	0.01	0.533	-0.02	0.01
stroke	Q1 [n=606; Y=13]	Q3 [n=771; Y=10]	0.72	0.50	0.516	0.27	1.94
stroke	Q1 [n=606; Y=13]	Q3 [n=771; Y=10]	0.01	0.00	0.003	0.00	0.02
stroke	Q1 [n=606; Y=13]	Q3 [n=771; Y=10]	0.02	0.01	0.008	0.01	0.03
stroke	Q1 [n=606; Y=13]	Q4 [n=787; Y=13]	0.00	0.01	0.777	-0.02	0.02
stroke	Q1 [n=606; Y=13]	Q4 [n=787; Y=13]	0.84	0.60	0.768	0.26	2.73
stroke	Q1 [n=606; Y=13]	Q4 [n=787; Y=13]	0.02	0.01	0.002	0.01	0.03
stroke	Q1 [n=606; Y=13]	Q4 [n=787; Y=13]	0.02	0.01	0.050	0.00	0.04
stroke	Q1 [n=659; Y=9]	Q2 [n=686; Y=8]	0.00	0.01	0.699	-0.01	0.01
stroke	Q1 [n=659; Y=9]	Q2 [n=686; Y=8]	0.83	0.48	0.698	0.32	2.13
stroke	Q1 [n=659; Y=9]	Q2 [n=686; Y=8]	0.01	0.00	0.004	0.00	0.02
stroke	Q1 [n=659; Y=9]	Q2 [n=686; Y=8]	0.01	0.00	0.002	0.01	0.02
stroke	Q1 [n=659; Y=9]	Q3 [n=748; Y=14]	0.01	0.01	0.434	-0.01	0.02
stroke	Q1 [n=659; Y=9]	Q3 [n=748; Y=14]	1.40	0.43	0.440	0.60	3.25
stroke	Q1 [n=659; Y=9]	Q3 [n=748; Y=14]	0.02	0.01	0.000	0.01	0.03
stroke	Q1 [n=659; Y=9]	Q3 [n=748; Y=14]	0.01	0.00	0.003	0.00	0.02
stroke	Q1 [n=659; Y=9]	Q4 [n=762; Y=16]	0.01	0.01	0.344	-0.01	0.02
stroke	Q1 [n=659; Y=9]	Q4 [n=762; Y=16]	1.52	0.46	0.359	0.62	3.75
stroke	Q1 [n=659; Y=9]	Q4 [n=762; Y=16]	0.02	0.01	0.000	0.01	0.03
stroke	Q1 [n=659; Y=9]	Q4 [n=762; Y=16]	0.01	0.00	0.007	0.00	0.02
Thrombotic	Q1 [n=646; Y=15]	Q2 [n=705; Y=25]	0.01	0.01	0.352	-0.01	0.03
thrombotic	Q1 [n=646; Y=15]	Q2 [n=705; Y=25]	1.36	0.34	0.365	0.70	2.68
Thrombotic	Q1 [n=646; Y=15]	Q2 [n=705; Y=25]	0.04	0.01	0.000	0.02	0.05
Thrombotic	Q1 [n=646; Y=15]	Q2 [n=705; Y=25]	0.03	0.01	0.000	0.01	0.04
Thrombotic	Q1 [n=646; Y=15]	Q3 [n=747; Y=32]	0.01	0.01	0.516	-0.02	0.04
thrombotic	Q1 [n=646; Y=15]	Q3 [n=747; Y=32]	1.25	0.36	0.535	0.62	2.55
Thrombotic	Q1 [n=646; Y=15]	Q3 [n=747; Y=32]	0.05	0.01	0.000	0.03	0.06
Thrombotic	Q1 [n=646; Y=15]	Q3 [n=747; Y=32]	0.04	0.01	0.001	0.01	0.06
Thrombotic	Q1 [n=646; Y=15]	Q4 [n=757; Y=49]	0.02	0.02	0.344	-0.02	0.05
thrombotic	Q1 [n=646; Y=15]	Q4 [n=757; Y=49]	1.41	0.40	0.387	0.65	3.06
Thrombotic	Q1 [n=646; Y=15]	Q4 [n=757; Y=49]	0.06	0.01	0.000	0.04	0.08
Thrombotic	Q1 [n=646; Y=15]	Q4 [n=757; Y=49]	0.04	0.02	0.005	0.01	0.07
Thrombotic	Q1 [n=650; Y=8]	Q2 [n=722; Y=26]	0.02	0.01	0.023	0.00	0.04
thrombotic	Q1 [n=650; Y=8]	Q2 [n=722; Y=26]	2.34	0.42	0.042	1.03	5.32
Thrombotic	Q1 [n=650; Y=8]	Q2 [n=722; Y=26]	0.03	0.01	0.000	0.02	0.05
Thrombotic	Q1 [n=650; Y=8]	Q2 [n=722; Y=26]	0.01	0.01	0.007	0.00	0.03
Thrombotic	Q1 [n=650; Y=8]	Q3 [n=727; Y=21]	0.01	0.01	0.150	0.00	0.03
thrombotic	Q1 [n=650; Y=8]	Q3 [n=727; Y=21]	1.79	0.43	0.177	0.77	4.14
Thrombotic	Q1 [n=650; Y=8]	Q3 [n=727; Y=21]	0.03	0.01	0.000	0.01	0.04
Thrombotic	Q1 [n=650; Y=8]	Q3 [n=727; Y=21]	0.01	0.01	0.007	0.00	0.03
Thrombotic	Q1 [n=650; Y=8]	Q4 [n=756; Y=66]	0.07	0.01	0.000	0.04	0.09
thrombotic	Q1 [n=650; Y=8]	Q4 [n=756; Y=66]	4.72	0.41	0.000	2.10	10.60

Thrombotic	Q1 [n=650; Y=8]	Q4 [n=756; Y=66]	0.08	0.01	0.000	0.06	0.11
Thrombotic	Q1 [n=650; Y=8]	Q4 [n=756; Y=66]	0.02	0.01	0.011	0.00	0.03
Thrombotic	Q1 [n=695; Y=28]	Q2 [n=705; Y=27]	0.00	0.01	0.848	-0.02	0.02
thrombotic	Q1 [n=695; Y=28]	Q2 [n=705; Y=27]	0.95	0.26	0.848	0.57	1.60
Thrombotic	Q1 [n=695; Y=28]	Q2 [n=705; Y=27]	0.04	0.01	0.000	0.02	0.05
Thrombotic	Q1 [n=695; Y=28]	Q2 [n=705; Y=27]	0.04	0.01	0.000	0.03	0.05
Thrombotic	Q1 [n=695; Y=28]	Q3 [n=732; Y=26]	-0.01	0.01	0.487	-0.03	0.01
thrombotic	Q1 [n=695; Y=28]	Q3 [n=732; Y=26]	0.83	0.27	0.485	0.49	1.40
Thrombotic	Q1 [n=695; Y=28]	Q3 [n=732; Y=26]	0.04	0.01	0.000	0.02	0.05
Thrombotic	Q1 [n=695; Y=28]	Q3 [n=732; Y=26]	0.04	0.01	0.000	0.03	0.06
Thrombotic	Q1 [n=695; Y=28]	Q4 [n=723; Y=40]	0.01	0.01	0.241	-0.01	0.04
thrombotic	Q1 [n=695; Y=28]	Q4 [n=723; Y=40]	1.33	0.25	0.247	0.82	2.18
Thrombotic	Q1 [n=695; Y=28]	Q4 [n=723; Y=40]	0.06	0.01	0.000	0.04	0.07
Thrombotic	Q1 [n=695; Y=28]	Q4 [n=723; Y=40]	0.04	0.01	0.000	0.03	0.06
Thrombotic	Q1 [n=606; Y=11]	Q2 [n=691; Y=16]	0.00	0.01	0.641	-0.01	0.02
thrombotic	Q1 [n=606; Y=11]	Q2 [n=691; Y=16]	1.21	0.42	0.648	0.53	2.77
Thrombotic	Q1 [n=606; Y=11]	Q2 [n=691; Y=16]	0.02	0.01	0.000	0.01	0.03
Thrombotic	Q1 [n=606; Y=11]	Q2 [n=691; Y=16]	0.02	0.01	0.003	0.01	0.03
Thrombotic	Q1 [n=606; Y=11]	Q3 [n=771; Y=30]	0.02	0.01	0.029	0.00	0.04
thrombotic	Q1 [n=606; Y=11]	Q3 [n=771; Y=30]	2.30	0.45	0.066	0.95	5.58
Thrombotic	Q1 [n=606; Y=11]	Q3 [n=771; Y=30]	0.04	0.01	0.000	0.03	0.06
Thrombotic	Q1 [n=606; Y=11]	Q3 [n=771; Y=30]	0.02	0.01	0.015	0.00	0.03
Thrombotic	Q1 [n=606; Y=11]	Q4 [n=787; Y=64]	0.07	0.02	0.000	0.04	0.10
thrombotic	Q1 [n=606; Y=11]	Q4 [n=787; Y=64]	4.69	0.57	0.006	1.54	14.27
Thrombotic	Q1 [n=606; Y=11]	Q4 [n=787; Y=64]	0.09	0.01	0.000	0.06	0.11
Thrombotic	Q1 [n=606; Y=11]	Q4 [n=787; Y=64]	0.02	0.01	0.070	0.00	0.04
Thrombotic	Q1 [n=659; Y=13]	Q2 [n=686; Y=19]	0.01	0.01	0.484	-0.01	0.02
thrombotic	Q1 [n=659; Y=13]	Q2 [n=686; Y=19]	1.28	0.36	0.489	0.64	2.57
Thrombotic	Q1 [n=659; Y=13]	Q2 [n=686; Y=19]	0.03	0.01	0.000	0.01	0.04
Thrombotic	Q1 [n=659; Y=13]	Q2 [n=686; Y=19]	0.02	0.01	0.000	0.01	0.03
Thrombotic	Q1 [n=659; Y=13]	Q3 [n=748; Y=36]	0.03	0.01	0.007	0.01	0.05
thrombotic	Q1 [n=659; Y=13]	Q3 [n=748; Y=36]	2.27	0.33	0.012	1.19	4.31
Thrombotic	Q1 [n=659; Y=13]	Q3 [n=748; Y=36]	0.05	0.01	0.000	0.03	0.06
Thrombotic	Q1 [n=659; Y=13]	Q3 [n=748; Y=36]	0.02	0.01	0.000	0.01	0.03
Thrombotic	Q1 [n=659; Y=13]	Q4 [n=762; Y=53]	0.04	0.01	0.006	0.01	0.06
thrombotic	Q1 [n=659; Y=13]	Q4 [n=762; Y=53]	2.37	0.40	0.032	1.08	5.22
Thrombotic	Q1 [n=659; Y=13]	Q4 [n=762; Y=53]	0.06	0.01	0.000	0.04	0.08
Thrombotic	Q1 [n=659; Y=13]	Q4 [n=762; Y=53]	0.03	0.01	0.008	0.01	0.05

RR: relative risk. CI: confidence interval.
Adjusted for all demographic, comorbidity, and clinical variables listed in Supplemental Table 2 including *categorical age, sex, race, temperature, oxygen saturation, systolic blood pressure, diabetes, myocardial infarction, heart failure, stroke, dementia, chronic obstructive pulmonary disease, renal disease, hypertension, in-hospital anti-coagulant use, inpatient anti-platelet use, inpatient steroid use, inpatient azithromycin and/or hydroxychloroquine.*

Supplemental Table V: Statistical analysis

Cluster cohort (n=2,908)	Analysis was performed in using R 4.0.3 (R core team, 2020). Agglomerative hierarchical **clustering** was used to detect patterns in the MHS cohort based on the distribution of biomarker quartiles of Gower distances in an unsupervised fashion using *cluster package*. All **outcomes** were stratified by cluster using the *R hclust package*. We calculated **adjusted risk** of AIS, other thrombotic events and mortality by biomarkers quartiles, after adjusting for baseline demographics, comorbidities, and clinical variables (Supplemental Table 4) using inverse-probability weighted logistic regression estimated using the R *tmle* package. **Distributions and significance tests** were automatically calculated using TableOne, an open-source Python library designed to automate and standardize the process of generating summary statistics for scientific papers. Categorical and continuous variables are automatically detected, with p-values calculated using parametric tests unless specified as exact test. Categorical variables are described as number of patients and relative percentage. Normal and non-normal continuous variables are distinguished using two statistical tests: Hartigans Dip Test to identify possible multimodal distributions and Tukey's rule indicates far outliers. Normal continuous variables are reported with mean and standard deviations, with p-values assess from parametric tests. Non-normal continuous variables are reported by median and interquartile ranges, with p-values assess from nonparametric tests.
Validation cohort (n=158)	Chi squared and Fisher's exact tests were used to analyze aggregate categorical data in the validation cohort

Supplemental Table VI: Minimum information about clinical artificial intelligence modeling: the MI-CLAIM checklist

Study design (Part 1)	**Completed: page number**
The clinical problem in which the model will be employed is clearly detailed in the paper.	■ see *Introduction* section
The research question is clearly stated.	■ see *Introduction* section
The characteristics of the cohorts (training and test sets) are detailed in the text.	■ see *Methods* and *Supplemental Material Table 5*
The cohorts (training and test sets) are shown to be representative of real-world clinical settings.	■ see *Methods* section
The state-of-the-art solution used as a baseline for comparison has been identified and detailed.	■ Not applicable as we are not comparing model performance but rather are use the model for exploratory purposes
Data and optimization (Parts 2, 3)	**Completed: page number**
The origin of the data is described and the original format is detailed in the paper.	■ see *Methods* section
Transformations of the data before it is applied to the proposed model are described.	■ see*Supplemental Material Table 5*
The independence between training and test sets has been proven in the paper.	■ Inherent in model used
Details on the models that were evaluated and the code developed to select the best model are provided.	■ *see Supplemental Material Table 5*
Is the input data type structured or unstructured?	☐ Structured ■Unstructured
Model performance (Part 4)	**Completed: page number**
The primary metric selected to evaluate algorithm performance (e.g., AUC, F-score, etc.), including the justification for selection, has been clearly stated.	■ *see Supplemental Material Table 4*
The primary metric selected to evaluate the clinical utility of the model (e.g., PPV, NNT, etc.), including the justification for selection, has been clearly stated.	■ see *Results section* and *Supplemental Material Tables 4 and 5*
The performance comparison between baseline and proposed model is presented with the appropriate statistical significance.	■ Not applicable as we are not comparing model performance but rather are use the model for exploratory purposes
Model examination (Part 5)	**Completed: page number**
Examination technique 1[a]	■ Visual analysis of the model dendrogram and biomarker quartile output was performed as depicted in *Supplemental Material Tables 1 and 2*
Examination technique 2[a]	■ Hubert Index was used to determine optimal number of clusters
A discussion of the relevance of the examination results with respect to model/algorithm performance is presented.	■ *See supplemental Material Table 1*
A discussion of the feasibility and significance of model interpretability at the case level if examination methods are uninterpretable is presented.	■ See *Discussion* section
A discussion of the reliability and robustness of the model as the underlying data distribution shifts is included.	■ See *Discussion* section
Reproducibility (Part 6): choose appropriate tier of transparency	
Tier 1: complete sharing of the code	■(full code can be made available upon reasonable request)
Tier 2: allow a third party to evaluate the code for accuracy/fairness; share the results of this evaluation	☐
Tier 3: release of a virtual machine (binary) for running the code on new data without sharing its details	☐
Tier 4: no sharing	☐