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# SARS-CoV-2 and Stroke Characteristics:

## A Report from the multinational COVID-19 Stroke Study Group

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# METHODS

# Methods; Supplemental Document 1.

## Detailed Study Design

This multicenter, multinational observational study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE),<sup>1</sup> and Enhancing the QUALity and Transparency Of health Research (EQUATOR) guidelines.<sup>2</sup> The study protocol was designed by the investigators at the Neuroscience Institute of Geisinger Health System, Pennsylvania, USA, and received approval by the Institutional Review Board of Geisinger Health System and other participating institutions when it was required. Investigators from North America (Canada and six states of the United States), South America (Brazil and Mexico), Europe (Belgium, Croatia, Czech Republic, Finland, France, Germany, Greece, Ireland, Italy, Norway, Portugal, Spain, Sweden, and Switzerland), Asia and the Middle East (India, Iran, Iraq, Israel, Lebanon, Singapore, South Korea, Turkey, and the United Arab Emirate), Oceania (Australia and New Zealand), and Africa (Egypt, Nigeria, and Uganda) responded to our invitation. The centers were included by non-probability sampling and data were recruited until June 10th, 2020. The core investigators invited their existing networks and collaborators from several countries through phone calls, emails, and announcements on social media platforms for professionals. The investigators and collaborators further introduced the study to local societies for physicians, academic health systems, hospitals that were designated as COVID-19 centers, services in charge of stroke patients, and other related organizations, sometimes using local languages. The authors also invited many stroke clinic investigators in other affected countries. In the USA, our collaborators from seven health systems accepted our invitation. Tertiary centers from health systems in New York, Pennsylvania, Tennessee, North Carolina, Virginia, and California provided data. In New Zealand, the data collection was led by the National Stroke Register team, which is supported by the National Stroke Network and the New Zealand Ministry of Health. Stroke physicians from all districts (Auckland, Bay of Plenty, Canterbury, Capital and Coast, Counties Manukau, Hawke's Bay, Lakes, Mid Central, Nelson Marlborough, Northland District, South Canterbury, Southern, Tairāwhiti, Taranaki, Waikato, Waitemata, West Coast, Wairarapa, Whanganui, and Hutt Valley) further verified the stroke events. In Iran, we communicated with the Departments of Neurology and Neurosurgery in main university hospitals according to the ranking by the Iranian Ministry of Health and Medical Education, geographical location, and whether the center was located in the SARS-CoV-2 infection hot spots. The local investigators further announced the invitation through the Iranian Stroke Organization and the National Society for Neurologists portals. We received data from 16 provinces (Tehran, East Azerbaijan, Khorasan, Guilan, Ardabil, Isfahan, Golestan, Kermanshah, Semnan, Hormozgan,

Kerman, Lorestan, Khuzestan, Markazi, Fars, and Ghazvin). In India, detailed data regarding the stroke were obtained from four states (Karnataka, Chhattisgarh, Ladakh, and Uttar Khand). Data from all Karnataka districts (Bengaluru, Mysuru, Belagavi, Kalaburgi, Vijayapura, Chikkaballapur, Bagalkote, Bidar, and Dakshina-Kannada) were obtained from the Government of Karnataka, Department of Health and Family Welfare in Bengaluru. Records of stroke were rechecked with Stroke Registry in Karnataka and individual communications with 15 tertiary centers in Bengaluru. In Lebanon, two health systems in Beirut, where over 75% of patients with SARS-CoV-2 diagnosis were hospitalized, participated in this study. In Italy, data from Sicily were provided by the Regional Health Authority of Sicily. We also received data from Genova. Multiple centers in Switzerland (Lugano, and Basel), Israel (Jerusalem), Portugal (Porto, Coimbra, and Lisbon), Spain (Valladolid, Barcelona, Lleida, and Seville), Greece (Athens), Germany (Frankfurt, and Bochum), France (Paris), Croatia (Zagreb), Brazil (São Paulo), Turkey (Istanbul), Finland (Helsinki), South Korea (Seoul), Australia (Adelaide, Melbourne, and Sydney), Uganda (Kampala), Egypt (Cairo) collaborated in this study. Collaborators from United Arab Emirates (Abu Dhabi) could not provide data by the deadline. Several centers reported no eligible patients for this study. Centers in Brazil, Canada, Croatia, Egypt, France, Germany, Greece, Iran, Israel, Italy, Portugal, Republic of Korea, Singapore, Spain, Switzerland, Turkey, and the United States reported data on their patients for the purpose of this study.



# Methods; Supplemental Document 2.

## Detailed Description of the Models

The patients were clustered based on the laboratory findings and comorbidities. We used clinicians' expert opinion (EX models), or unsupervised machine learning algorithms (ML models) for defining the clusters. The results of different models were compared through the contingency matrix (a.k.a contingency table).<sup>3</sup> We could not introduce any clustering based on the laboratory findings. The models for clustering the patients based on the comorbidities are as follows:

### A. Models based on the expert opinion (EX models)

Patients were categorized based on the number of the existing comorbidities. We either considered all comorbidities (Expert-All, EX-A models; including hypertension, diabetes mellitus, ischemic heart disease, atrial fibrillation, carotid stenosis, chronic kidney disease, cardiac ejection fraction less than 40%, active neoplasm, rheumatological diseases, history of transient ischemic attack or stroke, and current smoking), or selected number of vascular comorbidities (Expert-Selected, EX-S models; including hypertension, diabetes mellitus, ischemic heart disease, atrial fibrillation, carotid stenosis, chronic kidney disease, previous transient ischemic attack or stroke, and current smoking). We further clustered the patients under each of these models to two (EX-A<sub>2</sub> and EX-S<sub>2</sub>) or three (EX-A<sub>3</sub> and EX-S<sub>3</sub>) subgroups.

1. EX-A<sub>2</sub>: based on expert opinion and including all comorbidities, in two subgroups.
  - a. Subgroup a: zero or one comorbidity,
  - b. Subgroup b: more than one comorbidity.
2. EX-S<sub>2</sub>: based on expert opinion and including selected comorbidities, in two subgroups.
  - a. Subgroup a: zero or one comorbidity,
  - b. Subgroup b: more than one comorbidity.
3. EX-A<sub>3</sub>: based on expert opinion and including all comorbidities, in three subgroups.
  - a. Subgroup a: zero comorbidity,
  - b. Subgroup b: one or two comorbidities,
  - c. Subgroup c: more than two comorbidities.
4. EX-S<sub>3</sub>: based on expert opinion and including selected comorbidities, in three subgroups.
  - a. Subgroup a: zero comorbidity,
  - b. Subgroup b: one or two comorbidities,
  - c. Subgroup c: more than two comorbidities.

### B. Models based on machine learning algorithms (ML models)

We used unsupervised machine learning algorithms for clustering. Hierarchical and K-means clustering (ML-K models) and spectral clustering (ML-S models) were used. We grouped the patients to two (ML-K<sub>2</sub> and ML-S<sub>2</sub>), three (ML-K<sub>3</sub> and ML-S<sub>3</sub>), four (ML-K<sub>4</sub> and ML-S<sub>4</sub>), and five (ML-K<sub>5</sub> and ML-S<sub>5</sub>) clusters.

**Methods**

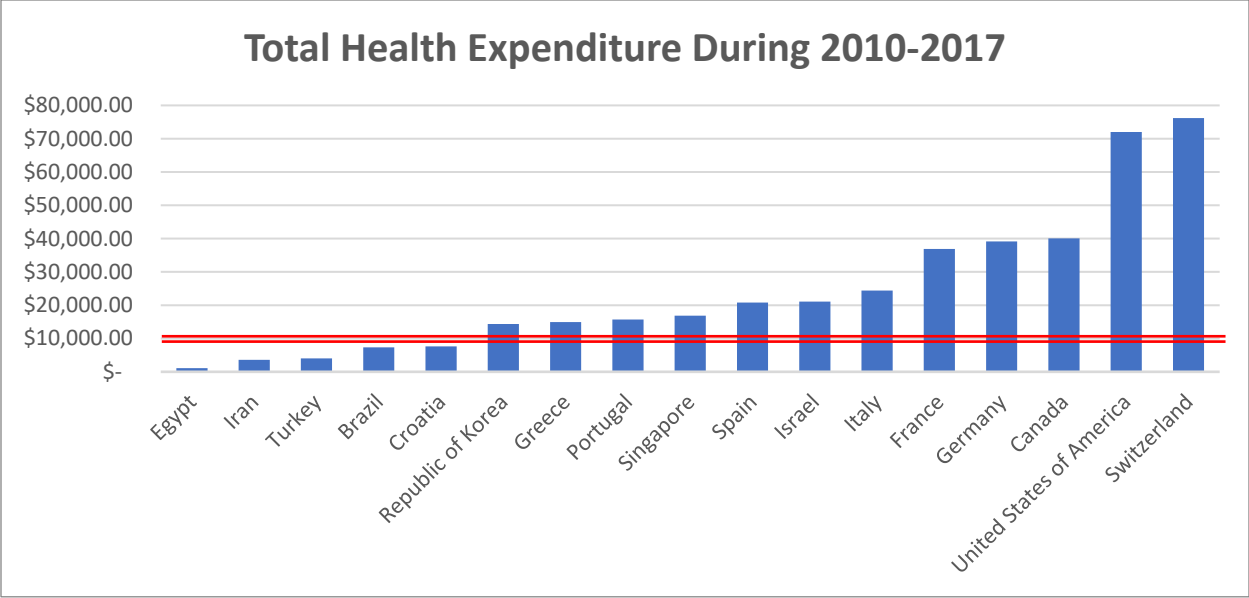
**Supplemental Table 1 &**

**Supplemental Figure 1**

**Country Health Expenditures**

**Supplemental Table 1.** Annual country health expenditures during 2010 – 2017, according to WHO Health Expenditure reports. These countries provided reports of stroke among SARS-CoV-2 infected patients.

Countries	Current Health Expenditure (CHE) per Capita in US\$							
	2010	2011	2012	2013	2014	2015	2016	2017
United States of America	\$7,957.28	\$8,169.91	\$8,441.00	\$8,647.64	\$9,068.00	\$9,538.07	\$9,941.35	\$10,246.14
Switzerland	\$8,021.81	\$9,572.17	\$9,286.55	\$9,689.67	\$10,014.71	\$9,807.80	\$9,835.96	\$9,956.26
Germany	\$4,597.24	\$5,021.63	\$4,754.66	\$5,094.42	\$5,290.72	\$4,617.49	\$4,734.18	\$5,033.45
Canada	\$5,044.14	\$5,361.24	\$5,408.93	\$5,345.32	\$5,081.56	\$4,539.14	\$4,518.14	\$4,754.95
France	\$4,593.39	\$4,933.40	\$4,652.29	\$4,900.39	\$4,987.87	\$4,204.09	\$4,256.96	\$4,379.73
Israel	\$2,211.02	\$2,410.75	\$2,376.65	\$2,648.82	\$2,788.50	\$2,640.31	\$2,856.18	\$3,144.63
Italy	\$3,214.55	\$3,387.58	\$3,125.61	\$3,195.55	\$3,190.09	\$2,708.84	\$2,736.26	\$2,840.13
Singapore	\$1,513.57	\$1,704.37	\$1,863.08	\$2,114.62	\$2,237.40	\$2,326.27	\$2,489.91	\$2,618.71
Spain	\$2,775.14	\$2,894.76	\$2,588.67	\$2,628.86	\$2,671.28	\$2,351.53	\$2,390.63	\$2,506.46
Republic of Korea	\$1,374.27	\$1,521.49	\$1,575.86	\$1,712.08	\$1,910.74	\$1,925.47	\$2,040.41	\$2,283.07
Portugal	\$2,213.10	\$2,207.70	\$1,918.60	\$1,959.42	\$1,986.89	\$1,724.53	\$1,802.77	\$1,908.03
Greece	\$2,573.74	\$2,354.01	\$1,968.48	\$1,834.34	\$1,724.53	\$1,464.73	\$1,499.35	\$1,516.59
Brazil	\$891.76	\$1,025.49	\$950.93	\$974.50	\$1,009.83	\$776.15	\$795.66	\$928.80
Croatia	\$1,126.37	\$1,132.50	\$1,029.97	\$889.94	\$909.37	\$795.52	\$840.91	\$902.14
Iran	\$440.85	\$524.69	\$519.30	\$413.73	\$382.71	\$375.13	\$454.19	\$475.48
Turkey	\$539.33	\$531.66	\$524.82	\$552.41	\$527.20	\$454.61	\$468.65	\$444.65
Egypt	\$111.44	\$123.26	\$143.38	\$140.33	\$153.79	\$180.82	\$151.47	\$105.77



**Supplemental Figure 1.** Distribution of total health expenditures during 2010-2017 by country, according to WHO Health Expenditure. These countries provided reports of stroke among SARS-CoV-2 infected patients.

# RESULTS

# **Results**

## **Acute Ischemic Stroke;**

### **Demographics**

#### **Supplemental Tables 3-5**

### Results; Supplemental Table 3. Subgroups of AIS patients younger or older than 55-year-old

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, comparing those younger versus older than 55. **Blue ink indicates the post-hoc p values.**

Parameter	Age <55-year-old N = 67 (36.2%)	Age >55-year-old N = 256 (79.3%)	P-value
Sex; Female; N (%)	29 (41.8)	102 (39.8)	0.77
Large Vessel Occlusion; N (%)	30 (47.6)	96 (43.6)	0.58
Intravenous Thrombolysis; N (%)	11 (16.4)	33 (12.9)	0.45
Mechanical Thrombectomy; N (%)	8 (11.9)	16 (6.3)	0.11
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	8.0 [4.0 – 17.0]	9.0 [4.0 – 17.0]	0.68
Imaging Patterns			
Embollic/Large Vessel athero-Thromboembolism; N (%)	46 (78.0)	160 (81.2)	0.21
Lacune; N (%)	4 (6.8)	22 (11.2)	
Border-zone; N (%)	9 (15.3)	14 (7.1)	
Vasculitis Pattern; N (%)	0 (0.0)	1 (0.5)	
TOAST			
Large-Artery Atherosclerosis; N (%)	14 (31.1)	42 (33.6)	0.05
Cardio-embolism; N (%)	7 (15.6)	39 (31.2) <sup>A (0.04)</sup>	
Small-Vessel Occlusion; N (%)	4 (8.9)	13 (10.4)	
Stroke of Other Determined Etiology; N (%)	7 (15.6) <sup>B (0.02)</sup>	6 (4.8)	
Stroke of Undetermined Etiology; N (%)	13 (28.9)	25 (20.0)	
Interval Between Onset to Index Event; Median [IQR]; Days	4.0 [0.0 – 10.0]	3.0 [0.0 – 8.0]	0.22
Mechanical Ventilation; N (%)	18 (26.9)	67 (26.2)	0.91
Disposition*			
Discharged Home; N (%)	39 (59.4) <sup>B (0.002)</sup>	89 (38.9)	<0.001
In Hospital Mortality; N (%)	8 (12.5)	74 (31.8) <sup>A (0.01)</sup>	
Still in Hospital/Subacute Care; N (%)	18 (28.1)	70 (30.0)	
Length of Hospital Stay; Median (IQR); Days	12.0 [5.0 – 18.0]	7.0 [4.0 – 15.0]	0.05
Comorbidities			
Hypertension; N (%)	26 (39.4)	176 (69.3)	<0.001
Diabetes Mellitus; N (%)	20 (29.9)	91 (35.8)	0.36
Ischemic Heart Disease; N (%)	9 (13.8)	63 (27.3)	0.03
Atrial Fibrillation; N (%)	4 (6.1)	41 (16.1)	0.04
Carotid Stenosis; N (%)	3 (4.6)	35 (15.2)	0.03

Parameter	Age <55-year-old N = 67 (36.2%)	Age >55-year-old N = 256 (79.3%)	P-value
Chronic Kidney Disease; N (%)	12 (18.2)	30 (11.8)	0.17
Cardiac Ejection Fraction <40%; N (%)	4 (6.2)	20 (8.7)	0.51
Active Neoplasm; N (%)	4 (6.2)	17 (7.4)	0.74
Rheumatological Disease; N (%)	1 (1.5)	4 (1.7)	0.92
Prior Stroke or Transient Ischemic Attack; N (%)	1 (1.5)	4 (1.7)	0.92
Smoking; N (%)	8 (12.1)	45 (17.7)	0.28
<b>Laboratory Findings</b>			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	9.9 ± 4.8	9.8 ± 4.8	0.91
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	9.1 [7.3 – 11.6]	9.0 [6.7 – 11.1]	0.96
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.7 ± 4.7	7.7 ± 4.4	0.99
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.7 [4.8 – 9.1]	6.8 [4.8 – 9.3]	0.86
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	2.0 ± 2.3	1.6 ± 1.4	0.05
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.6 [1.2 – 2.2]	1.3 [0.9 – 1.9]	<0.001
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	315.9 ± 201.9	314.2 ± 487.5	0.98
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	259.5 [179.0 – 398.5]	219.0 [158.5 – 315.0]	0.02
Alanine Transaminase (ALT); Mean (SD); U/L	43.4 ± 60.4	69.3 ± 92.0	0.01
Alanine Transaminase (ALT); Median [IQR] ; U/L	17.1 [6.1 – 56.4]	34.3 [12.0 – 99.0]	0.02
Aspartate Transaminase (AST); Mean (SD); U/L	20.9 ± 16.2	35.2 ± 28.2	<0.001
Aspartate Transaminase (AST); Median [IQR] ; U/L	16.0 [10.4 – 25.0]	26.0 [15.0 – 44.0]	<0.001
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	68.0 ± 197.7	48.8 ± 53.6	0.46
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	30.0 [18.0 – 50.0]	33.0 [22.0 – 50.0]	0.38
Creatinine; Mean (SD); mg/dl	1.4 ± 1.5	1.5 ± 1.8	0.53
Creatinine; Median [IQR]; mg/dl	0.9 [0.8 – 1.2]	1.1 [0.9 – 1.5]	<0.001
C-Reactive Protein (CRP); Mean (SD); mg/L	87.0 ± 259.0	54.0 ± 55.0	0.34
C-Reactive Protein (CRP); Median [IQR]; mg/L	32.0 [20.0 – 48.0]	38.0 [25.0 – 60.0]	0.06
Lactate Dehydrogenase (LDH); Mean (SD); U/L	487.1 ± 334.5	635.3 ± 1716.0	0.64
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	397.5 [286.0 – 588.0]	371.0 [241.5 – 522.5]	0.44
Fibrinogen; Mean (SD); mg/dl	285.6 ± 266.5	547.8 ± 1181.4	0.27
Fibrinogen; Median [IQR]; mg/dl	338.5 [4.0 – 501.0]	220.0 [42.0 – 490.0]	0.70
D- Dimer; Mean (SD); ng/ml	1911.7 ± 3209.7	2884.7 ± 7135.6	0.47
D- Dimer; Median [IQR]; ng/ml	625.5 [426.0 – 2085.0]	1100.0 [585.0 – 2205.0]	0.22

\* Data on patients' disposition were sparse.



## Results; Supplemental Table 4. Subgroups of AIS patients younger or older than 65-year-old

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, comparing those younger versus older than 65. **Blue ink indicates the post-hoc p values.**

Parameter	Age <65-year-old N = 148 (45.8%)	Age >65-year-old N = 175 (54.2%)	P-value
Age; Mean (SD); Years	54 ± 10	79 ± 8	<0.001
Age; Median [IQR]; Years	57 [49 - 62]	77 [72 - 84]	<0.001
Sex; Female; N (%)	52 (35.1)	78 (44.6)	0.09
Large Vessel Occlusion; N (%)	62 (47.3)	64 (42.1)	0.38
Intravenous Thrombolysis; N (%)	29 (19.6)	15 (8.6)	0.004
Mechanical Thrombectomy; N (%)	14 (9.5)	10 (5.7)	0.20
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	8.0 [4.0 – 16.0]	11.0 [5.0 – 20.0]	0.15
Imaging Patterns			
Embollic/Large Vessel athero-Thromboembolism; N (%)	94 (80.3)	112 (80.6)	0.31
Lacune; N (%)	9 (7.7)	17 (12.2)	
Border-zone; N (%)	13 (11.1)	10 (7.2)	
Vasculitis Pattern; N (%)	1 (0.9)	0 (0.0)	
TOAST			
Large-Artery Atherosclerosis; N (%)	33 (38.8)	23 (27.1)	0.07
Cardio-embolism; N (%)	15 (17.6)	21 (36.5) <sup>A (0.006)</sup>	
Small-Vessel Occlusion; N (%)	8 (9.4)	9 (10.6)	
Stroke of Other Determined Etiology; N (%)	8 (9.4)	5 (5.9)	
Stroke of Undetermined Etiology; N (%)	21 (24.7)	17 (20.0)	
Interval Between Onset to Index Event; Median [IQR]; Days	4.0 [0.0 – 10.0]	2.0 [0.0 – 8.0]	0.10
Mechanical Ventilation; N (%)	42 (28.4)	43 (24.6)	0.44
Disposition*			
Discharged Home; N (%)	71 (52.2) <sup>B (0.002)</sup>	56 (34.8)	0.01
In Hospital Mortality; N (%)	29 (21.3)	53 (32.9) <sup>A (0.03)</sup>	
Still in Hospital/Subacute Care; N (%)	36 (26.5)	52 (32.3)	
Length of Hospital Stay; Median (IQR); Days	9.0 [5.0 – 18.0]	7.0 [4.0 – 14.0]	0.05
Comorbidities			
Hypertension; N (%)	77 (52.4)	125 (72.3)	<0.001
Diabetes Mellitus; N (%)	54 (36.5)	57 (32.9)	0.51
Ischemic Heart Disease; N (%)	25 (18.0)	47 (29.9)	0.02
Atrial Fibrillation; N (%)	12 (8.2)	33 (19.1)	0.01
Carotid Stenosis; N (%)	9 (6.5)	29 (18.5)	0.002

Parameter	Age <65-year-old N = 148 (45.8%)	Age >65-year-old N = 175 (54.2%)	P-value
Chronic Kidney Disease; N (%)	24 (16.3)	18 (10.4)	0.12
Cardiac Ejection Fraction <40%; N (%)	6 (4.3)	18 (11.5)	0.03
Active Neoplasm; N (%)	11 (7.9)	10 (6.4)	0.61
Rheumatological Disease; N (%)	1 (0.7)	4 (2.5)	0.22
Prior Stroke or Transient Ischemic Attack; N (%)	1 (0.7)	4 (2.5)	0.22
Smoking; N (%)	18 (12.2)	35 (20.2)	0.06
<b>Laboratory Findings</b>			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	9.8 ± 4.7	9.8 ± 5.0	0.96
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	9.1 [7.2 – 11.3]	8.9 [6.5 – 11.1]	0.54
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.7 ± 4.2	7.7 ± 4.7	0.97
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.9 [4.9 – 9.2]	6.5 [4.7 – 9.2]	0.52
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.8 ± 2.0	1.6 ± 1.3	0.32
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.4 [1.0 – 2.0]	1.3 [0.8 – 1.9]	0.06
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	306.5 ± 218.5	321.8 ± 571.5	0.77
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	266.0 [177.0 – 381.0]	207.0 [154.0 – 300.0]	0.03
Alanine Transaminase (ALT); Mean (SD); U/L	61.2 ± 81.1	65.4 ± 91.4	0.69
Alanine Transaminase (ALT); Median [IQR]; U/L	26.9 [7.0 – 80.4]	32.8 [12.0 – 96.0]	0.54
Aspartate Transaminase (AST); Mean (SD); U/L	27.2 ± 22.4	36.5 ± 29.6	0.003
Aspartate Transaminase (AST); Median [IQR]; U/L	21.0 [12.0 – 35.0]	27.0 [15.5 – 47.5]	0.01
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	61.4 ± 138.9	45.4 ± 54.8	0.21
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	32.5 [21.4 – 56.0]	32.0 [20.0 – 47.0]	1.00
Creatinine; Mean (SD); mg/dl	1.5 ± 2.2	1.6 ± 1.2	0.59
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.3]	1.2 [0.9 – 1.5]	0.004
C-Reactive Protein (CRP); Mean (SD); mg/L	70.0 ± 178.0	53.0 ± 60.0	0.27
C-Reactive Protein (CRP); Median [IQR]; mg/L	35.0 [25.0 – 60.0]	37.0 [24.0 – 55.0]	0.95
Lactate Dehydrogenase (LDH); Mean (SD); U/L	548.9 ± 788.5	653.6 ± 1975.0	0.68
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	420.0 [283.5 – 558.5]	358.0 [220.0 – 503.0]	0.14
Fibrinogen; Mean (SD); mg/dl	421.3 ± 674.7	528.5 ± 1347.3	0.64
Fibrinogen; Median [IQR]; mg/dl	346.0 [4.0 – 506.0]	166.4 [22.9 – 464.0]	0.30
D- Dimer; Mean (SD); ng/ml	2417.5 ± 6626.8	2874.2 ± 6284.3	0.69
D- Dimer; Median [IQR]; ng/ml	830.0 [510.0 – 2085.0]	1100.0 [578.0 – 2430.0]	0.09

\* Data on patients' disposition were sparse.

## Results; Supplemental Table 5. Subgroups of AIS patients based on sex.

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke among female versus male patients. **Blue ink indicates the post-hoc p values.**

Parameter	Female N = 130 (40.2%)	Male N = 193 (59.8%)	P-value
Age; Mean (SD); Years	68.8 ± 17.1	66.1 ± 13.7	0.13
Age; Median [IQR]; Years	73 [58 – 81]	66 [58 – 76]	0.14
Large Vessel Occlusion; N (%)	46 (39.3)	80 (48.2)	0.14
Intravenous Thrombolysis; N (%)	22 (16.9)	22 (11.4)	0.16
Mechanical Thrombectomy; N (%)	12 (9.2)	12 (6.2)	0.31
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	12.0 [5.0 – 19.0]	8.0 [4.0 – 16.0]	<0.001
Imaging Patterns			
Embollic/Large Vessel athero-Thromboembolism; N (%)	83 (81.4)	123 (79.9)	0.49
Lacune; N (%)	11 (10.8)	15 (9.7)	
Border-zone; N (%)	7 (6.9)	16 (10.4)	
Vasculitis Pattern; N (%)	1 (1.0)	0 (0.0)	
TOAST			
Large-Artery Atherosclerosis; N (%)	19 (28.4)	27 (35.9)	0.05
Cardio-embolism; N (%)	21 (31.3)	25 (24.3)	
Small-Vessel Occlusion; N (%)	3 (4.5)	14 (13.6)	
Stroke of Other Determined Etiology; N (%)	9 (13.4) <sup>B (0.02)</sup>	4 (3.9)	
Stroke of Undetermined Etiology; N (%)	15 (22.4)	23 (22.3)	
Interval Between Onset to Index Event; Median [IQR]; Days	1.0 [0 – 8.0]	4.0 [0 – 9.0]	0.55
Mechanical Ventilation; N (%)	35 (26.9)	50 (25.9)	0.84
Disposition*			
Discharged Home; N (%)	47 (39.2)	80 (45.2)	0.59
In Hospital Mortality; N (%)	35 (29.2)	47 (26.6)	
Still in Hospital/Subacute Care; N (%)	38 (31.7)	50 (28.2)	
Length of Hospital Stay; Median (IQR); Days	7.0 [4.0 – 17.0]	7.0 [4.0 – 15.0]	0.10
Comorbidities			
Hypertension; N (%)	80 (63.0)	122 (63.2)	0.97
Diabetes Mellitus; N (%)	46 (35.9)	65 (33.7)	0.68
Ischemic Heart Disease; N (%)	28 (23.9)	44 (24.6)	0.90
Atrial Fibrillation; N (%)	22 (17.3)	23 (11.9)	0.17
Carotid Stenosis; N (%)	14 (12.0)	24 (13.4)	0.72
Chronic Kidney Disease; N (%)	10 (7.9)	32 (16.6)	0.02

Parameter	Female N = 130 (40.2%)	Male N = 193 (59.8%)	P-value
Cardiac Ejection Fraction <40%; N (%)	12 (11.1)	11 (6.1)	0.13
Active Neoplasm; N (%)	7 (6.0)	14 (6.8)	0.55
Rheumatological Disease; N (%)	1 (0.9)	4 (2.2)	0.37
Prior Stroke or Transient Ischemic Attack; N (%)	2 (1.7)	3 (1.7)	0.98
Smoking; N (%)	12 (9.4)	41 (21.2)	0.01
Laboratory Findings			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	9.7 ± 5.0	9.9 ± 4.7	0.80
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	8.8 [6.5 – 10.8]	9.1 [7.2 – 11.6]	0.64
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.7 ± 4.9	7.7 ± 4.2	0.94
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.3 [4.6 – 9.2]	7.2 [4.9 – 9.4]	0.94
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.6 ± 0.8	1.7 ± 2.1	0.64
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.5 [1.0 – 2.2]	1.3 [0.9 – 1.8]	0.24
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	284.9 ± 199.0	334.6 ± 546.7	0.35
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	242.0 [162.0 – 353.0]	221.0 [161.0 – 313.0]	0.90
Alanine Transaminase (ALT); Mean (SD); U/L	47.4 ± 55.5	73.6 ± 100.2	0.01
Alanine Transaminase (ALT); Median [IQR] ; U/L	22.4 [4.0 – 74.0]	33.0 [12.3 – 109.0]	0.05
Aspartate Transaminase (AST); Mean (SD); U/L	32.1 ± 25.5	32.1 ± 27.7	0.98
Aspartate Transaminase (AST); Median [IQR] ; U/L	25.0 [14.0 – 44.0]	23.0 [14.0 – 40.0]	0.42
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	38.1 ± 36.0	63.4 ± 131.2	0.02
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	29.0 [19.0 – 41.0]	34.5 [22.0 – 56.5]	0.91
Creatinine; Mean (SD); mg/dl	1.4 ± 1.3	1.6 ± 1.9	0.31
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.5]	1.1 [0.9 – 1.5]	0.68
C-Reactive Protein (CRP); Mean (SD); mg/L	49.7 ± 65.4	69.3 ± 131.2	0.23
C-Reactive Protein (CRP); Median [IQR]; mg/L	33.0 [23.0 – 50.0]	40.0 [26.0 – 58.0]	0.33
Lactate Dehydrogenase (LDH); Mean (SD); U/L	438.6 ± 353.6	696.8 ± 1894.5	0.33
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	349.5 [277.5 – 467.0]	414.5 [241.0 – 556.0]	0.13
Fibrinogen; Mean (SD); mg/dl	286.7 ± 227.9	562.3 ± 1216.6	0.23
Fibrinogen; Median [IQR]; mg/dl	346.0 [56.0 – 477.0]	218.0 [3.9 – 561.0]	0.68
D- Dimer; Mean (SD); ng/ml	2979.3 ± 6778.1	2470.6 ± 6258.5	0.67
D- Dimer; Median [IQR]; ng/ml	1057.0 [510.0 – 2200.0]	992 [568.0 – 2180.0]	0.92

\* Data on patients' disposition were sparse.

# **Results**

## **Acute Ischemic Stroke;**

### **Outcome Measures**

#### **Supplemental Tables 6-10**

## Results; Supplemental Table 6. Subgroups of AIS patients according to the TOAST criteria

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, based on TOAST classification subgroups. [Blue ink indicates the post-hoc p values.](#)

Parameter	A: Large Artery Atherosclerosis N = 56 (32.9%)	B: Cardio-embolism N = 46 (27.1%)	C: Small artery occlusion N = 17 (10.0%)	D: Other Determined N = 13 (7.6%)	E: Undetermined N = 38 (22.4%)	P-value
Age; Mean (SD); Years	63 ± 15	72 ± 14 <a href="#">D (0.021)</a>	67 ± 18	57 ± 16	65 ± 18	0.01
Age; Median [IQR]; Years	64.0 [56.0 – 73.0]	75.0 [62.0 – 81.0]	75.0 [58.0 – 78.0]	54.0 [40.0 – 72.0]	64.0 [51.0 – 80.0]	0.07
Sex; Female; N (%)	19 (33.9)	21 (45.7)	3 (17.6)	9 (69.2) <a href="#">C (0.043)</a>	15 (39.5)	0.05
Large Vessel Occlusion; N (%)	46 (85.2) <a href="#">B (0.003)</a> <a href="#">D (&lt;0.001)</a> <a href="#">E (&lt;0.001)</a>	24 (53.3)	0 (0.0)	2 (18.2)	7 (20.0)	<0.001
Intravenous Thrombolysis; N (%)	14 (25.0)	8 (17.4)	0 (0.0)	2 (15.4)	4 (10.5)	0.12
Mechanical Thrombectomy; N (%)	10 (17.9)	10 (21.7)	0 (0.0)	1 (7.7)	2 (5.3)	0.07
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	9.0 [5.0 – 17.0]	13.0 [8.0 -20.0]	4.0 [2.0 -8.0]	14.0 [6.0 – 18.0]	7.0 [3.0 – 17.0]	0.10
Imaging Patterns						
Embolic/Large Vessel athero-Thromboembolism; N (%)	54 (96.4) <a href="#">C (&lt;0.001)</a> <a href="#">D (0.017)</a>	43 (93.5) <a href="#">C (&lt;0.001)</a>	4 (23.5)	9 (69.2)	34 (89.5) <a href="#">C (&lt;0.001)</a>	<0.001
Lacune; N (%)	0 (0.0)	1 (2.2)	13 (76.5) <a href="#">B (&lt;0.001)</a> <a href="#">D (0.001)</a> <a href="#">E (&lt;0.001)</a>	1 (7.7)	4 (10.5)	
Border-zone; N (%)	2 (3.6)	1 (2.2)	0 (0.0)	3 (23.1) <a href="#">A (0.044)</a> <a href="#">B (0.024)</a>	0 (0.0)	
Vasculitis Pattern; N (%)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	
Interval Between Onset to Index Event; Median [IQR]; Days	4.0 [1.0 – 10.0]	2.0 [0.0 – 11.0]	2.0 [0.0 – 6.0]	10.0 [4.0 – 17.0]	4.0 [0.0 – 12.0]	0.12
Mechanical Ventilation; N (%)	22 (29.3)	10 (21.7)	4 (23.5)	9 (69.2)	11 (28.9)	0.02
Disposition*						
Discharged Home; N (%)	24 (42.9)	16 (34.8)	11 (64.7)	8 (61.5)	9 (24.3)	0.12
In Hospital Mortality; N (%)	14 (25.0)	13 (28.3)	3 (17.6)	2 (15.4)	9 (24.3)	
Still in Hospital/Subacute Care; N (%)	18 (32.1)	17 (37.0)	3 (17.6)	3 (23.1)	19 (54.1)	
Length of Hospital Stay; Median (IQR); Days	6.0 [4.0 – 15.0]	7.0 [5.0 -14.0]	7.0 [5.0 – 16.0]	20.0 [4.0 – 35.0]	8.0 [6.0 – 26.0]	0.17
Comorbidities						
Hypertension; N (%)	30 (53.6)	35 (76.1) <a href="#">D (0.023)</a>	10 (58.8)	4 (30.8)	25 (65.8)	0.03
Diabetes Mellitus; N (%)	20 (35.7)	15 (32.6)	6 (35.3)	1 (7.7)	12 (31.6)	0.41
Ischemic Heart Disease; N (%)	11 (19.6)	21 (45.7)	3 (17.6)	1 (7.7)	2 (5.3)	<0.001

Parameter	A: Large Artery Atherosclerosis N = 56 (32.9%)	B: Cardio-embolism N = 46 (27.1%)	C: Small artery occlusion N = 17 (10.0%)	D: Other Determined N = 13 (7.6%)	E: Undetermined N = 38 (22.4%)	P-value
		A (0.048) E (<0.001)				
Atrial Fibrillation; N (%)	2 (3.6)	23 (50.0) A (<0.001) E (<0.001)	4 (23.5)	1 (7.7)	1 (2.6)	<0.001
Carotid Stenosis; N (%)	16 (28.6) E (0.029)	6 (13.0)	1 (5.9)	0 (0.0)	2 (5.3)	0.01
Chronic Kidney Disease; N (%)	8 (14.3)	3 (6.5)	6 (35.3) B (0.038)	1 (7.7)	3 (7.9)	0.03
Cardiac Ejection Fraction <40%; N (%)	5 (8.9)	8 (17.4)	1 (5.9)	1 (7.7)	5 (13.2)	0.61
Active Neoplasm; N (%)	2 (3.6)	9 (19.6) A (0.029)	1 (5.9)	0 (0.0)	0 (0.0)	<0.001
Rheumatological Disease; N (%)	0 (0.0)	3 (6.5)	1 (5.9)	0 (0.0)	0 (0.0)	0.32
Prior Stroke or Transient Ischemic Attack; N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0.48
Smoking; N (%)	11 (19.6)	5 (10.9)	2 (11.8)	0 (0.0)	4 (10.5)	0.34
Laboratory Findings						
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	10.2 ± 5.5	10.3 ± 4.5	9.9 ± 2.5	11.6 ± 8.1	8.5 ± 3.9	0.29
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	9.1 [7.1 – 11.3]	9.8 [7.7 – 12.5]	9.0 [7.9 – 11.8]	9.3 [5.0 – 17.1]	7.7 [5.9 – 10.2]	0.16
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	8.4 ± 4.8	7.9 ± 4.5	8.0 ± 2.7	9.7 ± 7.7	6.5 ± 3.7	0.24
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	7.2 [5.4 – 9.2]	8.0 [4.8 – 10.2]	7.0 [6.0 – 10.0]	7.4 [3.5 – 14.2]	5.9 [4.2 – 8.2]	0.16
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.5 ± 2.3	2.1 ± 1.3	2.0 ± 2.1	1.5 ± 0.7	2.1 ± 1.9	0.35
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.1 [0.8 – 1.5]	1.9 [1.2 – 2.6]	1.2 [1.0 – 2.0]	1.5 [0.9 – 2.2]	1.4 [1.0 – 2.6]	<0.001
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	258.0 ± 134.4	503.5 ± 992.7	220.7 ± 151.3	343.9 ± 166.9	416.6 ± 431.2	0.20
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	223.0 [165.0 – 312.0]	232.0 [155.0 – 320.0]	179.5 [107.5 – 273.5]	338.0 [244.0 – 429.0]	249.0 [196.0 – 395.0]	0.04
Alanine Transaminase (ALT); Mean (SD); U/L	63.5 ± 78.4	35.5 ± 53.3	51.0 ± 60.0	44.9 ± 75.5	66.5 ± 81.2	0.29
Alanine Transaminase (ALT); Median [IQR]; U/L	33.9 [8.0 – 85.0]	14.0 [4.0 – 31.0]	44.0 [9.0 – 62.0]	4.8 [1.2 – 43.7]	29.7 [10.9 – 104.3]	0.08
Aspartate Transaminase (AST); Mean (SD); U/L	36.5 ± 34.4	30.3 ± 23.0	25.4 ± 13.9	34.7 ± 38.3	24.3 ± 19.1	0.26
Aspartate Transaminase (AST); Median [IQR]; U/L	23.0 [12.0 – 44.2]	25.0 [12.0 – 43.0]	19.0 [14.0 – 38.3]	38.0 [19.0 – 52.0]	33.0 [24.0 – 50.0]	0.72
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	47.9 ± 51.1	46.2 ± 63.6	43.0 ± 50.1	39.3 ± 26.0	86.6 ± 260.6	0.60
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	33.0 [21.0 – 56.0]	30.5 [19.0 – 50.0]	28.0 [20.0 – 34.0]	38.0 [19.0 – 52.0]	33.0 [24.0 – 50.0]	0.79
Creatinine; Mean (SD); mg/dl	1.3 ± 0.8	1.1 ± 0.3	1.6 ± 1.4	1.3 ± 1.2	1.4 ± 1.2	0.43
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.3]	1.0 [0.9 – 1.3]	1.3 [1.1 – 1.4]	0.8 [0.6 – 1.2]	1.0 [0.8 – 1.3]	0.05
C-Reactive Protein (CRP); Mean (SD); mg/L	47.0 ± 52.0	49.0 ± 58.0	35.0 ± 18.0	42.0 ± 25.0	107 ± 325	0.37

Parameter	A: Large Artery Atherosclerosis N = 56 (32.9%)	B: Cardio-embolism N = 46 (27.1%)	C: Small artery occlusion N = 17 (10.0%)	D: Other Determined N = 13 (7.6%)	E: Undetermined N = 38 (22.4%)	P-value
C-Reactive Protein (CRP); Median [IQR]; mg/L	41.0 [25.0 – 52.0]	36.0 [21.0 – 45.0]	30.0 [23.0 – 44.0]	37.0 [23.0 – 60.0]	36.0 [26.0 – 72.0]	0.75
Lactate Dehydrogenase (LDH); Mean (SD); U/L	1064.6 ± 2880.1	542.6 ± 1114.4	371.2 ± 202.7	474.7 ± 472.4	321.5 ± 185.6	0.53
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	458.0 [319.0 – 668.5]	315.0 [224.0 – 454.0]	268.0 [203.0 – 600.0]	337.0 [201.0 – 610.0]	326.0 [185.0 – 426.0]	0.18
Fibrinogen; Mean (SD); mg/dl	522.7 ± 1054.0	674.7 ± 1839.4	779.5 ± 918.3	157.2 ± 156.1	217.4 ± 338.1	0.73
Fibrinogen; Median [IQR]; mg/dl	76.0 [1.95 – 477.0]	200.5 [3.75 – 446.5]	429.5 [261.5 – 1297.5]	104.0 [2.7 – 353.0]	57.5 [4.0 – 220.0]	0.48
D- Dimer; Mean (SD); ng/ml	919.6 ± 956.4	2019.6 ± 2694.8	820.7 ± 593.0	1257.3 ± 761.9	1386.8 ± 1196.6	0.25
D- Dimer; Median [IQR]; ng/ml	486.5 [371.5 – 1422.5] B (0.039)	1100.0 [955.0 – 2355.0]	730.0 [480.0 – 1100.0]	949.5 [625.0 – 2200.0]	932.5 [513.5 – 2000.5]	0.03

\* Data on patients' disposition were sparse.



## Results; Supplemental Table 7. Subgroups of AIS patients according to the NIHSS scores.

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, based on NIHSS scores. [Blue ink indicates the post-hoc p values.](#)

Parameter	A: No Stroke Symptoms (NIHSS = 0) N = 20 (7.5%)	B: Minor Stroke (NIHSS = 1 to 4) N = 49 (18.4%)	C: Moderate Stroke (NIHSS 5 to 15) N = 117 (43.8%)	D: Moderate to Severe Stroke (NIHSS = 16 to 20) N = 35 (13.1%)	E: Severe Stroke (NIHSS = 21 to 42) N = 46 (17.2%)	P value
Age; Mean (SD); Years	67 ± 13	65 ± 17	66 ± 15	66 ± 16	69 ± 15	0.77
Age; Median [IQR]; Years	65 [60 – 76]	65 [55 – 75]	66 [56 – 77]	67 [57 – 78]	72 [60 – 81]	0.65
Sex; Female; N (%)	6 (30.0)	20 (40.8)	44 (37.6)	16 (45.7)	22 (47.8)	0.60
Large Vessel Occlusion; N (%)	1 (8.3)	8 (17.0)	49 (44.5) <sup>B (0.01)</sup>	23 (67.6) <sup>A (0.004)</sup> <sup>B (&lt;0.001)</sup>	31 (75.6) <sup>A (&lt;0.001)</sup> <sup>B (&lt;0.001)</sup> <sup>C (0.01)</sup>	<0.001
Intravenous Thrombolysis; N (%)	0 (0.0)	2 (4.1)	25 (21.4) <sup>B (0.04)</sup>	11 (31.4) <sup>B (0.004)</sup>	5 (10.9)	<0.001
Mechanical Thrombectomy; N (%)	0 (0.0)	1 (2.0)	8 (6.8)	9 (25.7) <sup>B (0.01)</sup> <sup>C (0.01)</sup>	6 (13.0)	<0.001
Imaging Patterns						
Embolic/Large Vessel athero-Thromboembolism; N (%)	4 (57.1)	31 (73.8)	85 (81.7)	24 (75.0)	39 (92.9)	<0.001
Lacune; N (%)	2 (28.6)	8 (19.0)	10 (9.6)	1 (3.1)	1 (2.4)	
Border-zone; N (%)	0 (0.0)	3 (7.1)	9 (8.7)	7 (21.9)	2 (4.8)	
Vasculitis Pattern; N (%)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
TOAST						
Large-Artery Atherosclerosis; N (%)	1 (14.3)	9 (25.7)	30 (43.5)	5 (19.2)	11 (36.7)	0.03
Cardio-embolism; N (%)	2 (28.6)	5 (14.3)	17 (24.6)	13 (50.0) <sup>B (0.03)</sup>	8 (26.7)	
Small-Vessel occlusion; N (%)	1 (14.3)	9 (25.7)	30 (43.5)	5 (19.2)	11 (36.7)	
Stroke of Other Determined Etiology; N (%)	0 (0.0)	3 (8.6)	3 (4.3)	4 (15.4)	2 (6.7)	
Stroke of Undetermined Etiology; N (%)	3 (42.9)	10 (28.6)	13 (18.8)	4 (15.4)	7 (23.3)	
Interval Between Onset to Index Event; Median [IQR]; Days	3.0 [0.0 – 12.0]	3.0 [0.0 – 10.0]	4.0 [1.0 – 8.0]	3.0 [0.0 – 10.0]	1.0 [0.0 – 10.0]	0.64

Parameter	A: No Stroke Symptoms (NIHSS = 0) N = 20 (7.5%)	B: Minor Stroke (NIHSS = 1 to 4) N = 49 (18.4%)	C: Moderate Stroke (NIHSS 5 to 15) N = 117 (43.8%)	D: Moderate to Severe Stroke (NIHSS = 16 to 20) N = 35 (13.1%)	E: Severe Stroke (NIHSS = 21 to 42) N = 46 (17.2%)	P value
Mechanical Ventilation; N (%)	2 (10.0)	8 (16.3)	25 (21.4)	12 (34.3)	29 (63.0) <sup>A (0.001)</sup> B (<0.001) C (<0.001)	<0.001
Disposition*						
Discharged Home; N (%)	5 (62.5)	28 (62.2) <sup>D (0.001)</sup> E (0.001)	52 (47.3) <sup>D (0.24)</sup> E (0.02)	6 (17.6)	9 (20.5)	<0.001
In Hospital Mortality; N (%)	1 (12.5)	5 (11.1)	18 (16.4)	19 (55.9) <sup>B (&lt;0.001)</sup> C (<0.001)	23 (52.3) <sup>B (&lt;0.001)</sup> C (<0.001)	
Still in Hospital/Subacute Care; N (%)	2 (25.0)	12 (26.7)	40 (36.4)	9 (26.5)	12 (27.3)	
Length of Hospital Stay; Median (IQR); Days	8.0 [2.0 – 22.0]	6.0 [4.0 – 12.0]	9.0 [5.0 – 17.0]	6.0 [4.0 – 14.0]	7.0 [5.0 – 15.0]	0.44
Comorbidities						
Hypertension; N (%)	14 (73.7)	34 (69.4)	78 (66.7)	23 (65.7)	29 (60.9)	0.86
Diabetes Mellitus; N (%)	9 (45.0)	13 (26.5)	41 (35.0)	13 (37.1)	16 (34.8)	0.65
Ischemic Heart Disease; N (%)	1 (10.0)	2 (4.3)	33 (29.7) <sup>B (0.01)</sup>	12 (36.4) <sup>B (0.002)</sup>	11 (26.2) <sup>B (0.04)</sup>	<0.001
Atrial Fibrillation; N (%)	4 (21.1)	4 (8.2)	12 (10.3)	11 (31.4) <sup>C (0.02)</sup>	9 (17.4)	0.02
Carotid Stenosis; N (%)	0 (0.0)	10 (21.7)	16 (14.4)	3 (9.1)	7 (16.7)	0.35
Chronic Kidney Disease; N (%)	3 (15.8)	8 (16.3)	16 (13.7)	7 (20.0)	3 (6.5)	0.48
Cardiac Ejection Fraction <40%; N (%)	2 (20.0)	3 (6.5)	9 (8.1)	2 (6.1)	4 (9.5)	0.68
Active Neoplasm; N (%)	0 (0.0)	0 (0.0)	11 (9.9)	3 (9.1)	3 (7.1)	0.21
Rheumatological Disease; N (%)	0 (0.0)	1 (2.2)	3 (2.7)	1 (3.0)	0 (0.0)	0.83
Prior Stroke or Transient Ischemic Attack; N (%)	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0.88
Smoking; N (%)	2 (10.5)	8 (16.3)	22 (18.8)	5 (14.3)	6 (13.0)	0.83
Laboratory Findings						
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	8.6 ± 3.5	9.6 ± 5.6	9.8 ± 4.4	9.2 ± 4.1	11.1 ± 5.0	0.24
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	7.7 [6.7 – 9.8]	7.7 [6.3 – 9.9]	8.9 [6.9 – 11.3]	9.3 [7.2 – 10.7]	10.5 [8.1 – 12.7]	0.03

Parameter	A: No Stroke Symptoms (NIHSS = 0) N = 20 (7.5%)	B: Minor Stroke (NIHSS = 1 to 4) N = 49 (18.4%)	C: Moderate Stroke (NIHSS 5 to 15) N = 117 (43.8%)	D: Moderate to Severe Stroke (NIHSS = 16 to 20) N = 35 (13.1%)	E: Severe Stroke (NIHSS = 21 to 42) N = 46 (17.2%)	P value
	E (0.001)					
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.0 ± 3.6	7.2 ± 5.1	7.9 ± 4.4	7.4 ± 3.7	8.5 ± 4.2	0.56
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.2 [5.1 – 8.6]	6.0 [4.5 – 8.2]	7.2 [5.0 – 9.1]	7.1 [4.8 – 9.2]	8.4 [5.3 – 10.5]	0.16
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.4 ± 1.5	1.7 ± 1.1	1.6 ± 1.2	2.1 ± 2.9	1.9 ± 2.4	0.68
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.1 [0.8 – 1.4]	1.3 [1.0 – 2.2]	1.4 [0.9 – 1.9]	1.4 [0.9 – 2.1]	1.3 [0.8 – 2.0]	0.42
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	419.9 ± 714.5	379.0 ± 395.7	334.2 ± 609.9	281.5 ± 129.4	264.8 ± 115.7	0.68
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	220.0 [177.0 – 390.0]	263.5 [169.0 – 395.0]	205.0 [149.0 – 313.0]	239.0 [171.0 – 397.0]	247.0 [190.0 – 348.0]	0.32
Alanine Transaminase (ALT); Mean (SD); U/L	105.6 ± 177.7	34.5 ± 45.9	63.9 ± 80.3	58.0 ± 84.3	50.1 ± 51.2	0.04
Alanine Transaminase (ALT); Median [IQR]; U/L	28.8 [15.3 – 153.7]	16.7 [4.0 – 49.0]	28.7 [11.0 – 82.5]	36.5 [3.1 – 75.0]	26.4 [4.6 – 110.0]	0.24
Aspartate Transaminase (AST); Mean (SD); U/L	30.9 ± 22.3	23.6 ± 20.2	33.1 ± 26.2	28.1 ± 23.7	41.5 ± 32.7	0.02
Aspartate Transaminase (AST); Median [IQR]; U/L	25.0 [14.0 – 40.0]	22.4 [12.4 – 31.8]	25.0 [14.2 – 42.0]	21.0 [10.7 – 39.0]	28.9 [15.0 – 57.0]	0.08
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	61.3 ± 50.5	50.0 ± 66.8	46.5 ± 45.6	33.9 ± 20.8	39.5 ± 39.0	0.32
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	43.0 [29.0 – 71.0]	32.5 [23.0 – 47.0]	31.5 [21.0 – 54.0]	31.0 [15.0 – 46.0]	33.0 [16.0 – 48.0]	0.33
Creatinine; Mean (SD); mg/dl	1.5 ± 1.2	1.0 ± 0.3	1.5 ± 1.3	1.2 ± 0.9	1.6 ± 1.1	0.05
Creatinine; Median [IQR]; mg/dl	1.0 [0.9 – 1.3] B (0.039)	0.9 [0.8 – 1.2] E (0.021)	1.2 [0.9 – 1.5]	1.0 [0.8 – 1.2]	1.2 [0.9 – 1.6]	<0.001
C-Reactive Protein (CRP); Mean (SD); mg/L	57.0 ± 41.0	46.0 ± 52.0	50.0 ± 51.0	45.0 ± 31.0	47.0 ± 40.0	0.91
C-Reactive Protein (CRP); Median [IQR]; mg/L	43.0 [29.0 – 75.0]	35.0 [23.0 – 49.0]	37.0 [24.0 – 51.0]	35.0 [24.0 – 55.0]	36.0 [26.0 – 56.0]	0.83
Lactate Dehydrogenase (LDH); Mean (SD); U/L	531.6 ± 254.9	551.9 ± 1136.0	457.2 ± 707.3	511.9 ± 412.3	1119.4 ± 3301.0	0.57
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	523.0 [312.0 – 736.0]	324.0 [203.0 – 483.0]	344.0 [200.0 – 490.0]	404.0 [241.0 – 681.0]	399.5 [315.0 – 490.0]	0.19
Fibrinogen; Mean (SD); mg/dl	509.3 ± 196.3	409.1 ± 740.9	575.3 ± 1556.1	133.9 ± 149.3	465.0 ± 298.2	0.88
Fibrinogen; Median [IQR]; mg/dl	563.0 [438.0 – 626.0] B (0.032) D (0.010)	44.0 [3.5 – 403.0]	58.0 [2.5 – 400.0]	76.0 [2.5 – 216.0]	419.0 [366.0 – 477.0]	0.01
D- Dimer; Mean (SD); ng/ml	7020.9 ± 11983.6	1025.6 ± 1087.5	3277.8 ± 9087.7	1757.3 ± 952.1	2033.5 ± 3027.9	0.08
D- Dimer; Median [IQR]; ng/ml	2343.0 [821.0 – 3477.0]	651.0 [347.0 – 1402.0]	950.0 [510.0 – 2165.0]	2048.0 [626.0 – 2448.0]	1100.0 [629.0 – 2175.0]	0.02

\* Data on patients' disposition were sparse.

**Results; Supplemental Table 8. Subgroups of AIS patients according to the presence or absence of large vessel occlusion.**

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, based on the absence versus presence of large vessel occlusion. [Blue ink indicates the post-hoc p values.](#)

Parameter	Other Strokes N = 157 (55.5%)	Large Vessel Occlusion N = 126 (44.5%)	P-value
Age; Mean (SD); Years	68 ± 16.1	65.7 ± 14.4	0.22
Age; Median [IQR]; Years	70 [58 – 79]	66 [57 – 75]	0.14
Sex; Female; N (%)	71 (45.2)	46 (36.5)	0.14
Intravenous Thrombolysis; N (%)	14 (8.9)	28 (22.2) <sup>A (0.002)</sup>	0.002
Mechanical Thrombectomy; N (%)	0 (0.0)	24 (19.0)	<0.001
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	6.0 [3.0 – 12.0]	15.0 [8.0 – 21.0]	<0.001
Imaging Patterns			
Embollic/Large Vessel athero-Thromboembolism; N (%)	99 (73.3)	99 (88.4) <sup>A (0.003)</sup>	<0.001
Lacune; N (%)	12 (17.0) <sup>B (&lt;0.001)</sup>	2 (1.8)	
Border-zone; N (%)	12 (8.9)	11 (9.8)	
Vasculitis Pattern; N (%)	1 (0.7)	0 (0.0)	
TOAST			
Large-Artery Atherosclerosis; N (%)	8 (9.6)	46 (58.2) <sup>A (&lt;0.001)</sup>	<0.001
Cardio-embolism; N (%)	21 (25.3)	24 (30.4)	
Small-Vessel Occlusion; N (%)	17 (20.5)	0 (0.0)	
Stroke of Other Determined Etiology; N (%)	9 (10.8) <sup>B (0.04)</sup>	2 (2.5)	
Stroke of Undetermined Etiology; N (%)	28 (33.7) <sup>B (&lt;0.001)</sup>	7 (8.9)	
Interval Between Onset to Index Event; Median [IQR]; Days	3.0 [0.0 – 9.0]	3.0 [0.0 – 8.0]	0.55
Mechanical Ventilation; N (%)	42 (26.8)	36 (28.6)	0.73
Disposition*			
Discharged Home; N (%)	66 (44.6)	46 (37.7)	0.24
In Hospital Mortality; N (%)	35 (23.6)	40 (32.8)	
Still in Hospital/Subacute Care; N (%)	47 (31.8)	36 (29.5)	
Length of Hospital Stay; Median (IQR); Days	8.0 [5.0 – 17.0]	6.0 [4.0 – 15.0]	0.10
Comorbidities			
Hypertension; N (%)	106 (68.4)	79 (62.7)	0.32
Diabetes Mellitus; N (%)	56 (35.9)	45 (35.7)	0.98
Ischemic Heart Disease; N (%)	27 (18.2)	40 (33.6) <sup>A (0.004)</sup>	<0.001

Parameter	Other Strokes N = 157 (55.5%)	Large Vessel Occlusion N = 126 (44.5%)	P- value
Atrial Fibrillation; N (%)	19 (12.3)	21 (16.7)	0.29
Carotid Stenosis; N (%)	17 (11.5)	18 (15.1)	0.38
Chronic Kidney Disease; N (%)	27 (17.4)	14 (11.1)	0.14
Cardiac Ejection Fraction <40%; N (%)	12 (8.1)	8.0 (6.7)	0.67
Active Neoplasm; N (%)	8 (5.4)	9 (7.6)	0.47
Rheumatological Disease; N (%)	2 (1.4)	3 (2.5)	0.48
Prior Stroke or Transient Ischemic Attack; N (%)	2 (1.4)	2 (1.7)	0.83
Smoking; N (%)	23 (14.8)	24 (19)	0.35
<b>Laboratory Findings</b>			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	9.8 ± 4.6	10.0 ± 5.1	0.69
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	8.6 [6.7 – 11.5]	9.5 [6.8 – 11.1]	0.64
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.6 ± 4.2	7.8 ± 4.7	0.77
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.5 [4.9 – 9.4]	7.3 [4.7 – 9.1]	0.94
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.7 ± 1.2	1.7 ± 2.2	0.82
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.4 [1 – 2.1]	1.3 [0.9 – 1.9]	0.24
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	334.1 ± 563.6	297.8 ± 332.4	0.54
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	206.0 [150.0 – 307.5]	249.0 [165.0 – 340.0]	0.90
Alanine Transaminase (ALT); Mean (SD); U/L	55.5 ± 78.6	62.9 ± 66.5	0.43
Alanine Transaminase (ALT); Median [IQR]; U/L	20.0 [6.1 – 75.0]	36.0 [13.1 – 109.0]	0.05
Aspartate Transaminase (AST); Mean (SD); U/L	31.6 ± 24.0	31.5 ± 28.1	0.98
Aspartate Transaminase (AST); Median [IQR]; U/L	25.5 [14.0 – 43.5]	22.0 [14.0 – 36.0]	0.42
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	56.6 ± 141.5	46.6 ± 55.9	0.49
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	32.0 [22.0 – 46.0]	32.5 [21.0 – 50.0]	0.91
Creatinine; Mean (SD); mg/dl	1.5 ± 1.4	1.3 ± 0.9	0.27
Creatinine; Median [IQR]; mg/dl	1.0 [0.9 – 1.5]	1.1 [0.9 – 1.4]	0.69
C-Reactive Protein (CRP); Mean (SD); mg/L	71.3 ± 183.8	47.4 ± 54.8	0.17
C-Reactive Protein (CRP); Median [IQR]; mg/L	35.0 [25.0 – 61.0]	36.0 [24.0 – 50.0]	0.33
Lactate Dehydrogenase (LDH); Mean (SD); U/L	470.9 ± 801.3	824.1 ± 2308.0	0.26
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	347.0 [237.0 – 457.0]	418.0 [241.0 – 588.0]	0.13
Fibrinogen; Mean (SD); mg/dl	346.3 ± 540.8	612.9 ± 1468.5	0.33
Fibrinogen; Median [IQR]; mg/dl	89.5 [3.8 – 457.0]	219.5 [ 3.3 – 483.0]	0.68
D- Dimer; Mean (SD); ng/ml	2825.8 ± 7596.3	1909.8 ± 2877.1	0.43
D- Dimer; Median [IQR]; ng/ml	982.0 [592.5 – 2012.5]	935.0 [510.0 – 2180.0]	0.92

\* Data on patients' disposition were sparse.

## Results; Supplemental Table 9. Subgroups of patients according to the imaging patterns.

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with a stroke, based on the neuroimaging pattern found when evaluating the patient. Blue ink indicates the post-hoc p values.

Parameter	Embolic/Large Vessel Athero-Thromboembolism N = 206 (80.5%)	Lacune N = 26 (10.2%)	Border-zone N = 23 (9.0%)	Vasculitis Pattern N = 1 (0.4%)	P-value
Age; Mean (SD); Year	67 ± 15	72 ± 18	62 ± 18	57 ± 0	0.17
Age; Median [IQR]; Year	68 [58 – 78]	73 [62 – 88]	59 [49 – 77]	57 [57 – 57]	0.41
Sex; Female; N (%)	83 (40.3)	11 (42.3)	7 (30.4)	1 (100.0)	0.49
Large Vessel Occlusion; N (%)	99 (50.0) <sup>A</sup> (<0.001)	23 (92.0)	12 (52.2) <sup>C</sup> (0.01)	1 (100.0)	0.001
Intravenous Thrombolysis; N (%)	34 (16.5)	1 (3.8)	2 (8.7)	0 (0.0)	0.28
Mechanical Thrombectomy; N (%)	23 (11.2)	0 (0.0)	1 (4.3)	0 (0.0)	0.24
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	11.0 [5.0 – 19.0]	5.0 [2.0 – 8.0]	14.0 [6.0 – 17.0]	0.0 [0.0 – 0.0]	0.03
TOAST Criteria					
Large-Artery Atherosclerosis; N (%)	54 (37.5)	0 (0.0)	2 (33.3)	0 (0.0)	<0.001
Cardio-embolism; N (%)	43 (29.9)	1 (5.3)	1 (16.7)	1 (100.0)	
Small-Vessel Occlusion; N (%)	4 (2.8)	13 (68.4) <sup>A</sup> (<0.001)	0 (0.0)	0 (0.0)	
Stroke of Other Determined Etiology; N (%)	9 (6.3)	1 (5.3)	3 (50.0) <sup>A</sup> (<0.001) <sup>B</sup> (0.03)	0 (0.0)	
Stroke of Undetermined Etiology; N (%)	34 (23.6)	4 (21.1)	0 (0.0)	0 (0.0)	
Interval Between Onset to Index Event; Median [IQR]; Day	3.0 [0.0 – 10.0]	1.0 [0.0 – 6.0]	5.0 [1.0 – 7.0]	23.0 [23.0 – 23.0]	0.39
Mechanical Ventilation; N (%)	63 (30.6)	8 (30.8)	6 (26.1)	0 (0.0)	0.89
Disposition*					
Discharged Home; N (%)	79 (38.5)	14 (53.8)	10 (43.5)	1 (100.0)	0.44
In Hospital Mortality; N (%)	62 (30.2)	3 (11.5)	6 (26.1)	0 (0.0)	
Still in Hospital/Subacute Care; N (%)	64 (31.2)	9 (34.6)	7 (30.4)	0 (0.0)	
Length of Hospital Stay; Median (IQR); Day	7.0 [5.0 – 16.0]	6.0 [4.0 – 14.0]	15.0 [5.0 – 16.0]	37.0 [37.0 – 37.0]	0.52
Comorbidities					
Hypertension; N (%)	130 (63.4)	16 (61.5)	18 (78.3)	1 (100.0)	0.45
Diabetes Mellitus; N (%)	66 (32.2)	8 (30.8)	10 (43.5)	1 (100.0)	0.35
Ischemic Heart Disease; N (%)	56 (27.3)	6 (23.1)	3 (13.0)	0 (0.0)	0.45

Parameter	Embolic/Large Vessel Athero-Thromboembolism N = 206 (80.5%)	Lacune N = 26 (10.2%)	Border-zone N = 23 (9.0%)	Vasculitis Pattern N = 1 (0.4%)	P-value
Atrial Fibrillation; N (%)	34 (16.6)	4 (15.4)	2 (8.7)	1 (100.0)	0.10
Carotid Stenosis; N (%)	33 (16.1)	1 (3.8)	2 (8.7)	0 (0.0)	0.30
Chronic Kidney Disease; N (%)	25 (12.2)	5 (19.2)	8 (34.8) <sup>A</sup> (0.01)	1 (100.0)	0.003
Cardiac Ejection Fraction <40%; N (%)	16 (7.8)	2 (7.7)	1 (4.3)	1 (100.0)	0.61
Active Neoplasm; N (%)	16 (7.8)	2 (7.7)	0 (0.0)	0 (0.0)	0.57
Rheumatological Disease; N (%)	4 (2.0)	1 (3.8)	0 (0.0)	0 (0.0)	0.81
Prior Stroke or Transient Ischemic Attack; N (%)	2 (1.0)	0 (0.0)	1 (4.3)	0 (0.0)	0.50
Smoking; N (%)	33 (16.1)	2 (7.7)	5 (21.7)	0 (0.0)	0.55
Laboratory Findings					
White Blood Cell Count; Mean (SD); x10 <sup>9</sup> /L	10.2 ± 5.2	9.5 ± 2.6	9.4 ± 3.4	7.1 ± 0.0	0.79
White Blood Cell Count; Median [IQR]; x10 <sup>9</sup> /L	9.1 [6.7 – 11.8]	8.8 [7.6 – 11.0]	9.8 [7.0 – 11.6]	7.1 [7.1 – 7.1]	0.40
Neutrophil Count; Mean (SD); x10 <sup>9</sup> /L	7.9 ± 4.8	7.6 ± 2.5	7.7 ± 3.2	5.3 ± 0.0	0.94
Neutrophil Count; Median [IQR]; x10 <sup>9</sup> /L	7.0 [4.7 – 9.3]	7.1 [5.9 – 8.8]	8.0 [5.2 – 9.1]	5.3 [5.3 – 5.3]	0.18
Lymphocyte Count; Mean (SD); x10 <sup>9</sup> /L	1.6 ± 1.3	1.7 ± 1.1	1.3 ± 0.5	1.0 ± 0.0	0.60
Lymphocyte; Median [IQR]; x10 <sup>9</sup> /L	1.4 [0.9 – 1.9]	1.3 [1.0 – 2.0]	1.2 [0.9 – 1.6]	1.0 [1.0 – 1.0]	0.65
Platelet Count; Mean (SD); x10 <sup>9</sup> /L	332.7 ± 520.1	283.1 ± 374.6	256.1 ± 176.7	268.0 ± 0.0	0.92
Platelet Count; Median [IQR]; x10 <sup>9</sup> /L	227.0 [163.0 – 328.0]	190.0 [145.0 – 261.0]	184.0 [135.0 – 338.0]	268.0 [268.0 – 268.0]	0.53
Alanine Transaminase (ALT); Mean (SD); U/L	55.2 ± 68.6	60.2 ± 68.3	67.4 ± 60.5	156.0 ± 0.0	0.45
Alanine Transaminase (ALT); Median [IQR]; U/L	23.0 [7.0 – 85.0]	45.5 [18.7 – 65.0]	43.7 [15.0 – 110.0]	156.0 [156.0 – 156.0]	0.06
Aspartate Transaminase (AST); Mean (SD); U/L	33.1 ± 28.6	22.2 ± 12.4	27.4 ± 24.8	77.0 ± 0.0	1.00
Aspartate Transaminase (AST); Median [IQR]; U/L	24.4 [13.0 – 44.0]	19.0 [12.4 – 35.0]	17.8 [13.0 – 37.5]	77.0 [77.0 – 77.0]	0.28
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	52.8 ± 120.1	41.3 ± 46.4	54.7 ± 57.5	13.0 ± 0.0	0.96
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	33.0 [21.0 – 51.0]	29.0 [18.0 – 38.0]	35.5 [20.7 – 65.5]	13.0 [13.0 – 13.0]	0.70
Creatinine; Mean (SD); mg/dl	1.4 ± 1.1	1.5 ± 1.4	1.4 ± 0.9	2.4 ± 0.0	0.71
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.4]	1.2 [0.9 – 1.5]	1.0 [0.9 – 1.9]	2.4 [2.4 – 2.4]	0.30
C-Reactive Protein (CRP); Mean (SD); mg/L	59.0 ± 148.0	40.0 ± 26.0	91.0 ± 133.0	20.0 ± 0.0	0.78

Parameter	Embolic/Large Vessel Athero-Thromboembolism N = 206 (80.5%)	Lacune N = 26 (10.2%)	Border-zone N = 23 (9.0%)	Vasculitis Pattern N = 1 (0.4%)	P-value
C-Reactive Protein (CRP); Median [IQR]; mg/L	36.0 [25.0 – 51.0]	30.0 [25.0 – 46.0]	48.0 [24.0 – 87.0]	20.0 [20.0 – 20.0]	0.62
Lactate Dehydrogenase (LDH); Mean (SD); U/L	679.4 ± 1885.7	345.2 ± 205.6	590.5 ± 335.5	312.0 ± 0.0	0.95
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	349.5 [222.0 – 490.0]	367.0 [201.0 – 561.0]	581.5 [341.5 – 839.5]	312.0 [312.0 – 312.0]	0.57
Fibrinogen; Mean (SD); mg/dl	511.5 ± 1213.3	217.4 ± 199.6	114.5 ± 223.6	NA	0.71
Fibrinogen; Median [IQR]; mg/dl	154.7 [3.8 – 450.0]	120.0 [104 – 403.0]	2.8 [2.6 – 226.5]	NA	0.54
D- Dimer; Mean (SD); ng/ml	1488.5 ± 1919.1	951.9 ± 701.9	1558.3 ± 1682.0	955.0 ± 0.0	0.89
D- Dimer; Median [IQR]; ng/ml	1000.0 [510.0 – 2100.0]	781.0 [480.0 – 1850.0]	625.0 [550.0 – 3500.0]	955.0 [955.0 – 955.0]	0.42

\* Data on patients' disposition were sparse.



**Results; Supplemental Table 10. Subgroups of AIS patients with stroke as the chief complaints versus others.**

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with a stroke, based on stroke as the chief complaint versus the presence of stroke following COVID-19 symptoms. [Blue ink indicates the post-hoc p values.](#)

Parameter	Stroke as Chief Complaint N = 104 (36.1%)	Stroke Following COVID-19 Symptoms N = 184 (63.9%)	P-value
Age; Mean (SD); Years	69 ± 15	66 ± 16	0.17
Age; Median [IQR]; Years	70 [60 – 79]	67 [56 - 78]	0.20
Sex; Female; N (%)	49 (47.1)	67 (36.4)	0.08
Large Vessel Occlusion; N (%)	43 (46.2)	75 (43.1)	0.62
Intravenous Thrombolysis; N (%)	18 (17.3)	24 (13.0)	0.33
Mechanical Thrombectomy; N (%)	8 (7.7)	14 (7.6)	0.98
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	10.0 [3.0 – 20.0]	9.0 [5.0 – 16.0]	0.94
Imaging Patterns			
Embollic/Large Vessel athero-Thromboembolism; N (%)	67 (79.8)	132 (81.0)	0.23
Lacune; N (%)	12 (14.3)	13 (8.0)	
Border-zone; N (%)	5 (6.0)	17 (10.4)	
Vasculitis Pattern; N (%)	0 (0.0)	1 (0.6)	
TOAST			
Large-Artery Atherosclerosis; N (%)	13 (25.5)	43 (38.7)	0.21
Cardio-embolism; N (%)	17 (33.3)	28 (25.2)	
Small-Vessel Occlusion; N (%)	8 (15.7)	9 (8.1)	
Stroke of Other Determined Etiology; N (%)	2 (3.9)	10 (9.0)	
Stroke of Undetermined Etiology; N (%)	11 (21.6)	21 (18.9)	
Mechanical Ventilation; N (%)	28 (26.9)	54 (29.3)	0.66
Disposition*			
Discharged Home; N (%)	36 (37.9)	72 (42.4)	0.02
In Hospital Mortality; N (%)	37 (38.9) <sup>B (0.006)</sup>	39 (22.9)	
Still in Hospital/Subacute Care; N (%)	22 (23.2)	59 (34.7)	
Length of Hospital Stay; Median (IQR); Days	6.0 [4.0 – 12.0]	9.0 [5.0 – 17.0]	
Comorbidities			
Hypertension; N (%)	69 (67.6)	122 (66.3)	0.82
Diabetes Mellitus; N (%)	35 (34.0)	67 (36.4)	0.68
Ischemic Heart Disease; N (%)	23 (25.3)	45 (26.0)	0.90

Parameter	Stroke as Chief Complaint N = 104 (36.1%)	Stroke Following COVID-19 Symptoms N = 184 (63.9%)	P-value
Atrial Fibrillation; N (%)	19 (18.6)	22 (12.0)	0.12
Carotid Stenosis; N (%)	10 (11.0)	28 (16.2)	0.25
Chronic Kidney Disease; N (%)	13 (12.7)	28 (15.2)	0.57
Cardiac Ejection Fraction <40%; N (%)	10 (11.0)	10 (5.8)	0.13
Active Neoplasm; N (%)	5 (5.5)	13 (7.5)	0.54
Rheumatological Disease; N (%)	2 (2.2)	3 (1.7)	0.80
Prior Stroke or Transient Ischemic Attack; N (%)	1 (1.1)	2 (1.2)	0.97
Smoking; N (%)	15 (14.7)	31 (16.8)	0.64
<b>Laboratory Findings</b>			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	10.2 ± 5.4	9.8 ± 4.5	0.54
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	8.9 [6.7 – 12.1]	9.0 [7.2 – 11.1]	0.94
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.7 ± 4.8	7.9 ± 4.2	0.75
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.4 [4.4 – 9.7]	7.2 [5.1 – 9.2]	0.39
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.7 ± 1.7	1.7 ± 1.7	0.90
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.4 [0.9 – 1.9]	1.3 [0.9 – 1.9]	0.81
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	263.4 ± 201.5	343.4 ± 557.7	0.10
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	224.0 [168.0 – 313.0]	222.0 [150.0 – 335.0]	0.93
Alanine Transaminase (ALT); Mean (SD); U/L	54.3 ± 92.7	65.3 ± 81.9	0.34
Alanine Transaminase (ALT); Median [IQR]; U/L	20.0 [7.0 – 75.0]	32.3 [10.0 – 99.0]	0.11
Aspartate Transaminase (AST); Mean (SD); U/L	32.9 ± 27.1	33.9 ± 27.8	0.78
Aspartate Transaminase (AST); Median [IQR]; U/L	24.6 [15.0 – 42.0]	25.0 [14.0 – 44.2]	0.96
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	58.1 ± 167.5	50.1 ± 53.0	0.58
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	27.5 [19.0 – 46.5]	33.0 [23.0 – 55.0]	0.05
Creatinine; Mean (SD); mg/dl	1.4 ± 1.1	1.5 ± 1.2	0.88
Creatinine; Median [IQR]; mg/dl	1.1 [0.9 – 1.5]	1.1 [0.9 – 1.5]	0.71
C-Reactive Protein (CRP); Mean (SD); mg/L	65.0 ± 210.0	56.0 ± 62.0	0.59
C-Reactive Protein (CRP); Median [IQR]; mg/L	32.0 [24.0 – 46.0]	38.0 [26.0 – 62.0]	0.07
Lactate Dehydrogenase (LDH); Mean (SD); U/L	398.6 ± 223.1	756.2 ± 2008.6	0.27
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	347.0 [216.0 – 507.0]	407.0 [258.0 – 574.0]	0.31
Fibrinogen; Mean (SD); mg/dl	520.1 ± 650.6	469.4 ± 1185.3	0.86
Fibrinogen; Median [IQR]; mg/dl	411.0 [53.9 – 594.0]	178.0 [3.8 – 471.0]	0.20
D- Dimer; Mean (SD); ng/ml	2444.7 ± 7368.7	2953.1 ± 6845.3	0.73
D- Dimer; Median [IQR]; ng/ml	691.0 [441.0 – 1100.0]	1259.5 [585.0 – 2460.0]	0.02

\* Data on patients' disposition were sparse.

# **Results**

## **Acute Ischemic Stroke**

### **Ecological Comparisons**

#### **Supplemental Tables 11-12**

### Results; Supplemental Table 11. Subgroups of AIS patients based on geographical regions

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, according to geographical regions. **Blue ink indicates the post-hoc p values.**

Parameter	A: Middle East N = 153 (47.4%)	B: Asia N = 6 (1.9%)	C: America N = 88 (27.2%)	D: Europe N = 76 (23.5%)	P-value
Age; Mean (SD); Years	67 ± 15	54 ± 20	68 ± 14	68 ± 16	0.19
Age; Median [IQR]; Years	68 [58 – 78]	48 [39 – 75]	66 [59 – 79]	70 [58 – 80]	0.39
Sex; Female; N (%)	58 (37.9)	1 (16.7)	38 (43.2)	33 (43.4)	0.50
Large Vessel Occlusion; N (%)	71 (48.3)	2 (40.0)	23 (41.1)	30 (40.0)	0.62
Intravenous Thrombolysis; N (%)	22 (14.4)	1 (16.7)	11 (12.5)	10 (13.2)	0.97
Mechanical Thrombectomy; N (%)	4 (2.6)	0 (0.0)	4 (4.5)	16 (21.1) <sup>A (&lt;0.001)</sup> <sub>C (0.004)</sub>	<0.001
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	12.0 [6.0 – 17.0]	7.0 [5.0 – 11.0]	7.0 [0.0 – 16.0]	8.0 [4.0 – 18.0]	0.06
Imaging Patterns					
Embolic/Large Vessel athero-Thromboembolism; N (%)	107 (75.4)	5 (83.3)	29 (87.9)	65 (86.7)	0.05
Lacune; N (%)	16 (11.3)	0 (0.0)	3 (9.1)	7 (9.3)	
Border-zone; N (%)	19 (13.4)	1 (16.7)	0 (0.0)	3 (4.0)	
Vasculitis Pattern; N (%)	0 (0.0)	0 (0.0)	1 (3.0)	0 (0.0)	
TOAST					
Large-Artery Atherosclerosis; N (%)	38 (53.5) <sup>D (&lt;0.001)</sup>	2 (33.3)	5 (26.3)	11 (14.9)	<0.001
Cardio-embolism; N (%)	15 (21.1)	1 (16.7)	3 (15.8)	27 (36.5)	
Small-Vessel Occlusion; N (%)	12 (18.3) <sup>D (0.02)</sup>	0 (0.0)	1 (5.3)	3 (4.1)	
Stroke of Other Determined Etiology; N (%)	5 (7.0)	0 (0.0)	2 (10.5)	6 (8.1)	
Stroke of Undetermined Etiology; N (%)	0 (0.0)	3 (50.0)	8 (42.1)	27 (36.5)	
Interval Between Onset to Index Event; Median [IQR]; Days	3.0 [0.0 – 8.0]	5.0 [4.0 – 6.0]	2.0 [0.0 – 7.0]	4.0 [0.0 – 14.0]	0.14
Mechanical Ventilation; N (%)	47 (30.7)	1 (16.7)	15 (17.0)	22 (28.9)	0.11
Disposition*					
Discharged Home; N (%)	74 (48.4)	0.0 (0.0)	28 (45.2)	25 (32.9)	<0.001
In Hospital Mortality; N (%)	46 (30.1)	1 (16.7)	16 (25.8)	19 (25.0)	
Still in Hospital/Subacute Care; N (%)	33 (21.6)	5 (83.3) <sup>A (0.003)</sup> <sub>C (0.04)</sub>	18 (29.0)	32 (42.1) <sup>A (0.007)</sup>	

Parameter	A: Middle East N = 153 (47.4%)	B: Asia N = 6 (1.9%)	C: America N = 88 (27.2%)	D: Europe N = 76 (23.5%)	P-value
Length of Hospital Stay; Median (IQR); Days	6.0 [4.0 – 10.0] C (0.047) D (0.047)	12.0 [12.0 – 14.0]	9.0 [4.0 – 14.0]	11.0 [5.0 – 18.0]	0.04
Comorbidities					
Hypertension; N (%)	93 (60.8)	2 (33.3)	56 (65.9)	51 (67.1)	0.33
Diabetes Mellitus; N (%)	53 (34.6)	1 (16.7)	34 (39.5)	23 (30.3)	0.50
Ischemic Heart Disease; N (%)	50 (32.7) <sup>C (0.02)</sup> D (0.04)	0 (0.0)	9 (14.8)	13 (17.1)	0.01
Atrial Fibrillation; N (%)	20 (13.1)	0 (0.0)	9 (10.6)	16 (21.1)	0.17
Carotid Stenosis; N (%)	17 (11.1)	0 (0.0)	7 (11.5)	14 (18.4)	0.32
Chronic Kidney Disease; N (%)	30 (19.6) <sup>C (0.01)</sup>	0 (0.0)	5 (5.9)	7 (9.2)	0.01
Cardiac Ejection Fraction <40%; N (%)	6 (3.9)	1 (16.7)	7 (11.5)	10 (13.2)	0.05
Active Neoplasm; N (%)	12 (7.8)	0 (0.0)	5 (8.2)	4 (5.3)	0.78
Rheumatological Disease; N (%)	0 (0.0)	0 (0.0)	0 (0.0)	5 (6.6)	<0.001
Prior Stroke or Transient Ischemic Attack; N (%)	2 (1.3)	0 (0.0)	2 (3.3)	1 (1.3)	0.75
Smoking; N (%)	28 (18.3)	0 (0.0)	16 (8.8)	9 (11.8)	0.38
Laboratory Findings					
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	10.3 ± 4.5	7.2 ± 3.2	9.0 ± 4.1	10.1 ± 5.9	0.15
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	9.6 [7.5 – 11.8]	6.3 [4.4 – 10.2]	7.9 [6.2 – 10.5]	8.5 [6.2 – 11.5]	0.02
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	8.2 ± 4.3	4.4 ± 2.6	7.2 ± 4.2	7.6 ± 5.0	0.11
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	7.6 [5.4 – 9.9]	3.7 [2.5 – 5.3]	6.3 [4.2 – 8.2]	6.0 [4.2 – 8.8]	0.01
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.5 ± 1.0	1.7 ± 0.5	1.6 ± 2.1	2.2 ± 2.2	0.05
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.3 [0.9 – 1.9]	1.6 [1.4 – 1.7]	1.2 [0.9 – 1.8]	1.4 [0.9 – 2.5]	0.14
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	230.5 ± 112.5 D (<0.001)	200.5 ± 86.8	295.6 ± 138.3 D (0.017)	506.0 ± 835.8	<0.001
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	192.0 [145.0 – 305.0] C (0.039)	181.5 [127.0 – 241.0]	268.0 [202.0 – 381.0]	244.5 [177.0 – 397.5]	<0.001
Alanine Transaminase (ALT); Mean (SD); U/L	59.7 ± 70.9	60.6 ± 70.5	78.1 ± 109.9	57.2 ± 91.3	0.50
Alanine Transaminase (ALT); Median [IQR] ; U/L	33.0 [9.0 – 97.0]	26.0 [11.0 – 113.4]	42.3 [16.2 – 102.0]	20.5 [3.1 – 57.5]	0.21
Aspartate Transaminase (AST); Mean (SD); U/L	34.1 ± 29.4	23.7 ± 14.3	30.9 ± 21.0	30.4 ± 27.5	0.62
Aspartate Transaminase (AST); Median [IQR] ; U/L	23.0 [14.6 – 43.0]	23.5 [14.2 – 34.0]	23.5 [15.0 – 40.0]	25.6 [7.7 – 40.0]	0.70
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	50.0 ± 49.0	101.7 ± 118.7	79.6 ± 188.3	38.9 ± 27.6	0.05

Parameter	A: Middle East N = 153 (47.4%)	B: Asia N = 6 (1.9%)	C: America N = 88 (27.2%)	D: Europe N = 76 (23.5%)	P-value
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	30.0 [20.0 – 46.0]	60.0 [35.0 – 86.0]	35.0 [21.0 – 67.0]	33.0 [23.0 – 46.0]	0.14
Creatinine; Mean (SD); mg/dl	1.51 ± 1.3	1.4 ± 0.9	1.9 ± 2.8	1.1 ± 0.6	0.04
Creatinine; Median [IQR]; mg/dl	1.12 [0.9 – 1.5]	1.0 [1.0 – 1.4]	1.1 [0.8 – 2.3]	1.0 [0.8 – 1.3]	0.06
C-Reactive Protein (CRP); Mean (SD); mg/L	50.0 ± 60.0	118.0 ± 138.0	98.0 ± 239.0	40.0 ± 24.0	0.02
C-Reactive Protein (CRP); Median [IQR]; mg/L	33.0 [24.0 – 49.0]	72.0 [45.0 – 94.0]	43.0 [24.0 – 82.0]	36.0 [24.0 – 50.0]	0.10
Lactate Dehydrogenase (LDH); Mean (SD); U/L	462.4 ± 186.8	541.5 ± 185.8	432.1 ± 278.6	911.6 ± 2623.2	0.40
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	426.5 [331.5 – 558.5] D (0.006)	504.0 [419.0 – 648.0] D (0.008)	384.0 [266.0 – 536.0]	270.0 [197.0 – 426.0]	0.03
Fibrinogen; Mean (SD); mg/dl	459.6 ± 759.0	43.5 ± 58.8	421.9 ± 214.8	560.3 ± 1377.8	0.70
Fibrinogen; Median [IQR]; mg/dl	166.8 [2.2 – 403.0] C (0.043) D (0.039)	23.0 [3.5 – 53.9] C (0.037)	464.0 [216.5 – 578.5]	210.0 [3.8 – 456.0]	0.01
D- Dimer; Mean (SD); ng/ml	1356.6 ± 3084.7	560.0 ± 265.5	4430.7 ± 9768.1	1659.8 ± 1167.4	0.09
D- Dimer; Median [IQR]; ng/ml	584.0 [427.0 – 1100.0]	550.0 [400.0 – 650.0]	1060.0 [565.0 – 2867.0]	1431.0 [730.0 – 2200.0]	0.01

\* Data on patients' disposition were sparse.

## Results; Supplemental Table 12. Subgroups of AIS patients according to the countries' health expenditure

Baseline characteristics, comorbidities, and laboratory findings among SARS-CoV-2 patients with an acute ischemic stroke, based on the countries' health expenditures. **Blue ink indicates the post-hoc p values.**

Parameter	Middle to high health expenditure N = 170 (52.6%)	Low health expenditure N = 153 (47.4%)	P-value
Age; Mean (SD); Years	68 ± 15	67 ± 15	0.65
Age; Median [IQR]; Years	69 [58 – 79]	68 [58 – 77]	0.83
Sex; Female; N (%)	74 (43.5)	56 (36.6)	0.21
Large Vessel Occlusion; N (%)	53 (39.0)	73 (49.7)	0.07
Intravenous Thrombolysis; N (%)	21 (12.4)	23 (15.0)	0.48
Mechanical Thrombectomy; N (%)	21 (12.4)	3 (2.0)	<0.001
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	8.0 [3.0 – 17.0]	11.0 [5.0 – 17.0]	0.02
Imaging Patterns			
Embolitic/Large Vessel athero-Thromboembolism; N (%)	100 (87.0) <sup>B (0.02)</sup>	106 (75.2)	0.02
Lacune; N (%)	10 (8.7)	16 (11.3)	
Border-zone; N (%)	4 (3.5)	19 (13.5) <sup>A (0.01)</sup>	
Vasculitis Pattern; N (%)	1 (0.9)	0 (0.0)	
TOAST			
Large-Artery Atherosclerosis; N (%)	19 (19.2)	37 (52.1) <sup>A (&lt;0.001)</sup>	<0.001
Cardio-embolism; N (%)	31 (31.3)	15 (21.1)	
Small-Vessel Occlusion; N (%)	4 (4.0)	13 (18.3) <sup>A (0.002)</sup>	
Stroke of Other Determined Etiology; N (%)	8 (8.1)	5 (7.0)	
Stroke of Undetermined Etiology; N (%)	37 (37.4) <sup>B (&lt;0.001)</sup>	1 (1.4)	
Interval Between Onset to Index Event; Median [IQR]; Days	3.0 [0.0 – 10.0]	3.0 [0.0 – 8.0]	0.69
Mechanical Ventilation; N (%)	38 (22.4)	47 (30.7)	0.09
Disposition*			
Discharged Home; N (%)	54 (37.5)	73 (47.7)	0.01
In Hospital Mortality; N (%)	35 (24.3)	47 (30.7)	
Still in Hospital/Subacute Care; N (%)	55 (38.2) <sup>B (0.002)</sup>	33 (21.6)	
Length of Hospital Stay; Median (IQR); Days	10.0 [5.0 – 17.0]	6.0 [4.0 – 10.0]	0.14
Comorbidities			
Hypertension; N (%)	109 (65.3)	93 (60.8)	0.41
Diabetes Mellitus; N (%)	59 (35.1)	52 (34.0)	0.83
Ischemic Heart Disease; N (%)	22 (15.4)	50 (32.7)	<0.001
Atrial Fibrillation; N (%)	25 (15.0)	20 (13.1)	0.63

Parameter	Middle to high health expenditure N = 170 (52.6%)	Low health expenditure N = 153 (47.4%)	P-value
Carotid Stenosis; N (%)	19 (13.3)	19 (12.4)	0.82
Chronic Kidney Disease; N (%)	11 (6.6)	21 (20.3)	<0.001
Cardiac Ejection Fraction <40%; N (%)	18 (12.6)	6 (3.9)	0.01
Active Neoplasm; N (%)	8 (5.6)	13 (8.5)	0.33
Rheumatological Disease; N (%)	4 (2.8)	1 (0.7)	0.15
Prior Stroke or Transient Ischemic Attack; N (%)	3 (2.1)	2 (1.3)	0.60
Smoking; N (%)	23 (13.8)	30 (19.6)	0.16
Laboratory Findings			
White Blood Cell Count x10 <sup>9</sup> /L; Mean (SD)	9.6 ± 5.0	10.1 ± 4.6	0.30
White Blood Cell Count x10 <sup>9</sup> /L; Median [IQR]	8.2 [6.2 – 10.8]	9.5 [7.4 – 11.8]	0.02
Neutrophil Count x10 <sup>9</sup> /L; Mean (SD)	7.3 ± 4.6	8.2 ± 4.3	0.11
Neutrophil Count x10 <sup>9</sup> /L; Median [IQR]	6.2 [4.2 – 8.7]	7.5 [5.3 -9.9]	<0.001
Lymphocyte Count x10 <sup>9</sup> /L; Mean (SD)	1.9 ± 2.2	1.5 ± 1.0	0.09
Lymphocyte x10 <sup>9</sup> /L; Median [IQR]	1.3 [0.9 – 2.0]	1.3 [1.0 – 1.9]	1.00
Platelet Count x10 <sup>9</sup> /L; Mean (SD)	393.4 ± 591.6	229.0 ± 110.6	<0.001
Platelet Count x10 <sup>9</sup> /L; Median [IQR]	247.0 [183.0 – 386.0]	191.0 [145.0 – 298.5]	<0.001
Alanine Transaminase (ALT); Mean (SD); U/L	65.8 ± 99.9	60.9 ± 70.6	0.65
Alanine Transaminase (ALT); Median [IQR]; U/L	26.9 [8.6 – 76.5]	40.0 [10.4 – 98.0]	0.46
Aspartate Transaminase (AST); Mean (SD); U/L	31.3 ± 24.0	33.0 ± 29.6	0.60
Aspartate Transaminase (AST); Median [IQR]; U/L	27.0 [14.0 – 40.0]	21.4 [14.0 – 39.0]	0.62
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	61.4 ± 135.2	43.5 ± 47.9	0.14
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	33.0 [22.0 – 53.0]	32.0 [20.0 – 46.0]	0.35
Creatinine; Mean (SD); mg/dl	1.52 ± 2.0	1.5 ± 1.3	0.95
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.4]	1.1 [0.9 – 1.5]	0.07
C-Reactive Protein (CRP); Mean (SD); mg/L	71.0 ± 170.0	50.0 ± 60.0	0.18
C-Reactive Protein (CRP); Median [IQR]; mg/L	39.0 [24.0 – 66.0]	33.0 [25.0 – 48.0]	0.11
Lactate Dehydrogenase (LDH); Mean (SD); U/L	667.0 ± 1861.5	473.8 ± 187.3	0.50
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	346.0 [205.0 – 522.0]	438.0 [336.0 – 600.0]	0.01
Fibrinogen; Mean (SD); mg/dl	514.4 ± 1061.6	171.7 ± 216.9	0.27
Fibrinogen; Median [IQR]; mg/dl	328.0 [53.9 – 506.0]	2.47 [2.1 – 373.0]	0.02
D- Dimer; Mean (SD); ng/ml	2879.1 ± 6884.8	1522.9 ± 3156.3	0.38
D- Dimer; Median [IQR]; ng/ml	1060.0 [585.0 – 2235.0]	600.0 [462.0 – 1100.0]	0.05

\* Data on patients' disposition were sparse.





# **Results**

**Structure of the Models: the proportion of the comorbidities under each subclass of the models**

**Supplemental Tables 13-18**

## Results; Supplemental Table 13. Dividing the SARS-CoV-2 infected acute ischemic stroke patients into 2 subgroups

The table shows the structure of the models for grouping the patients into 2 subgroups using machine learning (ML) and expert opinion (EX) models by considering the present comorbidities. ML-K<sub>2</sub> used hierarchal clustering and K-means, while ML-S<sub>2</sub> used spectral clustering, EX-A<sub>2</sub> used all 11 collected comorbidities and EX-S<sub>2</sub> used 8 selected comorbidities, to separate patients into 2 subgroups.

Model	Machine Learning						Clinician Expert Opinion					
	ML-K <sub>2</sub> (K-Mean)			ML-S <sub>2</sub> (Spectral)			EX-A <sub>2</sub> (All Comorbidities)			EX-S <sub>2</sub> (Selected Comorbidities)		
Comorbidities	A N = 112 (38.4%)	B N = 180 (61.6%)	P-value	A N = 173 (60.3%)	B N = 114 (39.7%)	P-value	A N = 115 (38.9%)	B N = 181 (61.1%)	P-value	A N = 137 (46.3%)	B N = 159 (53.7%)	P-value
Hypertension (%)	0.0	99.4	<0.001	37.6	95.6	<0.001	0.0	77.9	<0.001	0.0	81.1	<0.001
Diabetes Mellitus (%)	14.3	45.0	<0.001	7.5	72.8	<0.001	0.0	42.4	<0.001	0.0	44.1	<0.001
Ischemic Heart Disease (%)	14.3	30.6	0.002	7.5	50.9	<0.001	0.0	31.2	<0.001	0.0	32.4	<0.001
Atrial Fibrillation (%)	8.9	17.2	0.05	8.1	24.6	<0.001	0.0	18.2	<0.001	0.0	18.9	<0.001
Carotid Stenosis (%)	3.6	18.9	<0.001	5.8	23.7	<0.001	0.0	16.5	<0.001	0.0	17.1	<0.001
Chronic Kidney Disease (%)	12.5	15.0	0.55	16.2	11.4	0.26	0.0	17.	<0.001	12.2	14.4	0.63
Cardiac Ejection Fraction<40% (%)	1.8	12.2	0.002	4.0	14.9	0.001	0.0	10.4	0.01	0.0	10.8	0.003
Active Neoplasm (%)	5.4	8.3	0.34	4.0	12.3	0.01	0.0	9.1	0.01	0.0	9.5	0.01
Rheumatological Disease (%)	0.9	2.2	0.40	2.3	0.9	0.36	0.0	2.2	0.23	0.0	2.3	0.19
Previous Stroke/TIA (%)	1.8	1.7	0.94	1.2	2.6	0.35	0.0	2.2	0.23	0.0	2.3	0.19
Current Smoker (%)	6.3	22.8	<0.001	11.0	23.7	0.004	0.0	20.8	<0.001	0.0	21.6	<0.001

## Methods; Supplemental Table 14. Dividing the SARS-CoV-2 infected acute ischemic stroke patients into 3 subgroups

The table shows the structure of the models for grouping the patients into 3 subgroups using machine learning (ML) and experts opinion (EX) models by considering the present comorbidities. ML-K<sub>3</sub> used hierarchal clustering and K-means, while ML-S<sub>3</sub> used spectral clustering, EX-A<sub>3</sub> used all 11 collected comorbidities and EX-S<sub>3</sub> used 8 selected comorbidities, to separate patients into 3 subgroups.

Model	Machine Learning								Clinicians' Expert Opinion							
	ML-K <sub>3</sub> (K-Mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Comorbidities	A N = 99 (33.9%)	B N = 87 (29.8%)	C N = 106 (36.3%)	P-value	A N = 123 (42.9%)	B N = 44 (15.3%)	C N = 120 (41.8%)	P-value	A N = 65 (22.0%)	B N = 140 (47.3%)	C N = 91 (30.7%)	P-value	A N = 74 (25.0%)	B N = 147 (49.7%)	C N = 75 (25.3%)	P-value
Hypertension (%)	100.0	92.0	0.0	<0.001	98.4	90.9	10.8	<0.001	0.0	67.9	93.4	<0.001	0.0	72.8	97.3	<0.001
Diabetes Mellitus (%)	0.0	100.0	9.4	<0.001	41.5	77.3	9.2	<0.001	0.0	26.4	67.0	<0.001	0.0	29.3	73.3	<0.001
Ischemic Heart Disease (%)	25.3	41.4	9.4	<0.001	0.8	100.0	21.7	<0.001	0.0	13.6	58.2	<0.001	0.0	17.0	62.7	<0.001
Atrial Fibrillation (%)	18.2	16.1	8.5	0.11	13.0	38.6	7.5	<0.001	0.0	8.6	33.0	<0.001	0.0	9.5	37.3	<0.001
Carotid Stenosis (%)	13.1	24.1	3.8	<0.001	12.2	38.6	4.2	<0.001	0.0	7.9	29.7	<0.001	0.0	8.2	34.7	<0.001
Chronic Kidney Disease (%)	17.2	11.5	13.2	0.51	21.1	6.8	10.0	0.01	0.0	16.4	19.8	0.001	0.0	15.6	12.0	0.67
Cardiac Ejection Fraction<40% (%)	12.1	11.	1.9	0.01	10.6	18.2	2.5	0.003	0.0	4.3	19.8	<0.001	0.0	4.8	22.7	<0.001
Active Neoplasm (%)	8.1	10.3	3.8	0.20	4.1	22.7	5.0	<0.001	0.0	3.6	17.6	<0.001	0.0	8.2	12.0	<0.001
Rheumatological Disease (%)	3.0	1.1	0.9	0.46	3.3	0.0	0.8	0.22	0.0	1.4	3.3	0.27	0.0	2.7	1.3	0.32
Previous Stroke/TIA (%)	1.0	3.4	0.9	0.33	1.6	4.5	0.8	0.27	0.0	1.4	3.3	0.27	0.0	1.4	4.0	0.15
Current Smoker (%)	24.2	19.5	6.6	0.002	19.5	27.3	8.3	0.01	0.0	12.9	33.0	<0.001	0.0	14.3	36.0	<0.001

## Methods: Supplemental Table 15A. Dividing the SARS-CoV-2 infected acute ischemic stroke patients into 4 and 5 subgroups by Spectral clustering

The table shows the structure of the models for grouping the patients into 4 and 5 subgroups using machine learning (ML) models (spectral clustering) by considering the present comorbidities. ML-S<sub>4</sub> used spectral clustering to divide the patients into 4 groups while ML-S<sub>5</sub> separated the patients into 5 subgroups.

Models	Machine Learning										
	ML-S <sub>4</sub> (Spectral)					ML-S <sub>5</sub> (Spectral)					
Comorbidities	A N = 57 (19.3%)	B N = 112 (37.8%)	C N = 38 (12.8%)	D N = 89 (30.1%)	P-value	A N = 20 (6.8%)	B N = 89 (30.1%)	C N = 112 (37.8%)	D N = 19 (6.4%)	E N = 56 (18.9%)	P-value
Hypertension (%)	100.0	0.0	89.5	100.0	<0.001	95.0	100.0	0.0	84.2	100.0	<0.001
Diabetes Mellitus (%)	100.0	11.6	73.7	0.0	<0.001	85.0	0.0	13.4	52.6	100.0	<0.001
Ischemic Heart Disease (%)	10.5	11.6	100.0	16.9	<0.001	95.0	16.9	11.6	100.0	10.7	<0.001
Atrial Fibrillation (%)	10.5	8.0	44.7	11.2	<0.001	10.0	11.2	6.3	89.5	10.7	<0.001
Carotid Stenosis (%)	14.0	3.6	44.7	10.1	<0.001	85.0	10.1	3.6	5.3	12.5	<0.001
Chronic Kidney Disease (%)	14.0	12.5	7.9	18.0	0.46	15.0	18.0	12.5	0.0	14.3	0.34
Cardiac Ejection Fraction<40% (%)	7.0	1.8	21.1	11.2	0.001	15.0	11.2	1.8	26.3	7.1	0.002
Active Neoplasm (%)	1.8	3.6	26.3	6.7	<0.001	30.0	6.7	4.5	15.8	1.8	<0.001
Rheumatological Disease (%)	1.8	0.9	0.0	3.4	0.46	0.0	3.4	0.9	0.0	1.8	0.62
Previous Stroke/TIA (%)	1.8	0.9	5.3	1.1	0.32	5.0	1.1	0.9	5.3	1.8	0.50
Current Smoker (%)	14.0	6.3	31.6	23.6	<0.001	65.0	23.6	6.3	0.0	12.5	<0.001

## Methods: Supplemental Table 15B. Dividing the SARS-CoV-2 infected acute ischemic stroke patients into 4 and 5 subgroups based on K-Mean Clustering

The table shows the structure of the models for grouping the patients into 4 and 5 subgroups using machine learning (ML) models (K-Mean) by considering the present comorbidities. ML-S<sub>4</sub> used spectral clustering to divide the patients into 4 groups while ML-S<sub>5</sub> separated the patients into 5 subgroups.

	Machine Learning										
	ML-K <sub>4</sub> (K-Mean)					ML-K <sub>5</sub> (K-Mean)					
	A N= 74 (25.3%)	B N= 95 (32.5%)	C N= 62 (21.2%)	D N= 61 (20.9%)	P-Value	A N= 85 (29.1%)	B N= 39 (18.8%)	C N= 55 (18.8%)	D N= 49 (16.8%)	E N=64 (21.9%)	P-Value
Hypertension (%)	100.0	0.0	87.1	83.6	<0.001	0.0	74.4	81.8	83.7	100.0	<0.001
Diabetes Mellitus (%)	0.0	0.0	58.1	100.0	<0.001	0.0	33.3	100.0	59.2	0.0	<0.001
Ischemic Heart Disease (%)	0.0	9.5	100.0	0.0	<0.001	5.9	43.6	0.0	100.0	0.0	<0.001
Atrial Fibrillation (%)	13.5	8.4	27.4	9.8	0.006	0.0	100.0	0.0	4.1	0.0	<0.001
Carotid Stenosis (%)	10.8	4.2	29.0	13.1	<0.001	4.7	5.1	12.7	34.7	12.5	<0.001
Chronic Kidney Disease (%)	20.3	12.6	6.5	16.4	0.12	12.9	7.7	16.4	8.2	21.9	0.178
Cardiac Ejection Fraction<40% (%)	12.2	1.1	14.5	8.2	0.01	1.2	20.5	7.3	12.2	7.8	0.006
Active Neoplasm (%)	5.4	1.1	21.0	4.9	<0.001	0.0	7.7	5.5	22.4	6.3	<0.001
Rheumatological Disease (%)	4.1	1.1	0.	1.6	0.29	0.0	5.1	0.0	0.0	4.7	0.05
Previous Stroke/TIA (%)	1.4	1.1	3.2	1.6	0.76	1.2	2.6	1.8	2.0	1.6	0.99
Current Smoker (%)	23.0	7.4	25.8	13.1	0.006	5.9	7.7	14.5	36.7	21.9	<0.001

## Methods; Supplemental Table 16. Dividing the SARS-CoV-2 infected patients with intraparenchymal hemorrhage into 2 subgroups

The table shows the structure of the models for grouping the patients into 2 subgroups using machine learning (ML) and expert opinion (EX) models by considering the present comorbidities. ML-K<sub>2</sub> used hierarchal clustering and K-means, while ML-S<sub>2</sub> used spectral clustering, EX-A<sub>2</sub> used all 11 collected comorbidities and EX-S<sub>2</sub> used 8 selected comorbidities, to separate patients into 2 subgroups.

Model	Machine Learning						Clinicians' Expert Opinion					
	ML-K <sub>2</sub> (K-mean)			ML-S <sub>2</sub> (Spectral)			EX-A <sub>2</sub> (All Comorbidities)			EX-A <sub>2</sub> (Selected Comorbidities)		
Comorbidities	A N = 40 (70.2%)	B N = 17 (29.8%)	P-value	A N = 23 (34.3%)	B N = 44 (65.7%)	P-value	A N = 38 (55.9%)	B N = 30 (44.1%)	P-value	A N = 39 (57.4%)	B N = 29 (42.6%)	P-value
Hypertension (%)	55.0	88.2	0.02	78.3	56.8	0.08	42.1	90.0	<0.001	43.6	89.7	<0.001
Diabetes Mellitus (%)	2.5	94.1	<0.001	73.9	9.1	<0.001	2.6	66.7	<0.001	2.6	69.0	<0.001
Ischemic Heart Disease (%)	5.0	58.8	<0.001	43.5	4.5	<0.001	0.0	40.0	<0.001	0.0	41.4	<0.001
Atrial Fibrillation (%)	0.0	11.8	0.03	13.0	0.0	0.01	0.0	10.0	0.05	0.0	10.3	0.04
Carotid Stenosis (%)	0.0	11.8	0.03	8.7	0.0	0.05	0.0	6.7	0.11	0.0	6.9	0.10
Chronic Kidney Disease (%)	15.0	11.8	0.75	13.0	13.6	0.95	5.3	23.3	0.03	7.7	20.7	0.12
Cardiac Ejection Fraction<40% (%)	0.0	41.2	<0.001	21.7	4.5	0.03	0.0	23.3	0.002	0.0	24.1	0.001
Active Neoplasm (%)	0.0	23.5	0.001	13.0	2.3	0.08	0.0	13.3	0.20	0.0	13.8	0.02
Rheumatological Disease (%)	0.0	0.0	-	0.0	0.0	-	0.0	0.0	-	0.0	0.0	-
Previous Stroke/TIA (%)	0.0	0.0	-	0.0	0.0	-	0.0	0.0	-	0.0	0.0	-
Current Smoker (%)	10.0	29.4	0.07	26.1	11.4	0.12	0.0	36.7	<0.001	0.0	37.9	<0.001

## Methods; Supplemental Table 17. Dividing the SARS-CoV-2 infected patients with intraparenchymal hemorrhage into 3 subgroups

The table shows the structure of the models for grouping the patients into 3 subgroups using machine learning (ML) and experts' opinion (EX) models by considering the present comorbidities. ML-K<sub>3</sub> used hierarchal clustering and K-means, while ML-S<sub>3</sub> used spectral clustering, EX-A<sub>3</sub> used all 11 collected comorbidities and EX-S<sub>3</sub> used 8 selected comorbidities, to separate patients into 3 subgroups.

Model	Machine Learning								Clinicians' Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Comorbidities	A N = 23 (40.4%)	B N = 19 (33.3%)	C N = 15 (26.3%)	P-value	A N = 20 (29.9%)	B N = 28 (41.8%)	C N = 19 (28.4%)	P-value	A N = 19 (27.9%)	B N = 31 (45.6%)	C N = 18 (26.5%)	P-value	A N = 21 (30.9%)	B N = 33 (48.5%)	C N = 14 (20.6%)	P-value
Hypertension (%)	100	0	93.3	<0.001	75	100	0	<0.001	0	83.9	94.4	<0.001	0	90.9	92.9	<0.001
Diabetes Mellitus (%)	0	10.5	100	<0.001	70	17.9	10.5	<0.001	0	22.6	77	<0.001	0	24.2	92.9	<0.001
Ischemic Heart Disease (%)	8.7	0	66.7	<0.001	50	7.1	0	<0.001	0	6	55.6	<0.001	0	6.1	71.4	<0.001
Atrial Fibrillation (%)	0	0	13.3	0.06	10	3.6	0	0.31	0	3.2	11.1	0.24	0	3	14.3	0.11
Carotid stenosis (%)	0	0	13.3	0.06	10	0	0	0.09	0	0	11.1	0.06	0	0	14.3	0.02
Chronic Kidney Disease (%)	17.4	10.5	13.3	0.81	10	17.9	10.5	0.67	0	9.7	33.3	0.01	0	15.2	14.3	0.83
Cardiac Ejection Fraction<40% (%)	95.7	94.7	66.7	0.02	10	14.3	5.3	0.61	0	3.2	66.7	0.001	0	3	57.1	<0.001
Active Neoplasm (%)	4.3	0	20	0.06	15	3.6	0	0.11	0	0	22.2	0.003	0	0	28.6	<0.001
Rheumatological Disease (%)	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-
Previous stroke/TIA (%)	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-
Current Smoker (%)	21.7	0	26.7	0.06	30	17.9	0	0.04	0	9.7	44.4	<0.001	0	18.2	35.7	0.02



## Methods: Supplemental Table 18A. Dividing the SARS-CoV-2 infected patients with intraparenchymal hemorrhage into 4 and 5 subgroups by Spectral Clustering

The table shows the structure of the models for grouping the patients into 4 and 5 subgroups using machine learning (ML) models (spectral clustering) by considering the present comorbidities. ML-S<sub>4</sub> used spectral clustering to divide the patients into 4 groups while ML-S<sub>5</sub> separated the patients into 5 subgroups.

Model	Machine Learning										
	ML-S <sub>4</sub> (Spectral)					ML-S <sub>5</sub> (Spectral)					
Comorbidities	A N = 35 (52.2%)	B N = 10 (14.9%)	C N = 3 (4.5%)	D N = 19 (28.4%)	P-value	A N = 39 (58.2%)	B N = 2 (3.0%)	C N = 8 (11.9%)	D N = 15 (22.4%)	E N = 3 (4.5%)	P-value
Hypertension (%)	88.6	90.0	100.0	0.0	<0.001	53.8	100.0	87.5	66.7	100.0	0.16
Diabetes Mellitus (%)	25.7	100.0	0.0	10.5	<0.001	7.7	100.0	100.0	53.3	0.0	<0.001
Ischemic Heart Disease (%)	5.7	100.0	0.0	0.0	<0.001	5.1	100.0	100.0	0.0	0.0	<0.001
Atrial Fibrillation (%)	5.7	10.0	0.0	0.0	0.60	0.0	0.0	12.5	13.3	0.0	0.20
Carotid Stenosis (%)	0.0	20.0	0.0	0.0	0.01	0.0	50.0	12.5	0.0	0.0	0.001
Chronic Kidney Disease (%)	8.6	10.0	100.0	10.5	<0.001	7.7	0.0	12.5	13.3	100.0	<0.001
Cardiac Ejection Fraction<40% (%)	11.4	20.0	0.0	5.3	0.59	0.0	100.0	0.0	33.3	0.0	<0.001
Active Neoplasm (%)	2.9	30.0	0.0	0.0	0.01	0.0	100.0	12.5	6.7	0.0	<0.001
Rheumatological Disease (%)	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-
Previous Stroke/TIA (%)	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-
Current Smoker (%)	11.4	40.0	100.0	0.0	<0.001	2.6	0.0	50.0	20.0	100.0	<0.001

## Methods: Supplemental Table 18B. Dividing the SARS-CoV-2 infected patients with intraparenchymal hemorrhage into 4 and 5 subgroups by K-Mean clustering

The table shows the structure of the models for grouping the patients into 4 and 5 subgroups using machine learning (ML) models (K-Mean clustering) by considering the present comorbidities. ML-S<sub>4</sub> used spectral clustering to divide the patients into 4 groups while ML-S<sub>5</sub> separated the patients into 5 subgroups.

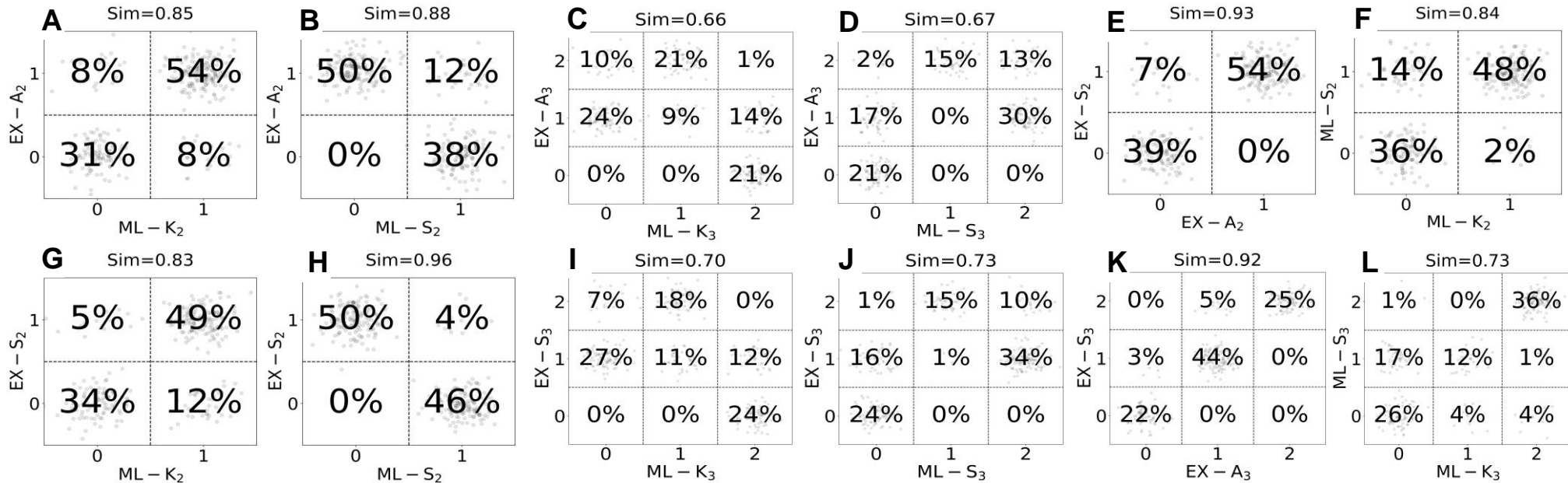
Models	Machine Learning										
	ML-K <sub>4</sub> (K-Mean)					ML-K <sub>5</sub> (K-Mean)					
	A N=10 17.5%	B N=7 (12.3%)	C N=18 (31.6%)	D N=22 (38.6%)	P-Value	A N=10 (17.5%)	B N=5 (8.8%)	C N=18 (31.6%)	D N=18 (31.6%)	E N=6 (10.5%)	P-Value
<b>Comorbidities</b>											
Hypertension (%)	90.0	85.7	0.0	100.0	<0.001	90.0	100.0	0.0	100.0	83.3	<0.001
Diabetes Mellitus (%)	80.0	85.7	5.6	9.1	<0.001	100.0	0.0	5.6	0.0	100.0	<0.001
Ischemic Heart Disease (%)	100.0	28.6	0.0	0.0	<0.001	100.0	0.0	0.0	11.1	0.0	<0.001
Atrial Fibrillation (%)	10.0	14.3	0.0	0.0	0.16	10.0	0.0	0.0	0.0	16.7	0.21
Carotid Stenosis (%)	10.0	14.3	0.0	0.0	0.16	20.0	0.0	0.0	0.0	0.0	0.04
Chronic Kidney Disease (%)	10.0	14.3	11.1	18.2	0.91	10.0	60.0	11.1	5.6	16.7	0.04
Cardiac Ejection Fraction<40% (%)	0.0	100.0	0.0	0.0	<0.001	20.0	20.0	0.0	0.0	66.7	<0.001
Active Neoplasm (%)	10.0	42.9	0.0	0.0	0.001	30.0	20.0	0.0	0.0	0.0	0.01
Rheumatological Disease (%)	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-
Previous Stroke/TIA (%)	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	-
Current Smoker (%)	40.0	14.3	0.0	18.2	0.5	40.0	100.0	0.0	0.0	0.0	<0.001

# **Results; Contingency Matrices**

**Supplemental Figures 2-3**

## Results; Supplemental Figure 2

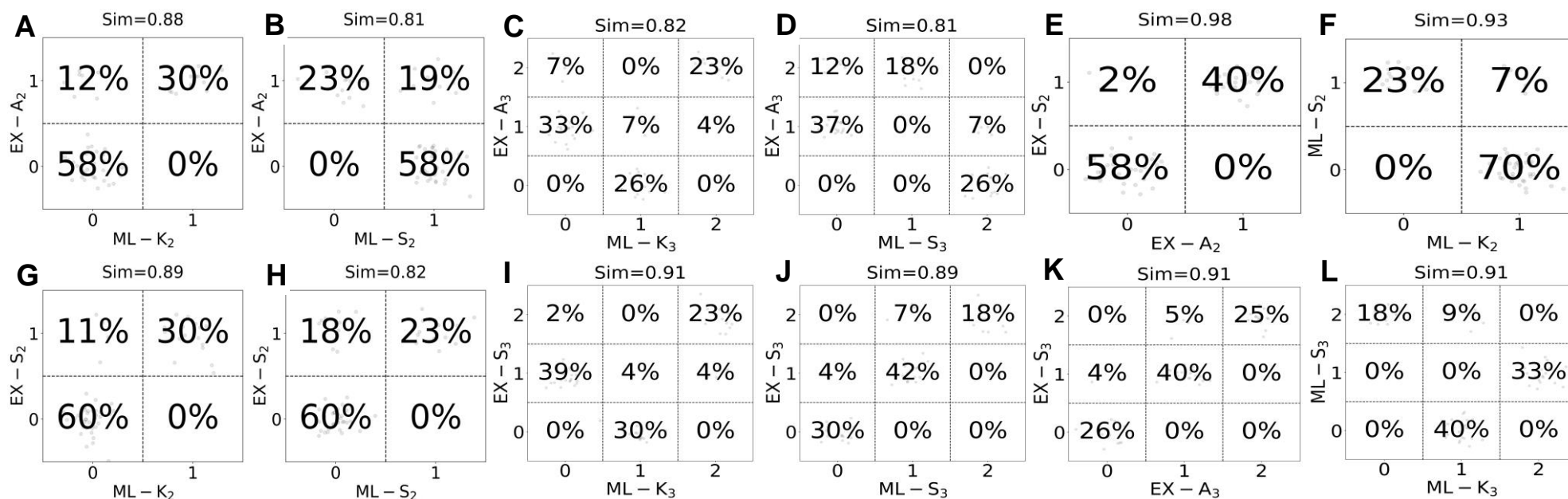
Contingency Matrices, models regarding the SARS-CoV-2 infected patients with acute ischemic stroke.



**Supplemental Figure 2.** The similarity of methods under different clustering models when grouping the patients with acute ischemic stroke into 2 and 3 subgroups. In models based on expert opinion (EX), EX-A included all 11 collected comorbidities and EX-S included 8 selected comorbidities. Patients were then clustered into two subgroups (EX-A<sub>2</sub> and EX-S<sub>2</sub>), with “0” referring to patients with zero or one comorbidities and “1” referring to patients with >1 comorbidity, or three subgroups (EX-A<sub>3</sub> and EX-S<sub>3</sub>), with “0” referring to patients without any known comorbidity, “1” referring to patients with one or two comorbidities, and “2” referring to patients with >2 comorbidities. In machine learning algorithms (ML) ML-K used hierarchal clustering and K-means, while ML-S used spectral clustering. Within each clustering, method patients were grouped into two (ML-K<sub>2</sub> and ML-S<sub>2</sub>) and three (ML-K<sub>3</sub> and ML-S<sub>3</sub>) clusters. Panel **A** shows the similarity between the 2 subgroups in EX-A<sub>2</sub> and ML-K<sub>2</sub>. Panel **B** shows the similarity between the 2 subgroups in EX-A<sub>2</sub> and ML-S<sub>2</sub>. Panel **C** shows the similarity between the 3 subgroups in EX-A<sub>3</sub> and ML-K<sub>3</sub>. Panel **D** shows the similarity between the 3 subgroups in EX-A<sub>3</sub> and ML-S<sub>3</sub>. Panel **E** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and EX-A<sub>2</sub>. Panel **F** shows the similarity between the 2 subgroups in ML-S<sub>2</sub> and ML-K<sub>2</sub>. Panel **G** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and ML-K<sub>2</sub>. Panel **H** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and ML-S<sub>2</sub>. Panel **I** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and ML-K<sub>3</sub>. Panel **J** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and ML-S<sub>3</sub>. Panel **K** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and EX-A<sub>3</sub>. Panel **L** shows the similarity between the 3 subgroups in ML-S<sub>3</sub> and ML-K<sub>3</sub>.

# Results; Supplemental Figure 3

Contingency Matrices, models regarding the SARS-CoV-2 infected patients with intraparenchymal hemorrhage.



**Supplemental Figure 3.** The similarity of methods under different clustering models when grouping the patients with intraparenchymal hemorrhage into 2 and 3 subgroups. In models based on experts' opinion (EX), EX-A included all 11 collected comorbidities and EX-S included 8 selected comorbidities. Patients were then clustered into two subgroups (EX-A<sub>2</sub> and EX-S<sub>2</sub>), with "0" referring to patients with zero or one comorbidities and "1" referring to patients with >1 comorbidity, or three subgroups (EX-A<sub>3</sub> and EX-S<sub>3</sub>), with "0" referring to patients without any known comorbidity, "1" referring to patients with one or two comorbidities, and "2" referring to patients with >2 comorbidities. In machine learning algorithms (ML) ML-K used hierarchal clustering and K-means, while ML-S used spectral clustering. Within each clustering, method patients were grouped into two (ML-K<sub>2</sub> and ML-S<sub>2</sub>) and three (ML-K<sub>3</sub> and ML-S<sub>3</sub>) clusters. Panel **A** shows the similarity between the 2 subgroups in EX-A<sub>2</sub> and ML-K<sub>2</sub>. Panel **B** shows the similarity between the 2 subgroups in EX-A<sub>2</sub> and ML-S<sub>2</sub>. Panel **C** shows the similarity between the 3 subgroups in EX-A<sub>3</sub> and ML-K<sub>3</sub>. Panel **D** shows the similarity between the 3 subgroups in EX-A<sub>3</sub> and ML-S<sub>3</sub>. Panel **E** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and EX-A<sub>2</sub>. Panel **F** shows the similarity between the 2 subgroups in ML-S<sub>2</sub> and ML-K<sub>2</sub>. Panel **G** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and ML-K<sub>2</sub>. Panel **H** shows the similarity between the 2 subgroups in EX-S<sub>2</sub> and ML-S<sub>2</sub>. Panel **I** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and ML-K<sub>3</sub>. Panel **J** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and ML-S<sub>3</sub>. Panel **K** shows the similarity between the 3 subgroups in EX-S<sub>3</sub> and EX-A<sub>3</sub>. Panel **L** shows the similarity between the 3 subgroups in ML-S<sub>3</sub> and ML-K<sub>3</sub>.

# **Results**

## **Acute Ischemic Stroke; Comparing the Patients among the Comorbidities' Subgroups**

**Supplemental Tables 19-20**

## Results; Supplemental Table 19. Subgroups of AIS patients clustered into 2 groups

Baseline characteristics and laboratory findings among SARS-CoV-2 patients with an ischemic stroke, based on grouping the patients into 2 subgroups using machine learning (ML) and expert opinion (EX) models. ML-K<sub>2</sub> used hierarchal clustering and K-means, while ML-S<sub>2</sub> used spectral clustering, to separate patients into 2 subgroups. EX-A<sub>2</sub> used all 11 collected comorbidities and EX-S<sub>2</sub> used 8 selected comorbidities, to separate patients into 2 subgroups. [Blue ink indicates the post-hoc p values.](#)

Model	Machine Learning						Expert Opinion					
	ML-K <sub>2</sub> (K-mean)			ML-S <sub>2</sub> (Spectral)			EX-A <sub>2</sub> (All comorbidities)			EX-S <sub>2</sub> (Selected Comorbidities)		
Parameter	A N = 112 (38.4%)	B N = 180 (61.6%)	P-value	A N = 173 (60.3%)	B N = 114 (39.7%)	P-value	A N = 115 (38.9%)	B N = 181 (61.1%)	P-value	A N = 137 (46.3%)	B N = 159 (53.7%)	P-value
Age; Mean (SD); Years	62 ± 17	70 ± 13	<0.001	66 ± 17	68 ± 13	0.20	61 ± 18	69 ± 14	<0.001	62 ± 17	69 ± 14	<0.001
Sex; Female; N (%)	45 (40.2)	70 (38.9)	0.08	66 (28.3)	48 (42.1)	0.50	79 (44.9)	83 (39.5)	0.29	86 (43.2)	76 (40.6)	0.61
Large Vessel Occlusion; N (%)	46 (48.4)	73 (42.7)	0.37	64 (42.1)	54 (50.0)	0.21	43 (43.9)	76 (44.4)	0.93	49 (41.2)	70 (46.7)	0.37
Intravenous Thrombolysis; N (%)	16 (14.3)	23 (12.8)	0.71	17 (9.8)	23 (17.5)	0.06	13 (7.4)	26 (12.4)	0.11	16 (8.0)	23 (12.3)	0.17
Mechanical Thrombectomy; N (%)	10 (8.9)	14 (7.8)	0.73	12 (6.9)	12 (10.5)	0.28	9 (5.1)	15 (7.1)	0.41	10 (5.0)	14 (7.5)	0.32
National Institutes of Health Stroke Scale (NIHSS) Score; Mean (SD)	12.0 ± 9.0	11.0 ± 8.0	0.52	11.0 ± 8.0	13.0 ± 8.0	0.11	11.0 ± 9.0	12.0 ± 9.0	0.95	11.0 ± 9.0	12.0 ± 8.0	0.87
Imaging Patterns												
Embollic/Large Vessel athero-Thromboembolism; N (%)	74 (83.1)	131 (79.4)		115 (79.3)	84 (80.8)		76 (83.5)	195 (92.9)		189 (95.0)	173 (92.5)	
Lacune; N (%)	10 (11.2)	15 (9.1)	0.44	18 (12.4)	8 (7.7)	0.38	10 (11.0)	16 (9.8)	0.43	14 (12.5)	12 (8.4)	0.56
Border-zone; N (%)	5 (5.6)	18 (10.9)		12 (8.3)	11 (10.6)		5 (5.5)	18 (11.0)		9 (8.0)	14 (9.8)	
Vasculitis Pattern; N (%)	0 (0.0)	1 (0.6)		0 (0.0)	1 (1.0)		0 (0.0)	1 (0.6)		0 (0.0)	1 (0.7)	
TOAST												
Large-Artery Atherosclerosis; N (%)	25 (38.5)	31 (29.8)		32 (31.1)	24 (35.8)		21 (30.0)	35 (34.7)		23 (28.4)	33 (36.7)	
Cardio-embolism; N (%)	11 (16.9)	35 (33.7)		19 (18.4)	27 (40.3)		10 (14.3)	36 (35.6)		23 (28.4)	33 (36.7)	
Small-Vessel Occlusion; N (%)	7 (10.8)	9 (8.7)	0.03	11 (10.7)	6 (9.0)	0.002	1 (2.7)	16 (12.0)	<0.001	13 (16.0)	33 (36.7)	0.001
Stroke of Other Determined Etiology; N (%)	9 (13.8)	4 (3.8)		12 (11.7)	1 (1.5)		11 (15.7)	2 (2.0)		11 (13.6)	2 (2.2)	
Stroke of Undetermined Etiology; N (%)	13 (20.0)	25 (24.0)		29 (28.2)	9 (13.4)		21 (30.0)	18 (17.8)		24 (29.6)	15 (16.7)	
Interval Between Onset to Index Event; Mean (SD); Days	6.0 ± 7.0	5.0 ± 6.0	0.19	6.0 ± 7.0	5.0 ± 7.0	0.68	7.0 ± 8.0	5.0 ± 6.0	0.07	7.0 ± 7.0	5.0 ± 6.0	0.15
Mechanical Ventilation; N (%)	36 (32.1)	47 (26.1)	0.27	51 (29.5)	32 (28.1)	0.80	22 (33.8)	63 (27.3)	0.30	27 (36.5)	58 (26.1)	0.09
Disposition*												
Discharged Home; N (%)	53 (48.6)	72 (40.2)		81 (47.4)	43 (37.7)		66 (42.0)	77 (36.7)		75 (41.7)	68 (36.4)	
In Hospital Mortality; N (%)	27 (24.8)	49 (27.4)	0.36	41 (24.0)	33 (28.9)	0.27	45 (28.7)	72 (34.3)	0.46	52 (28.9)	65 (34.8)	0.44
Still in Hospital/Subacute Care; N (%)	29 (26.6)	58 (32.4)		49 (28.7)	38 (33.3)		46 (29.3)	61 (29.0)		53 (29.4)	54 (28.9)	
Length of Hospital Stay; Mean (SD); Days	14.0 ± 15.0	11 ± 9.0	0.14	13.0 ± 14.0	11.0 ± 9.0	0.23	14.0 ± 15.0	11.0 ± 11.0	0.16	16.0 ± 17.0	11.0 ± 9.0	0.04
Laboratory Findings												
White Blood Cell Count; Mean (SD); x10 <sup>9</sup> /L	10.3 ± 5.3	9.5 ± 4.5	0.13	9.9 ± 5.2	9.8 ± 4.3	0.85	10.9 ± 7.3 <a href="#">8 (0.05)</a>	9.7 ± 4.6	0.05	10.7 ± 7.1	9.8 ± 4.5	0.13

Model	Machine Learning						Expert Opinion					
	ML-K <sub>2</sub> (K-mean)			ML-S <sub>2</sub> (Spectral)			EX-A <sub>2</sub> (All comorbidities)			EX-S <sub>2</sub> (Selected Comorbidities)		
Parameter	A N = 112 (38.4%)	B N = 180 (61.6%)	P-value	A N = 173 (60.3%)	B N = 114 (39.7%)	P-value	A N = 115 (38.9%)	B N = 181 (61.1%)	P-value	A N = 137 (46.3%)	B N = 159 (53.7%)	P-value
White Blood Cell Count; Median [IQR]; x10 <sup>9</sup> /L	9.2 [7.3 – 12.0]	8.9 [6.5 – 11.0]	0.33	8.9 [6.8 – 11.1]	9.2 [7.1 – 11.3]	0.38	9.5 [7.4 – 12.4]	9.0 [6.8 – 11.1]	0.04	9.5 [7.4 – 12.1]	9.0 [6.8 – 11.3]	0.13
Neutrophil Count; Mean (SD); x10 <sup>9</sup> /L	8.2 ± 4.6	7.4 ± 4.3	0.17	7.8 ± 4.6	7.6 ± 4.2	0.81	8.7 ± 6.6	7.5 ± 4.4	0.07	8.5 ± 6.5	7.6 ± 4.3	0.10
Neutrophil Count; Median [IQR]; x10 <sup>9</sup> /L	7.3 [5.0 – 10.7]	6.5 [4.7 – 9.0]	0.15	6.6 [4.8 – 9.1]	7.2 [5.0 – 9.4]	0.61	7.4 [4.9 – 10.7]	6.7 [4.8 – 9.1]	0.30	7.4 [4.9 – 10.3]	6.7 [4.8 – 9.2]	0.35
Lymphocyte Count; Mean (SD); x10 <sup>9</sup> /L	1.6 ± 1.5	1.5 ± 1.0	0.38	1.6 ± 1.3	1.5 ± 1.0	0.97	1.7 ± 1.6	1.5 ± 0.9	0.09	1.7 ± 1.6	1.5 ± 0.9	0.18
Lymphocyte; Median [IQR]; x10 <sup>9</sup> /L	1.4 [0.9 – 1.9]	1.3 [0.8 – 1.9]	0.31	1.3 [0.9 – 1.9]	1.3 [0.8 – 1.9]	0.94	1.4 [0.9 – 2.0]	1.3 [0.9 – 1.9]	0.39	1.4 [0.9 – 2.0]	1.3 [0.9 – 1.9]	0.74
Platelet Count; Mean (SD); x10 <sup>9</sup> /L	311.5 ± 354.4	318.1 ± 522.6	0.91	293.2 ± 319.2	349.1 ± 621.6	0.34	294.9 ± 323.6	289.7 ± 471.0	0.90	282.8 ± 308.8	302.0 ± 495.0	0.67
Platelet Count; Median [IQR]; x10 <sup>9</sup> /L	238.0 [171.0 – 350.0]	218.5 [154.0 – 318.0]	0.69	223.0 [163.0 – 338.0]	228.0 [156.0 – 320.0]	0.84	236.5 [164.0 – 337.0]	192.0 [150.0 – 300.0]	0.06	223.0 [156.0 – 326.0]	207.0 [154.0 – 310.0]	0.44
Alanine Transaminase (ALT); Mean (SD); U/L	70.9 ± 80.1	57.7 ± 74.8	0.19	60.3 ± 72.5	65.4 ± 83.1	0.61	69.9 ± 106.5	59.3 ± 73.6	0.31	71.1 ± 104.8	57.1 ± 72.4	0.17
Alanine Transaminase (ALT); Median [IQR]; U/L	45.7 [12.0 – 101.7]	27.4 [14.0 – 44.0]	0.03	38.5 [8.5 – 87.5]	27.4 [12.0 – 110.0]	0.24	25.0 [14.0 – 41.0]	24.8 [14.7 – 44.6]	0.24	25.0 [14.0 – 42.0]	24.6 [14.4 – 44.0]	0.11
Aspartate Transaminase (AST); Mean (SD); U/L	28.1 ± 24.4	33.2 ± 27.7	0.13	29.3 ± 24.4	35.4 ± 30.3	0.10	39.9 ± 93.3	34.3 ± 27.6	0.48	39.2 ± 88.4	34.4 ± 28.1	0.50
Aspartate Transaminase (AST); Median [IQR]; U/L	21.0 [13.0 – 35.0]	24.0 [14.0 – 44.0]	0.38	23.4 [14.0 – 36.0]	23.0 [14.0 – 48.0]	0.85	25.0 [14.0 – 41.0]	24.8 [14.7 – 44.6]	0.92	25.0 [14.0 – 42.0]	24.6 [14.4 – 44.0]	0.93
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	50.1 ± 49.2	54.9 ± 134.6	0.74	56.2 ± 131.9	47.2 ± 48.4	0.53	57.4 ± 117.8	54.5 ± 126.0	0.84	64.8 ± 159.1	45.7 ± 53.8	0.16
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	35.0 [23.0 – 56.0]	30.0 [20.0 – 46.5]	0.07	33.0 [21.0 – 50.0]	31.0 [21.0 – 50.0]	0.42	33.0 [23.0 – 50.0]	32.0 [20.0 – 46.0]	0.41	33.0 [23.0 – 51.0]	31.5 [20.0 – 46.0]	0.19
Creatinine; Mean (SD); mg/dl	1.4 ± 2.3	1.5 ± 1.2	0.76	1.5 ± 2.0	1.6 ± 1.3	0.53	1.5 ± 2.2	1.8 ± 1.7	0.29	1.5 ± 2.1	1.8 ± 1.7	0.27
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.3]	1.2 [0.9 – 1.5]	0.004	1.0 [0.8 – 1.3]	1.2 [0.9 – 1.6]	0.001	1.0 [0.8 – 1.3]	1.2 [0.9 – 1.6]	<0.001	1.0 [0.8 – 1.3]	1.2 [0.9 – 1.6]	0.001
C-Reactive Protein (CRP); Mean (SD); mg/L	59.0 ± 76.0	64.0 ± 167.0	0.77	69.0 ± 170.0	49.0 ± 41.0	0.27	57.4 ± 117.8	54.5 ± 126.0	0.84	64.8 ± 159.1	45.7 ± 53.8	0.09
C-Reactive Protein (CRP); Median [IQR]; mg/L	39.0 [27.0 – 60.0]	34.0 [23.0 – 53.0]	0.19	36.0 [25.0 – 56.0]	35.0 [23.0 – 51.0]	1.00	37.0 [27.0 – 54.0]	35.0 [24.0 – 55.0]	0.99	37.0 [27.0 – 56.0]	34.0 [23.0 – 52.0]	0.91
Lactate Dehydrogenase (LDH); Mean (SD); U/L	476.8 ± 277.2	720.4 ± 2129.1	0.33	397.4 ± 259.2	974.4 ± 2633.8	0.14	453.7 ± 379.7	718.0 ± 2046.1	0.22	455.2 ± 378.0	719.4 ± 2059.0	0.22
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	423.0 [281.0 – 610.0]	327.0 [203.0 – 478.0]	0.22	347.0 [224.0 – 490.0]	384.5 [237.0 – 523.0]	0.14	364.0 [250.0 – 558.0]	357.0 [219.0 – 490.0]	0.94	365.0 [250.0 – 558.0]	352.0 [218.0 – 489.5]	0.93
Fibrinogen; Mean (SD); mg/dl	290.7 ± 272.8	598.1 ± 1360.0	0.17	478.5 ± 1169.0	425.6 ± 845.8	0.83	341.8 ± 308.3	595.6 ± 1360.9	0.25	341.2 ± 304.3	616.3 ± 1411.0	0.22
Fibrinogen; Median [IQR]; mg/dl	219.5 [4.0 – 501.0]	178.0 [3.8 – 477.0]	0.74	216.0 [42.0 – 501.0]	149.0 [2.5 – 477.0]	0.54	317.0 [55.0 – 535.5]	178.0 [3.0 – 484.0]	0.44	331.0 [53.9 – 565.0]	149.0 [3.0 – 484.0]	0.31
D-Dimer; Mean (SD); ng/ml	2066.5 ± 2787.4	1430.1 ± 2033.0	0.18	1401.4 ± 1542.0	1747.8 ± 2441.0	0.38	1891.4 ± 2554.0	1727.7 ± 2348.0	0.71	1872.1 ± 2486.7	1741.2 ± 2428.0	0.77
D-Dimer; Median [IQR]; ng/ml	1059.5 [568.0 – 2235.0]	995.0 [526.0 – 1883.0]	0.33	904.5 [485.0 – 1970.0]	1060.0 [561.0 – 2165.0]	0.63	1008.0 [489.0 – 2200.0]	1060.0 [550.0 – 2085.0]	1.00	1040.0 [2200.0]	1027.0 [550.0 – 2085.0]	1.00

\* Data on patients' disposition were sparse.



## Results; Supplemental Table 20. Subgroups of AIS patients clustered into 3 groups

Baseline characteristics among SARS-CoV-2 patients with an ischemic stroke, based on the clustering of patients into 3 subgroups using machine learning (ML) and experts' opinion (EX) models. ML-K<sub>3</sub> used hierarchal clustering and K-means, while ML-S<sub>3</sub> used spectral clustering, to separate patients into 3 subgroups. EX-A<sub>3</sub> used all 11 collected comorbidities and EX-S<sub>3</sub> used 8 selected comorbidities, to separate patients into 3 subgroups. [Blue ink indicates the post-hoc p values.](#)

Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 99 (33.9%)	B N = 87 (29.8%)	C N = 106 (36.3%)	P-value	A N = 123 (42.9%)	B N = 44 (15.3%)	C N = 120 (41.8%)	P-value	A N = 65 (22.0%)	B N = 140 (47.3%)	C N = 91 (30.7%)	P-value	A N = 74 (25.0%)	B N = 147 (49.7%)	C N = 75 (25.3%)	P-value
Age; Mean (SD); Years	72 ± 13 <a href="#">C (&lt;0.001)</a>	68 ± 13 <a href="#">C (0.016)</a>	62 ± 17	<0.001	70 ± 14 <a href="#">C (&lt;0.001)</a>	70 ± 14 <a href="#">C (0.020)</a>	63 ± 17	<0.001	60 ± 18 <a href="#">B (0.001)</a> <a href="#">C (&lt;0.001)</a>	68 ± 14	70 ± 14	<0.001	59 ± 18 <a href="#">B (&lt;0.001)</a> <a href="#">C (&lt;0.001)</a>	69 ± 13	71 ± 13	<0.001
Sex; Female; N (%)	36 (36.4)	36 (41.4)	34 (40.6)	0.75	46 (37.4)	20 (45.5)	48 (40.0)	0.64	29 (44.6)	53 (37.9)	35 (38.5)	0.63	31 (41.9)	53 (36.1)	33 (44.0)	0.46
Large Vessel Occlusion; N (%)	38 (40.4)	36 (44.4)	46 (49.5)	0.47	41 (35.3)	22 (53.7)	55 (53.4)	0.01	26 (48.1)	50 (39.4)	43 (50.0)	0.26	31 (49.2)	52 (39.1)	36 (50.7)	0.20
Intravenous Thrombolysis; N (%)	10 (10.1)	15 (17.2)	14 (13.2)	0.36	10 (8.1)	12 (27.3)	15 (12.5)	0.01	6 (9.2)	14 (10.0)	19 (20.9)	0.03	7 (9.5)	17 (11.6)	15 (20.0)	0.12
Mechanical Thrombectomy; N (%)	6 (6.1)	8 (9.2)	10 (9.4)	0.63	7 (5.7)	4 (9.1)	13 (10.8)	0.34	5 (7.7)	9 (6.4)	10 (11.0)	0.46	6 (8.1)	9 (6.1)	9 (12.0)	0.32
National Institutes of Health Stroke Scale (NIHSS) Score; Mean (SD)	8 [4-16]	12 [6-18]	10 [5-19]	0.28	8 [4-16]	13 [7-20]	11 [5-19]	0.024	8 [4-22]	9 [4-16]	12 [6-20]	0.179	9 [4-22]	8 [4-16]	12 [6-19]	0.214
Imaging Patterns																
Embolic/Large Vessel athero-Thromboembolism; N (%)	75 (81.5)	59 (77.6)	71 (82.6)	0.49	81 (73.6)	35 (85.4)	83 (84.7)	0.22	41 (82.0)	97 (79.5)	67 (80.7)	0.31	47 (79.7)	102 (80.3)	56 (81.2)	0.72
Lacune; N (%)	9 (9.8)	6 (7.9)	10 (11.6)		12 (10.9)	4 (9.8)	10 (10.2)		4 (8.0)	17 (13.9)	5 (6.0)		7 (11.9)	14 (11.0)	5 (7.2)	
Border-zone; N (%)	8 (8.7)	10 (13.2)	5 (5.8)		16 (14.5)	2 (4.9)	5 (5.1)		5 (10.0)	8 (6.6)	10 (12.0)		5 (8.5)	11 (8.7)	7 (10.1)	
Vasculitis Pattern; N (%)	0.0 (0.0)	1 (1.3)	0.0 (0.0)		1 (0.9)	0.0 (0.0)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)	0.0 (0.0)		1 (1.2)	0.0 (0.0)	0.0 (0.0)	
TOAST																
Large-Artery Atherosclerosis; N (%)	14 (23.7)	19 (40.4)	23 (36.5)	0.08	23 (30.7)	6 (24.0)	27 (38.6)	0.003	16 (43.2)	21 (26.9)	19 (34.5)	<0.001	19 (43.2)	21 (26.6)	16 (34.0)	<0.001
Cardio-embolism; N (%)	20 (33.9)	15 (31.9)	11 (17.5)		17 (22.7)	15 (60.0) <a href="#">A (0.002)</a> <a href="#">C (0.001)</a>	14 (20.0)		5 (13.5)	13 (16.7) <a href="#">A (0.001)</a> <a href="#">B (&lt;0.001)</a>	28 (50.9)		5 (11.4)	18 (22.8)	23 (48.9) <a href="#">A (&lt;0.001)</a> <a href="#">B (0.007)</a>	
Small-Vessel Occlusion; N (%)	5 (8.5)	4 (8.5)	7 (11.1)		8 (10.7)	2 (8.0)	7 (10.0)		1 (2.7)	12 (15.4)	4 (7.3)		4 (9.1)	9 (11.4)	4 (8.5)	

Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 99 (33.9%)	B N = 87 (29.8%)	C N = 106 (36.3%)	P-value	A N = 123 (42.9%)	B N = 44 (15.3%)	C N = 120 (41.8%)	P-value	A N = 65 (22.0%)	B N = 140 (47.3%)	C N = 91 (30.7%)	P-value	A N = 74 (25.0%)	B N = 147 (49.7%)	C N = 75 (25.3%)	P-value
Stroke of Other Determined Etiology; N (%)	3 (5.1)	1 (2.1)	9 (14.3)	0.28	4 (5.3)	0.0 (0.0)	9 (12.9)	0.37	6 (16.2)	7 (9.0) C (0.002)	0.0 (0.0)	0.19	7 (15.9)	6 (7.6) C (0.009)	0.0 (0.0)	0.27
Stroke of Undetermined Etiology; N (%)	17 (28.8)	8 (17.0)	13 (20.6)		23 (30.7)	2 (8.0)	13 (18.6)		9 (24.3)	25 (32.1)	4 (7.3)		9 (20.5)	25 (31.6)	4 (8.5)	
Interval Between Onset to Index Event; Mean (SD); Days	5.0 ± 6.0	5.0 ± 7.0	7.0 ± 7.0	0.28	5.0 ± 6.0	6.0 ± 8.0	6.0 ± 7.0	0.37	7.0 ± 8.0	5.0 ± 6.0	5.0 ± 7.0	0.19	7.0 ± 7.0	5.0 ± 6.0	6.0 ± 7.0	0.27
Mechanical Ventilation; N (%)	25 (25.3)	24 (27.6)	34 (32.1)	0.55	31 (25.2)	13 (25.9)	39 (32.5)	0.27	22 (33.8)	38 (27.1)	25 (27.5)	0.39	27 (36.5)	37 (25.2)	21 (28.0)	0.16
Disposition*																
Discharged Home; N (%)	37 (37.8)	38 (43.7)	50 (48.5)	0.57	51 (41.8)	17 (38.6)	56 (47.1)	0.27	31 (50.8)	60 (43.2)	36 (39.6)	0.39	38 (54.3)	61 (41.8)	29 (37.3)	0.16
In Hospital Mortality; N (%)	27 (27.6)	25 (28.7)	24 (23.3)		30 (24.6)	17 (38.6)	27 (22.7)		14 (23.0)	33 (23.7)	30 (33.0)		14 (20.0)	37 (25.3)	36 (34.7)	
Still in Hospital/Subacute Care; N (%)	34 (34.7)	24 (27.6)	29 (28.2)		41 (33.6)	10 (22.7)	36 (30.3)		16 (26.2)	46 (33.1)	25 (27.5)		18 (25.7)	48 (32.9)	21 (28.0)	
Length of Hospital Stay; Mean (SD); Days	10.0 ± 8.0	12.0 ± 9.0	14.0 ± 15.0	0.11	12.0 ± 9.0	10.0 ± 7.0	13.0 ± 15.0	0.56	14.0 ± 15.0	12.0 ± 12.0	10.0 ± 8.0	0.28	16.0 ± 17.0 B (0.036)	11.0 ± 9.0	11.0 ± 8.0	0.03

\* Data on patients' disposition were sparse.

# **Results**

## **Intraparenchymal Hemorrhage; Comparing the Patients among the Comorbidities' Subgroups**

**Supplemental Tables 20-21**

**Supplemental Table 20. Dividing the IPH patients into 2 subgroups.** Baseline characteristics and laboratory findings among SARS-CoV-2 patients with a hemorrhagic stroke, when grouping the patients into 2 subgroups using machine learning (ML) and expert opinion (EX) models. ML-K<sub>2</sub> used hierarchal clustering and K-means, while ML-S<sub>2</sub> used spectral clustering, to separate patients into 2 subgroups. EX-A<sub>2</sub> used all 11 collected comorbidities and EX-S<sub>2</sub> used 8 selected comorbidities, to separate patients into 2 subgroups.

Model	Machine Learning						Expert Opinion					
	ML-K2 (K-mean)			ML-S2 (Spectral)			EX-A2 (All comorbidities)			EX-S2 (Selected Comorbidities)		
Parameter	A N = 40 (70.2%)	B N = 17 (29.8%)	P- value	A N = 23 (34.3%)	B N = 44 (65.7%)	P- value	A N = 38 (55.9%)	B N = 30 (44.1%)	P- value	A N = 39 (57.4%)	B N = 29 (42.6%)	P- value
Age; Mean (SD); Years	61 ± 19	63 ± 16	0.68	68 ± 16	61 ± 18	0.14	61 ± 18	67 ± 15	0.15	61 ± 18	67 ± 15	0.15
Age; Median [IQR]; Years	65 [49 – 73]	65 [57 – 75]	0.89	69 [57 – 82]	65 [52 – 73]	0.26	65 [48 – 73]	67 [57 – 82]	0.46	65 [49 – 73]	67 [57 – 82]	0.32
Sex; Female; N (%)	15 (37.5)	10 (58.8)	0.64	13 (56.5)	16 (36.4)	0.30	15 (39.5)	15 (50.0)	0.30	16 (41.0)	14 (48.3)	0.40
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	14.0 [3.0 – 19.0]	15.0 [12.0 – 23.0]	1.00	0.0 [0.0 – 14.0]	15.0 [3.0 – 20.0]	0.36	7.0 [0.0 – 21.0]	13.0 ± [0.0 – 16.0]	0.50	8.0 [0.0 – 21.0]	12.0 [0.0 – 15.0]	0.76
Intracerebral Hemorrhage (ICH) Score; Median [IQR]	3.0 [2.0 – 3.0]	3.0 [2.0 – 4.0]	0.49	4.0 [3.0 – 5.0]	3.0 [2.0 – 3.0]	0.09	3.0 [2.0 – 4.0]	3.0 [1.0 – 4.0]	0.87	3.0 [2.0 – 4.0]	3.0 [2.0 – 4.0]	0.72
Interval Between Onset to Index Event; Median [IQR]; Days	0.0 [0.0 – 7.0]	6.0 [0.0 – 12.0]	0.18	0.0 [0.0 – 10.0]	0.0 [0.0 – 8.0]	0.83	0.0 [0.0 – 11.0]	0.0 [0.0 – 7.0]	0.94	0.0 [0.0 – 11.0]	0.0 [0.0 – 8.0]	0.72
Mechanical Ventilation Onset; Median [IQR]; Days	2.0 [1.0 – 4.0]	1.0 [1.0 – 3.0]	1.00	2.0 [1.0 – 3.0]	2.0 [1.0 – 3.0]	1.00	1.0 [1.0 – 5.0]	2.0 [1.0 – 2.0]	0.70	1.0 [1.0 – 5.0]	2.0 [1.0 – 2.0]	0.70
Disposition *												
Discharged Home; N (%)	8 (22.9)	2 (11.8)		1 (6.3)	9 (23.1)		7 (23.3)	3 (11.5)		7 (22.6)	3 (12.0)	
In Hospital Mortality; N (%)	20 (57.1)	11 (64.7)	0.64	12 (75.0)	22 (56.4)	0.30	16 (53.3)	19 (73.1)	0.30	17 (54.8)	18 (72.0)	0.40
Still in Hospital/Subacute Care; N (%)	7 (20.0)	4 (23.5)		3 (18.8)	8 (20.5)		7 (23.3)	4 (15.4)		7 (22.6)	4 (16.0)	
Length of Hospital Stay; Median (IQR); Days	8.0 [4.0 – 18.0]	5.0 [2.0 – 33.0]	0.79	5.0 [4.0 – 23.0]	8.0 [3.0 – 21.0]	0.75	7.0 [3.0 – 23.0]	7.0 [4.0 – 17.0]	0.94	7.0 [3.0 – 23.0]	6.0 [4.0 – 19.0]	0.84
Laboratory Findings												
White Blood Cell Count; Mean (SD); x10 <sup>9</sup> /L	13.1 ± 12.9	10.1 ± 4.9	0.28	9.4 ± 4.6	12.8 ± 12.4	0.15	13.5 ± 13.4	9.4 ± 4.1	0.13	13.3 ± 13.2	9.4 ± 4.2	0.15
White Blood Cell Count; Median [IQR]; x10 <sup>9</sup> /L	10.1 [8.2 – 12.0]	8.6 [7.1 – 12.1]	0.05	8.6 [6.7 – 10.3]	10.0 [8.2 – 12.0]	0.11	10.1 [8.4 – 13.2]	8.6 [7.2 – 10.5]	0.03	10.0 [8.2 – 12.5]	8.7 [6.9 – 10.8]	0.06
Neutrophil Count; Mean (SD); x10 <sup>9</sup> /L	10.4 ± 12.0	7.9 ± 4.8	0.38	7.8 ± 4.5	10.1 ± 11.5	0.31	11.2 ± 12.5	7.3 ± 4.1	0.14	10.9 ± 12.3	7.4 ± 4.2	0.17
Neutrophil Count; Median [IQR]; x10 <sup>9</sup> /L	7.6 [5.5 – 9.8]	5.6 [4.7 – 9.7]	0.04	6.9 [4.7 – 9.4]	7.6 [5.4 – 10.3]	0.39	8.0 [6.8 – 12.2]	6.3 [4.7 – 9.0]	0.02	7.6 [5.6 – 12.2]	6.5 [4.8 – 9.7]	0.04
Lymphocyte Count; Mean (SD); x10 <sup>9</sup> /L	2.1 ± 2.3	1.6 ± 0.7	0.36	1.3 ± 0.7	2.0 ± 2.2	0.11	2.0 ± 2.4	1.5 ± 0.7	0.30	2.0 ± 2.3	1.4 ± 0.7	0.24
Lymphocyte; Median [IQR]; x10 <sup>9</sup> /L	1.3 [0.9 – 2.2]	1.7 [1.1 – 2.1]	0.35	1.0 [0.8 – 1.8]	1.4 [1.0 – 2.2]	0.87	1.2 [0.7 – 1.9]	1.4 [0.8 – 2.1]	0.79	1.2 [0.7 – 2.0]	1.4 [0.8 – 2.0]	1.00
Platelet Count; Mean (SD); x10 <sup>9</sup> /L	198.4 ± 104.5	195.4 ± 102.2	0.93	204.4 ± 87.0	192.5 ± 105.1	0.65	198.2 ± 111.1	199.9 ± 84.1	0.95	195.9 ± 110.0	202.5 ± 84.6	0.80

Model	Machine Learning						Expert Opinion					
	ML-K2 (K-mean)			ML-S2 (Spectral)			EX-A2 (All comorbidities)			EX-S2 (Selected Comorbidities)		
Parameter	A N = 40 (70.2%)	B N = 17 (29.8%)	P-value	A N = 23 (34.3%)	B N = 44 (65.7%)	P-value	A N = 38 (55.9%)	B N = 30 (44.1%)	P-value	A N = 39 (57.4%)	B N = 29 (42.6%)	P-value
Platelet Count; Median [IQR]; x10 <sup>9</sup> /L	172.0 [131.0 – 255.0]	178.0 [133.0 – 258.5]	0.76	178.5 [145.0 – 257.0]	174.0 [131.0 – 237.0]	0.87	168.5 [113.0 – 255.0]	182.0 [147.0 – 253.5]	0.79	167.0 [115.0 – 255.0]	184.0 [149.0 – 257.0]	0.59
Alanine Transaminase (ALT); Mean (SD); U/L	55.9 ± 73.7	36.2 ± 38.8	0.26	23.9 ± 24.9	57.1 ± 71.7	0.07	45.7 ± 72.1	43.5 ± 46.8	0.89	45.7 ± 72.1	43.5 ± 46.8	0.89
Alanine Transaminase (ALT); Median [IQR]; U/L	22.9 [8.0 – 81.0]	17.5 [6.2 – 56.2]	0.99	16.7 [6.4 – 33.8]	27.0 [8.1 – 81.2]	0.27	20.1 [6.2 – 55.0]	17.5 [7.0 – 69.3]	0.57	20.1 [6.2 – 55.0]	17.5 [7.0 – 69.3]	0.57
Aspartate Transaminase (AST); Mean (SD); U/L	33.7 ± 27.2	33.1 ± 19.9	0.93	31.4 ± 17.3	34.2 ± 26.5	0.20	28.5 ± 19.9	37.4 ± 25.1	0.16	29.2 ± 19.9	37.0 ± 25.5	0.22
Aspartate Transaminase (AST); Median [IQR]; U/L	26.0 [18.2 – 42.0]	27.6 [17.0 – 41.5]	0.84	27.1 [20.0 – 40.0]	27.5 [17.6 – 43.2]	0.91	23.0 [18.2 – 35.0]	33.0 [18.0 – 48.0]	0.17	24.0 [18.6 – 37.5]	32.5 [18.0 – 43.4]	0.28
Blood Urea Nitrogen (BUN); Mean (SD); mg/dl	84.1 ± 226.1	47.1 ± 45.6	0.40	140.8 ± 441.9	82.3 ± 215.1	0.57	93.3 ± 229.3	117.2 ± 399.8	0.79	91.2 ± 225.4	120.4 ± 407.4	0.75
Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl	26.0 [18.2 – 42.0]	27.6 [17.0 – 41.5]	0.30	35.0 [23.0 – 54.0]	29.5 [18.5 – 51.0]	0.47	31.5 [19.5 – 53.0]	33.0 [20.0 – 49.0]	0.89	33.0 [20.0 – 52.0]	33.5 [20.0 – 49.0]	0.91
Creatinine; Mean (SD); mg/dl	1.9 ± 2.3	2.3 ± 2.0	0.54	2.7 ± 2.6	1.8 ± 2.2	0.19	1.5 ± 1.7	2.7 ± 2.8	0.05	1.5 ± 1.7	2.8 ± 2.8	0.04
Creatinine; Median [IQR]; mg/dl	1.0 [0.8 – 1.3]	1.3 [1.1 – 3.1]	0.17	1.4 [1.0 – 4.3]	1.0 [0.8 – 1.3]	0.09	1.0 [0.8 – 1.3]	1.3 [1.0 – 4.1]	0.06	1.0 [0.8 – 1.2]	1.3 [1.1 – 4.3]	0.03
C-Reactive Protein (CRP); Mean (SD); mg/L	95.0 ± 272.0	63.0 ± 76.0	0.56	57.0 ± 69.0	92.0 ± 259.0	0.46	102.0 ± 276.0	51.0 ± 62.0	0.35	99.0 ± 271.0	52.0 ± 63.0	0.37
C-Reactive Protein (CRP); Median [IQR]; mg/L	32.0 [21.0 – 46.0]	39.0 [28.0 – 68.0]	0.30	38.0 [28.0 – 45.0]	33.0 [21.0 – 56.0]	0.50	36.0 [22.0 – 56.0]	36.0 [25.0 – 46.0]	0.79	35.0 [20.0 – 52.0]	33.5 [20.0 – 49.0]	1.00
Lactate Dehydrogenase (LDH); Mean (SD); U/L	341.0 ± 209.1	628.9 ± 758.7	0.25	417.8 ± 193.2	486.8 ± 612.3	0.65	357.7 ± 221.5	572.0 ± 656.6	0.24	357.7 ± 221.5	572.0 ± 656.6	0.24
Lactate Dehydrogenase (LDH); Median [IQR]; U/L	330.0 [164.0 – 457.0]	357.0 [284.0 – 580.0]	1.00	366.5 [284.0 – 560.0]	402.0 [164.0 – 579.0]	0.84	333.0 [164.0 – 507.0]	376.0 [284.0 – 484.0]	1.00	330.0 [164.0 – 507.0]	376.0 [284.0 – 580.0]	1.00
Fibrinogen; Mean (SD); mg/dl	747.0 ± 386.9	349.5 ± 190.2	0.17	651.7 ± 540.4	747.0 ± 386.9	0.81	848.8 ± 405.1	349.5 ± 190.2	0.09	848.8 ± 405.1	349.5 ± 190.2	0.09
Fibrinogen; Median [IQR]; mg/dl	719.5 [498.0 – 996.0]	349.5 [215.0 – 484.0]	0.40	484.0 [215.0 – 1256.0]	719.5 [498.0 – 996.0]	1.00	746.0 [693.0 – 1246.0]	349.5 [215.0 – 484.0]	0.43	746.0 [693.0 – 1246.0]	349.5 [215.0 – 484.0]	0.43
D- Dimer; Mean (SD); ng/ml	1882.9 ± 2216.0	4578.3 ± 4646.4	0.42	16670.9 ± 22877.3	1882.9 ± 2216.0	0.09	11967.3 ± 20130.3	3170.2 ± 3375.2	0.31	11065.7 ± 19329.9	3394.2 ± 3723.4	0.23
D- Dimer; Median [IQR]; ng/ml	1253.0 [391.5 – 2387.0]	3120.0 [836.0 – 9779.0]	0.55	3120.0 [836.0 – 49725.0]	1253.0 [391.5 – 2387.5]	0.13	2371.0 [483.0 – 6935.0]	2303.0 [836.0 – 3120.0]	1.00	2050.0 [483.0 – 6935.0]	2556.0 [836.0 – 3120.0]	1.00

\* Data on patients' disposition were sparse.

**Supplemental Table 21. Dividing the IPH patients to 3 subgroups.** Baseline characteristics and laboratory findings among SARS-CoV-2 patients with intraparenchymal hemorrhage when clustering of patients into 3 subgroups using machine learning (ML) and expert opinion (EX) models. ML-K<sub>3</sub> used hierarchal clustering and K-means, while ML-S<sub>3</sub> used spectral clustering, to separate patients into 3 subgroups. EX-A<sub>3</sub> used all 11 collected comorbidities and EX-S<sub>3</sub> used 8 selected comorbidities, to separate patients into 3 subgroups. Blue ink indicates the post-hoc p values.

Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 23 (40.4%)	B N = 19 (33.3%)	C N = 15 (26.3%)	P- value	A N = 20 (29.9%)	B N = 28 (41.8%)	C N = 19 (28.4%)	P value	A N = 19 (27.9%)	B N = 31 (45.6%)	C N = 18 (26.5%)	P- value	A N = 21 (30.9%)	B N = 33 (48.5%)	C N = 14 (20.6%)	P- value
Age; Mean (SD); Years	67 ± 13 B (0.03)	53 ± 21	64 ± 17	0.03	72 ± 14 C (0.005)	66 ± 14	49 ± 21	0.01	55 ± 19 B (0.019)	69 ± 15	64 ± 17	0.03	53 ± 19 B (0.001)	70 ± 13	63 ± 17	0.002
Age; Median [IQR]; Years	67 [59 – 78]	49 [45 – 68]	66 [51 – 82]	0.28	72 [63 – 83]	66 [57 – 74]	49 [45 – 68]	0.10	56 [47 – 68]	68 [60 – 78]	65 [52 – 82]	0.11	56 [45 – 68]	68 [65 – 78]	65 [51 – 82]	0.04
Sex; Female; N (%)	7 (30.4)	9 (47.4)	9 (60.0)	0.19	10 (50.0)	10 (35.7)	9 (47.4)	0.56	9 (47.4)	11 (35.5)	10 (55.6)	0.37	9 (42.9)	12 (36.4)	9 (64.3)	0.21
National Institutes of Health Stroke Scale (NIHSS) Score; Median [IQR]	16.0 [8.0 – 21.0]	6.0 [0.0 – 17.0]	15.0 [12.0 – 23.0]	0.17	0.0 [0.0 – 10.0] B (0.009)	16.0 [12.0 – 22.0]	6.0 [0.0 – 17.0]	0.03	1.0 [0.0 – 14.0]	5.0 [0.0 – 20.0]	15.0 [12.0 – 15.0]	0.09	1.0 [0.0 – 14.0]	8.0 [0.0 – 19.0]	15.0 [12.0 – 23.0]	0.11
Intracerebral Hemorrhage (ICH) Score; Median [IQR]	3.0 [2.0 – 3.0]	2.0 [2.0 – 4.0]	3.0 [3.0 – 4.0]	0.21	4.0 [3.0 – 5.0]	3.0 [2.0 – 3.0]	2.0 [2.0 – 4.0]	0.10	4.0 [2.0 – 5.0] B (0.010)	3.0 [2.0 – 3.0] C (0.026)	3.0 [2.0 – 4.0]	0.02	4.0 [2.0 – 4.0] B (0.019)	3.0 [2.0 – 3.0]	3.0 [2.0 – 5.0]	0.02
Interval Between Onset to Index Event; Median [IQR]; Days	0.0 [0.0 – 4.0]	1.0 [0.0 – 12.0]	6.0 [0.0 – 11.0]	0.31	0.0 [0.0 – 7.0]	0.0 [0.0 – 8.0]	1.0 [0.0 – 12.0]	0.88	0.0 [0.0 – 11.0]	0.0 [0.0 – 10.0]	4.0 [0.0 – 8.0]	0.81	0.0 [0.0 – 11.0]	0.0 [0.0 – 6.0]	5.0 [0.0 – 10.0]	0.61
Mechanical Ventilation Onset; Median [IQR]; Days	2.0 [1.0 – 2.0]	4.0 [1.0 – 5.0]	1.0 [1.0 – 2.0]	0.05	2.0 [1.0 – 2.0]	1.0 [1.0 – 2.0]	4.0 [1.0 – 5.0]	0.05	1.0 [1.0 – 4.0]	2.0 [1.0 – 4.0]	2.0 [1.0 – 2.0]	0.51	3.0 [1.0 – 5.0]	2.0 [1.0 – 2.0]	1.0 [1.0 – 2.0]	0.90
Disposition *																
Discharged Home; N (%)	6 (26.1)	2 (14.3)	2 (13.3)	0.15	1 (7.7)	7 (25.0)	2 (14.3)	0.07	2 (16.7)	7 (25.9)	1 (5.9)	0.32	2 (14.3)	7 (25.0)	1 (7.1)	0.25
In Hospital Mortality; N (%)	15 (8.7)	6 (42.9)	10 (66.7)		9 (62.9)	19 (67.9)	6 (42.9)		6 (50.0)	16 (59.3)	13 (76.5)		7 (50.0)	18 (64.3)	10 (71.4)	
Still in Hospital/Suba-cute Care; N (%)	2 (8.7)	6 (42.9)	3 (20.0)		3 (23.1)	2 (7.1)	6 (42.9)		4 (33.3)	4 (14.8)	3 (17.6)		5 (35.7)	3 (10.7)	3 (21.4)	
Length of Hospital Stay; Median [IQR]; Days	8.0 [3.0 – 19.0]	7.0 [5.0 – 24.0]	5.0 [3.0 – 29.0]	0.80	7.0 [4.0 – 29.0]	5.0 [3.0 – 17.0]	7.0 [5.0 – 24.0]	0.94	6.0 [6.0 – 18.0]	7.0 [3.0 – 21.0]	7.0 [2.0 – 29.0]	0.95	6.0 [4.0 – 23.0]	9.0 [4.0 – 19.0]	5.0 [2.0 – 31.0]	0.49

Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 23 (40.4%)	B N = 19 (33.3%)	C N = 15 (26.3%)	P- value	A N = 20 (29.9%)	B N = 28 (41.8%)	C N = 19 (28.4%)	P value	A N = 19 (27.9%)	B N = 31 (45.6%)	C N = 18 (26.5%)	P- value	A N = 21 (30.9%)	B N = 33 (48.5%)	C N = 14 (20.6%)	P- value
<b>Laboratory Findings</b>																
<b>White Blood Cell Count; Mean (SD); x10<sup>9</sup>/L</b>	14.5 ± 16.5	11.0 ± 5.6	10.2 ± 5.0	0.50	8.4 ± 3.2	10.9 ± 14.7	9.5 ± 5.6	0.17	11.2 ± 6.3	12.7 ± 13.5	9.6 ± 4.7	0.63	10.9 ± 5.9	12.3 ± 13.2	10.1 ± 5.2	0.79
<b>White Blood Cell Count; Median [IQR]; x10<sup>9</sup>/L</b>	10.8 [8.2 – 12.0]	9.5 [8.2 – 12.0]	8.4 [6.7 – 15.1]	0.10	8.4 [6.7 – 9.8]	10.9 [7.7 – 15.1]	9.5 [8.2 – 12.0]	0.06	10.3 [8.2 – 13.8]	9.3 [8.1 – 11.6]	8.7 [6.7 – 9.8]	0.16	10.0 [8.2 – 13.8]	9.3 [7.9 – 11.5]	8.4 [6.7 – 9.1]	0.11
<b>Neutrophil Count; Mean (SD); x10<sup>9</sup>/L</b>	11.2 ± 15.1	8.9 ± 5.7	8.0 ± 4.9	0.66	6.7 ± 3.4	8.4 ± 12.4	7.2 ± 5.7	0.37	10.1 ± 5.9	9.9 ± 12.5	7.6 ± 4.7	0.68	9.7 ± 5.5	9.6 ± 12.1	7.9 ± 5.1	0.85
<b>Neutrophil Count; Median [IQR]; x10<sup>9</sup>/L</b>	8.3 [5.5 – 9.8]	7.2 [5.3 – 9.4]	5.8 [4.6 – 12.2]	0.09	6.7 [4.7 – 7.2]	8.4 [5.5 – 12.2]	7.2 [5.3 – 9.4]	0.32	8.7 [5.6 – 12.8]	7.2 [5.5 – 9.7]	6.3 [4.6 – 8.5]	0.17	7.5 [6.8 – 12.2]	7.2 [5.3 – 9.7]	5.5 [4.6 – 7.1]	0.06
<b>Lymphocyte Count; Mean (SD); x10<sup>9</sup>/L</b>	2.5 ± 2.9	1.5 ± 0.8	1.6 ± 0.7	0.21	1.0 ± 0.7	1.5 ± 2.5	1.3 ± 0.8	1.0	1.3 ± 0.8	2.0 ± 2.4	1.6 ± 0.7	0.44	1.3 ± 0.8	2.0 ± 2.4	1.6 ± 0.7	0.47
<b>Lymphocyte; Median [IQR]; x10<sup>9</sup>/L</b>	1.4 [1.0 – 2.3]	1.3 [0.9 – 2.0]	1.7 [1.1 – 2.0]	0.62	1.0 [0.7 – 1.7]	1.5 [1.0 – 2.2]	1.3 [0.9 – 2.0]	0.73	1.2 [0.7 – 1.5]	1.0 [0.9 – 2.0]	1.7 [1.1 – 2.1]	0.34	1.2 [0.7 – 1.9]	1.0 [0.8 – 2.2]	1.7 [1.1 – 2.0]	0.28
<b>Platelet Count; Mean (SD); x10<sup>9</sup>/L</b>	198.7 ± 119.9	198.9 ± 81.9	194.3 ± 105.7	0.99	193.0 ± 90.3	165.5 ± 113.5	190.0 ± 81.9	0.61	215.8 ± 89.4	182.2 ± 106.8	212.2 ± 89.7	0.49	202.4 ± 91.6	192.4 ± 102.9	209.6 ± 99.0	0.87
<b>Platelet Count; Median [IQR]; x10<sup>9</sup>/L</b>	174.0 [115.0 – 237.0]	190.0 [151.0 – 255.0]	176.0 [133.0 – 272.0]	0.94	193.0 [150.0 – 272.0]	165.5 [115.0 – 236.0]	190.0 [151.0 – 255.0]	0.90	219.0 [167.0 – 255.0]	159.5 [115.0 – 237.0]	180.0 [145.0 – 272.0]	0.51	210.0 [151.0 – 255.0]	180.5 [138.0 – 243.5]	176.0 [133.0 – 272.0]	0.93
<b>Alanine Transaminase (ALT); Mean (SD); U/L</b>	72.0 ± 83.6	43.0 ± 59.8	29.0 ± 28.8	0.19	17.1 ± 24.3	55.0 ± 75.9	22.9 ± 59.8	0.20	33.1 ± 56.9	58.1 ± 74.5	33.4 ± 35.6	0.37	34.8 ± 54.5	57.8 ± 72.7	27.6 ± 30.1	0.31
<b>Alanine Transaminase (ALT); Median [IQR]; U/L</b>	61.1 [12.0 – 99.0]	22.9 [6.2 – 45.0]	17.0 [6.2 – 54.1]	0.60	17.1 [7.0 – 33.8]	55.0 [12.0 – 81.0]	22.0 [6.2 – 45.0]	0.48	21.5 [3.8 – 31.5]	19.0 [8.4 – 81.4]	12.0 [6.2 – 63.0]	0.61	21.5 [5.0 – 32.0]	19.0 [12.0 – 81.0]	10.0 [5.0 – 54.1]	0.56
<b>Aspartate Transaminase (AST); Mean (SD); U/L</b>	37.1 ± 28.2	27.8 ± 25.3	34.3 ± 20.0	0.60	24.7 ± 17.9	35.1 ± 25.2	22.0 ± 25.3	0.31	28.6 ± 26.1	36.2 ± 23.6	30.9 ± 19.6	0.59	29.1 ± 24.3	35.5 ± 23.9	31.8 ± 20.2	0.70
<b>Aspartate Transaminase (AST); Median [IQR]; U/L</b>	33.0 [22.0 – 46.0]	22.0 [15.0 – 26.0]	28.0 [18.0 – 43.0]	0.07	24.7 [18.0 – 40.0] B (0.024)	35.1 [25.0 – 48.0] C (0.020)	22.0 [15.0 – 26.0]	0.01	21.0 [15.6 – 31.1]	32.0 [22.0 – 46.0]	27.6 [17.0 – 38.0]	0.17	22.0 [18.2 – 35.0]	32.0 [20.0 – 46.0]	27.1 [18.0 – 36.0]	0.17

Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 23 (40.4%)	B N = 19 (33.3%)	C N = 15 (26.3%)	P- value	A N = 20 (29.9%)	B N = 28 (41.8%)	C N = 19 (28.4%)	P value	A N = 19 (27.9%)	B N = 31 (45.6%)	C N = 18 (26.5%)	P- value	A N = 21 (30.9%)	B N = 33 (48.5%)	C N = 14 (20.6%)	P- value
<b>Blood Urea Nitrogen (BUN); Mean (SD); mg/dl</b>	33.6 ± 25.7	142.9 ± 320.2	43.7 ± 45.0	0.21	34.0 ± 475.2	32.0 ± 23.1	31.0 ± 320.2	0.45	145.8 ± 333.1	124.6 ± 406.1	40.2 ± 45.2	0.63	132.5 ± 310.5	119.7 ± 398.9	43.0 ± 48.3	0.73
<b>Blood Urea Nitrogen (BUN); Median [IQR]; mg/dl</b>	25.0 [17.5 – 48.5]	31.0 [17.0 – 72.0]	34.0 [23.0 – 45.0]	0.45	34.0 [19.0 – 59.0]	32.0 [21.0 – 47.0]	31.0 [17.0 – 72.0]	0.79	29.0 [17.0 – 45.0]	34.5 [22.0 – 59.0]	32.5 [12.5 – 44.5]	0.92	29.0 [17.0 – 54.0]	33.0 [21.0 – 59.0]	38.0 [28.0 – 45.0]	0.99
<b>Creatinine; Mean (SD); mg/dl</b>	2.2 ± 2.7	1.4 ± 1.6	2.3 ± 2.1	0.45	1.3 ± 2.5	1.1 ± 2.7	1.0 ± 1.6	0.40	1.3 ± 1.7	2.1 ± 2.3	2.8 ± 2.8	0.24	1.3 ± 1.6	2.3 ± 2.8	2.6 ± 2.1	0.27
<b>Creatinine; Median [IQR]; mg/dl</b>	1.1 [1.0 – 1.4]	1.0 [0.8 – 1.2]	1.3 [1.0 – 4.3]	0.36	1.3 [1.0 – 2.0]	1.1 [1.0 – 3.7]	1.0 [0.8 – 1.2]	0.21	0.9 [0.7 – 1.0]	1.1 [1.0 – 1.4]	1.4 [1.1 – 4.3]	0.08	0.9 [0.7 – 1.2]	1.1 [1.0 – 1.7]	1.4 [1.1 – 4.3]	0.08
<b>C-Reactive Protein (CRP); Mean (SD); mg/L</b>	35.0 ± 19.0	165.0 ± 386.0	59.0 ± 77.0	0.25	38.0 ± 74.0	34.0 ± 21.0	33.0 ± 386.0	0.18	167.0 ± 402.0	45.0 ± 34.0	56.0 ± 75.0	0.19	150.0 ± 375.0	43.0 ± 34.0	62.0 ± 82.0	0.26
<b>C-Reactive Protein (CRP); Median [IQR]; mg/L</b>	33.0 [21.0 – 46.0]	33.0 [21.0 – 66.0]	38.0 [28.0 – 63.0]	0.57	38.0 [25.0 – 45.0]	34.0 [24.0 – 46.0]	33.0 [21.0 – 66.0]	0.77	35.0 [21.0 – 45.0]	33.0 [23.0 – 55.0]	38.0 [28.0 – 50.0]	0.83	35.0 [21.0 – 66.0]	34.0 [20.0 – 54.0]	38.0 [28.0 – 45.0]	0.63
<b>Lactate Dehydrogenase (LDH); Mean (SD); U/L</b>	312.6 ± 187.0	366.4 ± 235.1	628.9 ± 758.7	0.35	489.0 ± 207.7	318.0 ± 722.3	402.0 ± 235.1	0.75	397.4 ± 149.9	516.5 ± 696.6	404.6 ± 155.5	0.79	406.5 ± 192.1	522.9 ± 688.6	385.3 ± 157.0	0.75
<b>Lactate Dehydrogenase (LDH); Median [IQR]; U/L</b>	321.0 [182.5 – 433.0]	402.0 [164.0 – 564.0]	357.0 [284.0 – 580.0]	0.70	489.0 [256.0 – 580.0]	318.0 [284.0 – 457.0]	402.0 [164.0 – 564.0]	0.65	407.0 [275.5 – 535.0]	330.0 [120.0 – 580.0]	357.0 [284.0 – 580.0]	0.72	407.0 [273.0 – 564.0]	376.0 [120.0 – 580.0]	318.0 [284.0 – 489.0]	0.48
<b>Fibrinogen; Mean (SD); mg/dl</b>	774.5 ± 666.8	719.5 ± 37.5	349.5 ± 190.2	0.58	870.0 ± 545.9	303.0 ± 571.5	719.5 ± 37.5	0.83	898.3 ± 310.9	774.5 ± 666.8	349.5 ± 190.2	0.41	898.3 ± 310.9	774.5 ± 666.8	349.5 ± 190.2	0.41
<b>Fibrinogen; Median [IQR]; mg/dl</b>	774.5 [303.0 – 1246.0]	719.5 [693.0 – 746.0]	349.5 [215.0 – 484.0]	0.14	870.0 [484.0 – 1256.0]	303.0 [215.0 – 1246.0]	719.5 [693.0 – 746.0]	0.91	746.0 [693.0 – 1256.0]	774.5 [303.0 – 1246.0]	349.5 [215.0 – 484.0]	0.33	746.0 [693.0 – 1256.0]	774.5 [303.0 – 1246.0]	349.5 [215.0 – 484.0]	0.33
<b>D- Dimer; Mean (SD); ng/ml</b>	1518.7 ± 891.9	2101.4 ± 2834.9	4578.3 ± 4646.4	0.46	6167.5 ± 24190.8	2033.5 ± 1082.3	483.0 ± 2834.9	0.17	9634.6 ± 18039.5	11367.4 ± 21456.5	3603.8 ± 4265.2	0.79	9634.6 ± 18039.5	9586.2 ± 19681.0	4578.3 ± 4646.4	0.90



Model	Machine Learning								Expert Opinion							
	ML-K <sub>3</sub> (K-mean)				ML-S <sub>3</sub> (Spectral)				EX-A <sub>3</sub> (All Comorbidities)				EX-S <sub>3</sub> (Selected Comorbidities)			
Parameter	A N = 23 (40.4%)	B N = 19 (33.3%)	C N = 15 (26.3%)	P- value	A N = 20 (29.9%)	B N = 28 (41.8%)	C N = 19 (28.4%)	P value	A N = 19 (27.9%)	B N = 31 (45.6%)	C N = 18 (26.5%)	P- value	A N = 21 (30.9%)	B N = 33 (48.5%)	C N = 14 (20.6%)	P- value
D- Dimer; Median [IQR]; ng/ml	2017.0 [489.0 – 2050.0]	483.0 [300.0 – 2725.0]	3120 [836.0 – 9779.0]	0.68	6167.5 [836.0 – 49726.0]	2033.5 [1253.0 – 2585.0]	483.0 [300.0 – 2725.0]	0.41	2725.0 [300.0 – 6935.0]	2050.0 [2017.0 – 2556.0]	1978.0 [758.0 – 6449.5]	0.84	2725.0 [300.0 – 6935.0]	2033.5 [680.0 – 2556.]	3120.0 [836.0 – 9779.0]	0.57

\* Data on patients' disposition were sparse.

# **Discussion**

## **Literature Review: TOAST and Imaging finding**

**Supplemental Table 22**

**Discussion; Supplemental Table 22. TOAST subclasses and lacunar imaging findings in epidemiological studies**

Study	Population (Number)	Region	TOAST					Imaging pattern
			LA A (%)	SAO (%)	Cardioembolic (%)	Undetermined (%)	Other (%)	Lacunar (%)
<b>Ornello et al<sup>4</sup></b>	128172	Worldwide	23	22	22	26	3	-
		Asians	33	24	15	22	2	-
		White	19	20	28	27	4	-
		Hispanic	17	25	23	30	3	-
<b>O'Donnell et al<sup>5</sup></b>		Blacks	12	24	20	38	5	-
	3000	Worldwide	19	44	9	22	5	21
	422	High-income countries	18	30	26	21	4	29
	151	South America	4	18	16	46	15	13
	1146	Southeast Asia	11	53	2	31	3	22
	958	India	31	50	4	11	3	20
<b>O'Donnell et al<sup>6</sup></b>	323	Africa	14	27	25	14	20	16
	13447	Worldwide	-	-	-	-	-	26.9
	1917	Western Europe, North America, Australia	-	-	-	-	-	30
	1394	Eastern and central Europe, and Middle East	-	-	-	-	-	20.9
	1471	South America	-	-	-	-	-	18.9
	3987	China	-	-	-	-	-	36.4
	2850	South Asia	-	-	-	-	-	26.6
	855	Southeast Asia	-	-	-	-	-	13.9
	973	Africa	-	-	-	-	-	14
<b>Li et al<sup>7</sup></b>	2555	UK	10	12	38	32		
<b>Lutski et al<sup>8</sup></b>	3579	Israel	9	23	11	56	1	26
<b>Yesilot Barlas et al.<sup>9</sup></b>	3331	Europe (15- to 49-year-olds)	9.3	12	17	39	21	
<b>Ihle-Hansen et al.<sup>10</sup></b>	210	Norway	11	31	31	25	-	31
<b>Corso et al.<sup>11</sup></b>	1057	Italy	14	20	25	39	-	20
<b>Lai et al.<sup>12</sup></b>	1021	Taiwan				-	-	37
<b>Park et al.<sup>13</sup></b>	9417	Korea	36	22	21	-	-	-
<b>Lovett et al.<sup>14</sup></b>	1079	UK	14	20	25	36	-	-
<b>Yip et al<sup>15</sup></b>	676	Taiwan	17	29	20	29	6	29
<b>Czlonkowska et al.<sup>16</sup></b>	633	Poland	-	-	-	-	-	14
<b>Tanizaki et al<sup>17</sup></b>	298	Japan	-	-	18	-	-	56
<b>Schneider et al.<sup>18</sup></b>	362	US – Black	10	18	15	54	3	-
	1594	US – White	12	15	22	49	2	-
<b>Schulz et al.<sup>19</sup></b>	293	UK – Hospitalized	14	14	28	38	4	-
	345	UK – Non hospitalized	15	27	17	34	5	-
<b>Ghandehari et al.<sup>20</sup></b>	1392	Iran						19
<b>Krishnamurthi et al.<sup>21</sup></b>	1643	New Zealand	15	21	29	31	5	-
<b>Hauer et al.<sup>22</sup></b>	3311	Netherlands	24	19	14	34	6	-
<b>Alzamora et al.<sup>23</sup></b>	196	Spain	-	-	-	-	-	28
<b>Carrera et al.<sup>24</sup></b>	5759	Switzerland	-	15	-	-	-	-
<b>Nacu et al.<sup>25</sup></b>	228	Norway 15-49	3	14	28	35	19	-
	1126	Norway 50-74	14	16	24	43	1	-
	1130	Norway ≥75	11	8	40	37	1	-
<b>Bejot et al.<sup>26</sup></b>	332	France	35	26	24			-
<b>Kubo et al.<sup>27</sup></b>	430	Japan	-	-	-	-	-	54
<b>Di Carlo et al.<sup>28</sup></b>	2740	Europe	-	-	-	-	-	26
<b>Kolominsky-Rabas et al.<sup>29</sup></b>	531	Germany	13	22	26	35	1	-
<b>Hajat et al.<sup>30</sup></b>	1181	UK	9	27	27	24	3	-
<b>Senel et al.<sup>31</sup></b>	2534	Turkey	18	20	22	33	4	-
	2314	Iran	10	3	16	58	10	-
<b>Chung et al.<sup>32</sup></b>	2702	Korea	37	22	20	11		-

Study	Population (Number)	Region	TOAST					Imaging pattern
			LA A (%)	SAO (%)	Cardioembolic (%)	Undetermined (%)	Other (%)	Lacunar (%)
Harris et al. <sup>33</sup>	235	Indonesia	59	26	2	9	1	-
Rukn et al. <sup>34</sup>	4735	The Middle East and North Africa (MENA)	46?	24	17	-	-	-
	5809	Non-MENA (Worldwide)	35?	21	24	-	-	-
Saber et al. <sup>35</sup>	512	Iran	14	22	15	43	4	-
Porcello Marrone et al. <sup>36</sup>	688	Brazil	32	18	28	16	4	-
Tsai et al. <sup>37</sup>	13254	Chinese	43	18	8	-	-	24
	12689	White	26	22	25	-	-	28
Sarfo et al. <sup>38</sup>	515	Nigeria & Ghana < 50-year-old	40	28	11	-	-	-
	1603	Nigeria & Ghana ≥50-year-old	32	39	7	-	-	-
Wafa et al. <sup>39</sup>	3088	UK	11	25	26	34	2	-
Khorvash et al. <sup>40</sup>	1910	Iran	8	25	21	43	2	-
Khealani et al. <sup>41</sup>	874	Pakistan	31	25	10	32		-
Kumral et al. <sup>42</sup>	1529	Turkey		13	-	-	-	13
Lee et al. <sup>43</sup>	1567	Korea	42	31	8	16	1	-
Grau et al. <sup>44</sup>	5017	Germany	20	20	25	-	-	-

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