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Characteristics of a COVID-19 Cohort With Large Vessel Occlusion: A Multicenter International Study

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Authors

Jabbour, Pascal
Dmytriw, Adam A
Sweid, Ahmad
et al.

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Pascal Jabbour, MD [*]
Adam A. Dmytriw, MD, MPH, MSc [‡]
Ahmad Sweid, MD [*]
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Nader Sourour, MD [¶]
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Ajit S. Puri, MD [‡‡‡‡]
Bijoy K. Menon, MD [§§§§]
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Guglielmo Pero, MD [††††††††]
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Sanjeev Nayak, MD [||||||||||||]
Leonardo Renieri, MD [¶¶¶¶¶¶¶]
Mohamed A. Aziz-Sultan, MD [‡]
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Aman B. Patel, MD [‡]
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Jonathan A. Grossberg, MD [‡‡‡‡‡‡‡‡]
Hassan Saad, MD [‡‡‡‡‡‡‡‡]
M. Reid Gooch, MD [*]
Nabeel A. Herial, MD, MPH [*]
Robert H. Rosenwasser, MD [*]
Stavropoula Tjoumakaris, MD [*]
Ambooj Tiwari, MD, MPH [†††††††††§§§§§]

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Characteristics of a COVID-19 Cohort With Large Vessel Occlusion: A Multicenter International Study

BACKGROUND: The mechanisms and outcomes in coronavirus disease (COVID-19)–associated stroke are unique from those of non–COVID-19 stroke.

OBJECTIVE: To describe the efficacy and outcomes of acute revascularization of large vessel occlusion (LVO) in the setting of COVID-19 in an international cohort.

METHODS: We conducted an international multicenter retrospective study of consecutively admitted patients with COVID-19 with concomitant acute LVO across 50 comprehensive stroke centers. Our control group constituted historical controls of patients presenting with LVO and receiving a mechanical thrombectomy between January 2018 and December 2020.

RESULTS: The total cohort was 575 patients with acute LVO; 194 patients had COVID-19 while 381 patients did not. Patients in the COVID-19 group were younger (62.5 vs 71.2; $P < .001$) and lacked vascular risk factors (49, 25.3% vs 54, 14.2%; $P = .001$). Modified thrombolysis in cerebral infarction 3 revascularization was less common in the COVID-19 group (74, 39.2% vs 252, 67.2%; $P < .001$). Poor functional outcome at discharge (defined as modified Ranklin Scale 3-6) was more common in the COVID-19 group (150, 79.8% vs 132, 66.7%; $P = .004$). COVID-19 was independently associated with a lower likelihood of achieving modified thrombolysis in cerebral infarction 3 (odds ratio [OR]: 0.4, 95% CI: 0.2-0.7; $P < .001$) and unfavorable outcomes (OR: 2.5, 95% CI: 1.4-4.5; $P = .002$).

CONCLUSION: COVID-19 was an independent predictor of incomplete revascularization and poor outcomes in patients with stroke due to LVO. Patients with COVID-19 with LVO were younger, had fewer cerebrovascular risk factors, and suffered from higher morbidity/mortality rates.

KEY WORDS: COVID-19, SARS-CoV-2, Central nervous system, Cerebrovascular disease, Hypercoagulable

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One of the peculiar features of coronavirus disease (COVID-19) is the increased incidence of thrombotic events in multiple organ systems due to multiple factors including the presence of the angiotensin-converting enzyme (ACE)-2 receptor on the surface of the vascular endothelium and the hypercoagulable state because of immune dysregulation.[1-26] Great efforts have been invested in understanding the disease better and elucidating its manifestation and pathophysiology.[1-26] We have learned a lot about the effect of COVID-19 on the central nervous system, particularly acute ischemic stroke (AIS). There remain limited data on the safety and outcomes of acute revascularization of large vessel occlusion (LVO) in patients with COVID-19. In this international multicenter series, we describe the safety and efficacy of acute revascularization of LVO in the setting of patients with COVID-19 compared with non-COVID-19 patients with LVO. We also examine the characteristics of patients with COVID-19 and identify predictors of complete revascularization and unfavorable outcomes. To the best of our knowledge, this is the largest multicenter study of patients

ABBREVIATIONS: ACE, angiotensin-converting enzyme; **AIS,** acute ischemic stroke; **ASPECTS,** Alberta Stroke Program Early Computed Tomography Score; **ET,** endotracheal; **GWTG,** get with the guidelines; **LVO,** large vessel occlusion; **MT,** mechanical thrombectomy; **mTICI,** modified thrombolysis in cerebral infarction; **NIHSS,** National Institutes of Health Stroke Scale; **sICH,** symptomatic intracerebral hemorrhage; **TICI,** thrombolysis in cerebral infarction; **tPA,** tissue plasminogen activator; **WHO,** World Health Organization.

Supplemental digital content is available for this article at neurosurgery-online.com.

with COVID-19 with LVO receiving mechanical thrombectomy (MT).

METHODS

We conducted an international multicenter retrospective study of patients with COVID-19 with AIS and LVO between February 25 and December 30, 2020 across 48 thrombectomy comprehensive stroke centers, predominantly from North America and Europe. The institutional review board of participating institutions reviewed and approved the study, and patient consent was waived. The remaining methods section is attached as **Supplemental Digital Content**, http://links.lww.com/NEU/C851.

Data Sharing Statement

The relevant anonymized patient-level data are available on reasonable request from the authors.

Ethical Approval

All procedures performed in the studies involving human participants were per the institutional review board ethical standards and national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent

The study protocol was reviewed and approved by the University institutional review board. Following our institutional guidelines, all protected health information was removed, and individual patient consent was not required in the analysis of case series.

RESULTS

The total cohort composite was 575 patients, with 194 patients having concomitant COVID-19 and LVO and 381 patients having only LVO as a control group from 48 centers (Figure). The data are presented in Table 1.

There was a significant difference in the mean age of the patients with relatively younger patients in the COVID-19 cohort compared with the non–COVID-19 cohort (62.5 + 15.3 years vs 71.2 + 15.9 years; $P < .001$). In addition, there was a significantly higher proportion of patients less than or equal to 50 years (30, 18.5% vs 41, 10.8%; $P = .015$). There was a lower proportion of female patients in the COVID-19 group (84, 43.3% vs 305, 80.1%; <0.001). The functional status at stroke onset was significantly different, with a lower proportion of functional independence in the COVID-19 group (modified Ranklin Scale [mRS] 0-2: 153, 90.0% vs 367, 96.3%; 0.002).

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*Department of Neurological Surgery, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA; ‡Interventional Neuroradiology & Endovascular Neurosurgery Service, Mass General Brigham Partners, Harvard Medical School, Boston, Massachusetts, USA; §Department of Interventional Neuroradiology, Rothschild Foundation Hospital, Paris, France; ‖Department of Neurosurgery, Good Samaritan Hospital Medical Center, West Islip, New York, USA; ¶Department of Interventional Neuroradiology, Pitié-Salpêtrière Hospital, Paris, France; #Department of Radiology, New York University Langone Medical Center, New York, New York, USA; **Department of Interventional Neuroradiology & Neuroendovascular Surgery, Miami Cardiac and Vascular Institute, Baptist Hospital of Miami, Miami, Florida, USA; ††Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan, USA; ‡‡Department of Interventional Neuroradiology, Hospital Clinico Universitario de Valladolid, Valladolid, Spain; §§Department of Neurosurgery, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA; ‖‖Department of Neurosurgery, Advocate Aurora Health, Chicago, Illinois, USA; ¶¶Department of Neuroscience, Valley Baptist Medical Center/University of Texas Rio Grande Valley, Harlingen, Texas, USA; ##Department of Neurosurgery, Baylor College of Medicine, Houston, Texas, USA; ***Department of Neurosurgery, University of Texas Medical Branch, Galveston, Texas, USA; †††Department of Neurosurgery, Firoozgar Hospital, Tehran, Iran; ‡‡‡Departments of Neurological Surgery, Radiology, Mechanical Engineering, and Stroke & Applied Neuroscience Center, University of Washington, Seattle, Washington, USA; §§§Department of Neurosurgery, University of Michigan, Ann Arbor, Michigan, USA; ‖‖‖Department of Neurosurgery & Neuroradiology, University of Miami & Jackson Memorial Hospital, Miami, Florida, USA; ¶¶¶Department of Biomedical Engineering, American University of Beirut, Beirut, Lebanon; ###Department of Neurology and Neuroradiology, Alexandria University Hospital, Al Attarin, Egypt; ****Departments of Neurological Surgery and Stroke & Applied Neuroscience Center, University of Washington, Seattle, Washington, USA; ††††Division of Neuroradiology, Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia, USA; ‡‡‡‡Division of Neurointerventional Radiology, Department of Radiology, UMass Memorial Medical Center, Worcester, Massachusetts, USA; §§§§Calgary Stroke Program, Cumming School of Medicine, Calgary, Alberta, Canada; ‖‖‖‖Department of Medicine (Neurology), Prisma Health Upstate, USC, Greenville, South Carolina, USA; ¶¶¶¶Department of Neurological Surgery, University of Southern California, Los Angeles, California, USA; ####Department of Neurology, UT Health Science Center, Houston, Texas, USA; *****Department of Neurointerventional Radiology, San Francisco General Hospital, San Francisco, California, USA; †††††Department of Neurology, Brookdale University Hospital, Brooklyn, New York, USA; ‡‡‡‡‡Department of Neurology, Jamaica Medical Center, Richmond Hill, New York, USA; §§§§§Department of Neurology, NYU Lutheran Hospital, Brooklyn, New York, USA; ‖‖‖‖‖Department of Neurology, Sinai Grace Hospital, Detroit, Michigan, USA; ¶¶¶¶¶Department of Neurology, St. Joseph Mercy Health, Ann Arbor, Michigan, USA; #####Department of Neurosurgery, University of New York at Buffalo, Buffalo, New York, USA; ******Department of Neurology, Robert Wood Johnson University Hospital, New Brunswick, New Jersey, USA; ††††††Department of Neurology, University Emergency Hospital Bucharest, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; ‡‡‡‡‡Department of Neurology, Hospital Universitari, Bellvitge, Barcelona, Spain; §§§§§§Stroke Unit, Neuroscience Department, Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona, Spain; ‖‖‖‖‖Department of Neurology, Hospital Clínic, Barcelona, Spain; ¶¶¶¶¶¶Department of Neurology, Hospital Clínico Universitario, Valladolid, Spain; ######Stroke Unit, Department of Neurology, Vall d'Hebron Research Institute, Barcelona, Spain; *******Departament de Medicina, Universitat Autónoma de Barcelona, Barcelona, Spain; †††††††Department of Neuroradiology, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; ‡‡‡‡‡‡Department of Neurology, Eastern Region, Northwell Health, Long Island, New York, New York, USA; §§§§§§§Department of Neurology, Radiology, and Neurosurgery, Westchester Medical Center at New York Medical College, Valhalla, New York, USA; ‖‖‖‖‖‖‖Department of Radiology, University Hospital of North Midlands, Stoke-on-Trent, UK; ¶¶¶¶¶¶¶Department of Radiology, Neurovascular Unit, Careggi University Hospital, Florence, Italy; #######Departments of Neurology and Radiology, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, USA; ********Cooper Neurological Institute, Cooper University Hospital, Camden, New Jersey, USA; †††††††Department of Physics, University of Toronto, Toronto, Ontario, Canada; ‡‡‡‡‡‡‡Department of Neurosurgery, Emory University, Atlanta, Georgia, USA

Correspondence:
Pascal Jabbour, MD,
Division of Neurovascular Surgery and Endovascular Neurosurgery,
Thomas Jefferson University Hospital,
901 Walnut Street 3rd Floor,
Philadelphia PA 19107, USA.
Email: pascal.jabbour@jefferson.edu

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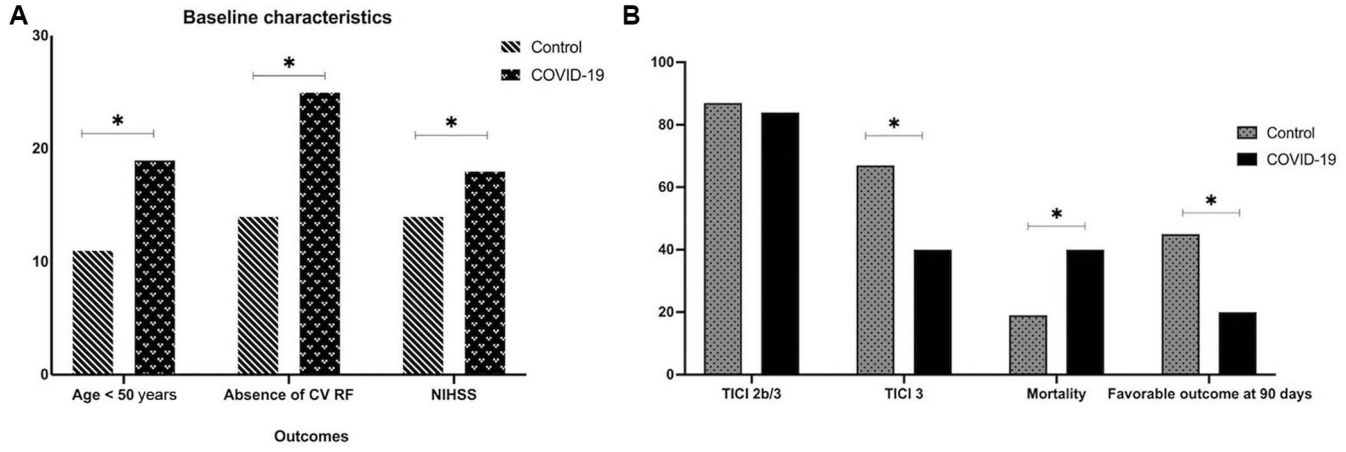

FIGURE. A, *Bar graph showing a comparative analysis between COVID-19 group and the control group for baseline characteristics.* B, *Bar graph showing a comparative analysis between COVID-19 group and the control group for outcomes. COVID-19, coronavirus disease; TICI, thrombolysis in cerebral infarction.*

Comorbidities

Chronic heart disease (35, 18.0% vs 131, 34.4% vs; $P < .001$) and atrial fibrillation (47, 24.2% vs 148, 39.6%; $P < .001$) were lower while diabetes mellitus type II was significantly higher (59, 30.4% vs 86, 22.9%; $P = .050$) in the COVID-19 group. Hypertension, chronic lung disease, and chronic liver disease frequency were similar between both groups. Moreover, lack of traditional cerebrovascular risk factors was observed at a higher proportion in the COVID-19 group (49, 25.3% vs 54, 14.2%; $P = .001$).

COVID-19 Characteristics

The severity of COVID-19 on stroke onset was moderate in 75.5% of cases (139), severe in 15.8% (29), and critical in 8.7% (16). The mean duration between COVID-19 symptoms and stroke onset was 9.1 + 11.6 days, and 34.1% cases (62) of the COVID-19 group had a stroke as the initial manifestation of the COVID-19 disease.

Stroke Characteristics

The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) at admission was lower in the COVID-19 group (8 vs 9; $P \leq .001$) while the National Institutes of Health Stroke Scale (NIHSS) score at admission was higher in the COVID-19 group (17.5; vs 14; $P \leq .001$) (Figure A).

The mean number of involved vessels (1.5 + 0.8; vs 1.2 + 0.5; $P = .004$) and involvement of more than 1 vessel (32, 32.6% vs 79, 20.8%; $P = .006$) were higher in the COVID-19 group. Regarding location of the occlusion (anterior vs posterior circulation), there was no significant difference between both groups (anterior circulation: 89, 91.8% vs 341, 89.9%; $P = .597$).

The duration between stroke onset to hospital admission (in hours) was lower in the COVID-19 group (4.5 + 5.1 hours; vs 7.1 + 5.8 hours; $P \leq .001$) while door to arterial access was higher in the COVID-19 group (1.6 + 1.9 hours vs 1.2 + 1.3 hours; $P = .005$).

Stroke Treatment

For stroke treatment, tissue plasminogen activator (tPA) administration was similar between both groups (62, 34.3% vs 130, 34.8%; $P = .907$). A higher proportion of MT procedures were performed under general anesthesia in the COVID-19 group (58, 31.5% vs 72, 19.1%; $P \leq 0.001$).

The number of thrombectomy attempts was similar between both groups (1.9 + 1.4 vs 1.9 + 1.2; $P = .859$). Extracranial stenting was similar, whereas intracranial stenting was higher in the control group (7, 3.6% vs 39, 10.2%; $P = .005$).

The procedure duration to complete the MT procedure was prolonged by 11 mins in the COVID-19 group (62.2 + 47.3 vs 51.9 + 31.9; $P = .002$). Favorable revascularization (modified thrombolysis in cerebral infarction [mTICI] 2b-3) was similar between both groups (158, 83.6% vs 326, 86.9%; $P = .284$). However, complete revascularization (mTICI 3) was observed at a lower proportion in the COVID-19 group (74, 39.2% vs 252, 67.2%; $P < .001$).

Complications, Functional Outcomes, and Mortality

There was no significant difference in symptomatic intracerebral hemorrhage (sICH) (8, 4.1% vs 20, 5.3%; $P = .683$) nor was there a significant difference in NIHSS score at 24 hours post-thrombectomy (10 vs 11; $P = .710$) between both groups.

The length of hospital stay was longer in the COVID-19 group by 9.4 days (17.8 + 19.3 days vs 8.4 + 8.6 days; $P \leq .001$). Poor functional outcome at discharge (150, 79.8% vs 132, 66.7%; $P = .004$) was observed more frequently in the COVID-19 group, and favorable functional outcome at 90 days (20, 18.9% vs 144, 47.4%; $P < .001$) was observed less frequently in the COVID-19 group.

TABLE 1. Baseline Characteristics and Technical and Procedural Outcomes in Patients With Acute Ischemic Stroke in the Setting of COVID-19

Variable	Cohort—patients with COVID-19 Mean (SD, range) N (%), mean ± SD; 95% CI; Median (range) (n = 194)	Non-COVID-19 patients Mean N (%), mean ± SD; 95% CI; median (range) (n = 381)	*P*-value
Baseline characteristics			
Age (y)	62.5 + 15.3; 60.0-64.8	71.2 + 15.9; 69.5-72.8	**<.001**
Age <50 y	30 (15.5)	41 (10.8)	**.015**
Sex (female)	84 (43.3)	305 (80.1)	**<.001**
Prestroke mRS			**.002**
0-2	153 (90.0)	367 (96.3)	
3-5	17 (10.0)	14 (3.7)	
Comorbidities			
Hypertension	119 (61.3)	266 (69.8)	.098
Chronic heart disease	35 (18.0)	131 (34.4)	**<.001**
Chronic lung disease	44 (22.7)	75 (19.7)	.402
Chronic kidney disease	19 (9.8)	6 (6.9)	.446
Chronic liver disease	10 (5.2)	10 (2.6)	.148
Diabetes mellitus type II	59 (30.4)	86 (22.6)	**.050**
Atrial fibrillation	47 (21.6)	148 (38.8)	**<.001**
New onset atrial fibrillation	13 (6.7)		
Absence of cerebrovascular risk factors	49 (25.3)	54 (14.2)	**.001**
COVID-19 characteristics			
Severity per WHO classification			
Moderate	139 (75.5)		
Severe	29 (15.8)		
Critical	16 (8.7)		
Stroke as initial presentation of COVID-19	62 (32)		
Duration between COVID-19 diagnosis and stroke onset (d)	9.1 + 11.6; 7.3-10.8		
Stroke characteristics			
ASPECTS	8; 8.0-9.0	9; 9.0-10.0	**<.001**
No. of involved LVO	1.5 + 0.8; 1.3-1.6	1.2 + 0.5; 1.2-1.3	**.004**
No. of involved LVO			**.006**
One vessel	66 (67.3)	300 (79.2)	
More than 1 vessel	32 (32.7)	79 (20.8)	
Stroke location (anterior circulation)	89 (90.8)	341 (90)	.597
Stroke onset to hospital door (h)	4.5 + 5.1; 3.6-5.3	7.1 + 5.8; 6.3-7.8	**<.001**
Door to arterial access (h)	1.6 + 1.9; 1.3-1.9	1.2 + 1.3; 1.0-1.3	**.005**
NIHSS at admission	17.5; 15.0-19.0	14.0; 13.0-15.0	**<.001**
Stroke treatment			
Tissue plasminogen activator	62 (32)	130 (34.1)	.907
Airway control (intubation)	58 (29.9)	72 (18.9)	**<.001**
No. of thrombectomy passes	1.9 + 1.4; 1.7-2.1	1.9 + 1.2; 1.8-2.0	.859
Stenting	13 (6.7)	53 (13.9)	**.086**
Intracranial	7 (3.6)	39 (10.2)	**.005**
Extracranial	6 (3.1)	14 (3.7)	.813
Procedure duration (min)	62.2 + 47.3; 55.4-68.9	51.9 + 31.9; 48.7-55.2	**.002**
mTICI score			
2B-3	158 (81.4)	326 (85.6)	.284
3	74 (38.1)	252 (66.1)	**<.001**
Outcomes			
Complications			**.002**
Asymptomatic	9 (4.6)	54 (14.2)	
Symptomatic	11 (5.7)	22 (5.8)	
sICH	8 (4.1)	20 (5.3)	.683
NIHSS 24 h after MT	10.0; 7.0-12.0	11.0; 9.0-13.0	.710
Length of hospital stay (d)	17.8 + 19.3; 14.8-20.8	8.4 + 8.6; 7.5-9.2	**<.001**

TABLE 1. Continued.

Variable	Cohort—patients with COVID-19 Mean (SD, range) N (%), mean ± SD; 95% CI; Median (range) (n = 194)	Non-COVID-19 patients Mean N (%), mean ± SD; 95% CI; median (range) (n = 381)	*P*-value
mRS at discharge (3-6)	150 (77.3)	132 (34.6)	**.004**
mRS at 90 d (0-3)	20 (10.3)	144 (37.8)	**<.001**
Mortality (in hospital)	75 (38.7)	70 (18.4)	**<.001**

ASPECTS, Alberta Stroke Program Early Computed Tomography Score; COVID-19, coronavirus disease; LVO, large vessel occlusion; mRS, modified Ranklin Scale; MT, mechanical thrombectomy; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; sICH, symptomatic intracerebral hemorrhage; WHO, World Health Organization.
Bold values indicate statistically significant value $P \leq .05$.

Mortality rate was higher by more than 2-fold in the COVID-19 group (75, 40.3% vs 70, 18.5%; $P < .001$) (Figure B).

Predictors of Revascularization mTICI 3

Univariate and multivariate analyses are presented in Table 2. Factors associated with good revascularization outcomes were female sex (odds ratio [OR]: 3.0, 95% CI: 1.7-5.4; $P < .001$), COVID-19 positivity (OR: 0.2, 95% CI: 0.3-0.5; $P < .001$), chronic heart disease (OR: 2.3, 95% CI: 1.4-4.1; $P = .003$), ASPECTS (OR: 1.2, 95% CI: 1.0-1.3; $P = .001$), number of vessels involved (OR: 0.7, 95% CI: 0.5-0.9; $P = .017$), and NIHSS score at admission (OR: 0.9, 95% CI: 0.9-1.0; $P = .05$) before propensity score analysis. After matching, female sex (OR: 1.7, 95% CI: 1.0-2.8; $P = .02$), COVID-19 positivity (OR: 0.3, 95% CI: 0.2-0.6; $P < .001$), ASPECTS (OR: 1.2, 95% CI: 1.1-1.4; $P = .005$), and NIHSS at admission (OR: 1.0, 95% CI: 0.9-1.0; $P = .03$) remained statistically significant in addition to chronic kidney diseases (OR: 2.7, 95% CI: 1.1-6.5; $P = .026$). Moreover, multivariate analysis performed after matching showed that the independent predictors of good revascularization are female sex (OR: 2.2, 95% CI: 1.2-3.9; $P = .007$), COVID positivity (OR: 0.4, 95% CI: 0.2-0.8; $P = .004$), chronic kidney diseases (OR: 3.0, 95% CI: 1.1-8.0; $P = .034$), and ASPECTS (OR: 1.2, 95% CI: 1.0-1.4; $P = .014$) (Table 2).

Predictors of Unfavorable Outcomes (modified Ranklin Scale 3-6)

Univariate and multivariate analyses are presented in Table 3. Factors associated with unfavorable outcomes were COVID-19 positivity (OR: 1.9, 95% CI: 1.2-3.1; $P = .004$), ASPECTS

TABLE 2. Univariate and Multivariable Analyses for Variables Associated With Revascularization mTICI 3 Before and After Propensity Score Analysis

	Univariate			Univariate after propensity score analysis			Multivariate		
Variable	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Sex (female)	3.0	1.7-5.4	**<.001**	1.7	1.0-2.8	**.02**	2.2	1.2-3.9	**.007**
Decreasing age	1.0	0.9-1.0	.195						
COVID-19	0.3	0.2-0.5	**<.001**	0.3	0.2-0.6	**<.001**	0.4	0.2-0.8	**.004**
Chronic heart disease	2.3	1.4-4.1	**.003**						
Chronic kidney disease	1.5	0.6-3.6	.348	2.7	1.1-6.5	**.026**	3.0	1.1-8.0	**.034**
ASPECTS	1.2	1.0-1.3	**.001**	1.2	1.1-1.4	**.005**	1.2	1.0-1.4	**.014**
Atrial fibrillation	1.4	0.9-2.0	.054						
No. of vessels involved	0.7	0.5-0.9	**.017**						
LVO location (anterior circulation)	0.9	0.5-1.7	.749						
Tissue plasminogen activator	1.0	0.7-1.4	.060						
NIHSS at admission	0.9	0.9-1.0	**.050**	1.0	0.9-1.0	**.03**			
Onset to door	1.0	0.9-1.0	.070						
Onset to arterial access	1.0	0.9-1.0	.229						

ASPECTS, Alberta Stroke Program Early Computed Tomography Score; COVID-19, coronavirus disease; LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.
Bold values indicate statistically significant value $P \leq .05$.

TABLE 3. Univariate and Multivariate Analyses for Variables Associated With Unfavorable Outcomes (mRS 3-6) Before and After Propensity Score Analysis

	Univariate			Univariate after propensity score analysis			Multivariate after propensity score analysis		
Variable	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Sex (female)	0.9	0.6-1.5	.736						
Increasing age	1.0	1.0-1.0	.012	1.0	1.0-1.0	**.038**	1.0	1.0-1.1	**.016**
COVID-19	1.9	1.2-3.1	**.004**	2.5	1.3-5.1	**.008**	2.6	1.1-5.8	**.025**
NIHSS at admission	1.1	1.1-1.1	**<.001**	1.1	1.1-1.2	**<.001**	1.1	1.0-1.1	**.005**
Baseline functional status	1.6	1.1-2.4	.011	2.3	1.1-4.9	**.026**			
Chronic heart disease	0.8	0.5-1.5	.619						
Chronic lung disease	0.9	0.5-1.6	.821						
Chronic kidney disease	1.5	0.6-3.5	.348						
Chronic liver disease	2.6	0.6-11.7	.205						
Hypertension	1.4	0.8-2.2	.186						
Diabetes mellitus type II	1.4	0.8-2.4	.180	2.5	1.2-5.5	**.019**			
Atrial fibrillation	0.8	0.5-1.3	.359						
ASPECTS	0.8	0.7-0.9	**.002**	0.7	0.6-0.9	**.005**			
No. of vessels involved	1.1	0.7-1.7	.578						
LVO location (anterior circulation)	1.2	0.5-2.8	.682						
Tissue plasminogen activator	0.8	0.5-1.2	.267						
Onset to door	1.0	0.9-1.0	.280	1.0	1.0-1.0	**.045**			
Onset to arterial access	0.9	0.9-1.0	**.031**	1.0	1.0-1.0	**.035**			
General ET intubation	0.8	0.5-1.4	.448						
Stenting	0.9	0.5-1.9	.908						
Procedure duration	1.0	0.9-1.0	.053						
TICI 2B-3	0.4	0.2-0.8	**.009**	0.6	0.4-0.9	**.015**	0.6	0.4-1.0	**.042**

ASPECTS, Alberta Stroke Program Early Computed Tomography Score; COVID-19, coronavirus disease; ET, endotracheal; LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; TICI, thrombolysis in cerebral infarction.
Bold values indicate statistically significant value $P < .05$

(OR: 0.8, 95% CI: 0.7-0.9; $P = .002$), NIHSS score at admission (OR: 1.1, 95% CI: 1.1-1.1; $P < .001$), onset to arterial access time (OR: 0.9, 95% CI: 0.9-1.0; $P = .031$), and thrombolysis in cerebral infarction (TICI) 2b-3 revascularization (OR: 0.4, 95% CI: 0.2-0.8; $P = .009$) before propensity score analysis. After matching, COVID-19 positivity (OR: 2.5, 95% CI: 1.3-5.1; $P = .008$), ASPECTS (OR: 0.7, 95% CI: 0.6-0.9; $P = .005$), NIHSS at admission (OR: 1.1, 95% CI: 1.1-1.2; $P < .001$), onset to arterial access time (OR: 1.0, 95% CI: 1.0-1.0; $P = .035$), and TICI 2b-3 revascularization (OR: 0.6, 95% CI: 0.4-0.9; $P = .015$) remained statistically significant in addition to increasing age (OR: 1.0, 95% CI: 1.0-1.0; $P = .038$), baseline functional status (OR: 2.3, 95% CI: 1.1-4.9; $P = .026$), diabetes mellitus type 2 (OR: 2.5, 95% CI: 1.2-5.5; $P = .019$), and onset to door time (OR: 1.0, 95% CI: 1.0-1.0; $P = .045$). Moreover, multivariate analysis performed after matching showed that the independent predictors of unfavorable outcomes are COVID positivity (OR: 2.6, 95% CI: 1.1-5.8; $P = .025$), increasing age (OR: 1.0, 95% CI: 1.0-1.1; $P = .016$), NIHSS at admission (OR: 1.1, 95% CI: 1.0-1.1; $P = .005$), and TICI 2b-3 (OR: 0.6, 95% CI: 0.4-1.0; $P = .042$) (Table 3).

DISCUSSION

Key Points

This multicenter, comparative, retrospective study demonstrates that patients with COVID-19 with concomitant LVO have a grim prognosis, with a mortality rate reaching 40%. Moreover, COVID-19 increases the likelihood by 2.5-fold for unfavorable outcomes; in addition, it decreases the likelihood to achieve complete revascularization by 60%. Our findings further corroborate past series reporting poor outcomes in patients developing AIS in the setting of COVID-19.[27-34] Moreover, previous efforts have demonstrated that COVID-19 was an independent predictor for LVO, poor outcomes, and increased mortality.[33,35-37] The degree of recovery after an AIS is dependent on a complex set of factors that can be categorized into patient's characteristics (baseline functional status and comorbidities), stroke characteristics (severity and time lag to treat), concomitant pathologies, and complications. Ischemic brain tissue is highly vulnerable and requires optimal conditions for a potential recovery. The milieu produced by COVID-19 is the complete opposite of an optimal condition. COVID-19 induces vasculopathy, hypercoagulable state, myocarditis, arrhythmias, thrombotic

microangiopathy, coagulopathy and thrombocytopenia, tropism to endothelial cells through ACE-2 receptor, and inhibition of angiotensin (1-7) production.[1-26] It has been proposed that down-regulation of ACE-2 leading to both arteriopathy and thrombosis may play a central role in the development of stroke during COVID-19.[38,39]

Apart from establishing that COVID-19 is an independent predictor of poor functional outcomes and reduces the likelihood of achieving complete revascularization, it is imperative to define the characteristics of such subjects developing LVO in the setting of COVID-19. Such an effort will enhance our understanding of the disease and may aid in improving prognostication.

Beginning with the patients' characteristics, the mean age of the COVID-19 group was significantly lower than the control group by 8.7 years. Numerous publications spanning across heterogeneous geographic areas reported similar findings.[30,33,35,40-45] Similarly, the difference remains significant, almost by 10 years, compared with the Contact Aspiration vs Stent Retriever for Successful Revascularization (ASTER) trial (71.1 years) and the study by Al Kasab et al (72 years).[46,47] Moreover, the proportion of patients 50 years and younger was 2-fold higher compared with the control group. The reported incidence of LVO in young patients in non–COVID-19 settings ranges between 3.3% and 5%, whereas in the COVID-19 setting, it ranges between 16% and 19% (current study).[48] The latter figures are almost 4-fold higher than the general population. Similar to previously reported data,[31,33] sex preponderance was observed in this study with more men (by 2.8-fold) in the COVID-19 group. For comorbidities, patients with COVID-19 were more likely to lack cerebrovascular risk factors. Such findings have been previously reported by a group from New York and other institutions.[40,43]

Interpretation and Generalizability

Interestingly, only 75% of the patients who developed LVO had moderate COVID-19 severity according to the World Health Organization classification.[49] It is paramount to emphasize that immune dysregulation resulting in a cytokine storm is a factor that has a pathophysiological significance in the development of stroke in COVID-19 disease.[50-52] In addition, the duration between stroke onset and COVID-19 symptoms was 9 days; this includes patients who had a stroke as the initial manifestation of COVID-19, which constituted 34.1%.[53] The Global COVID-19 Stroke Registry reported a median latency period between symptom onset and stroke of 7 days (IQR: 2-15).[33] Historical data have consistently demonstrated an increased incidence of ischemic stroke during pandemics, often occurring within several days of the infection.[54,55] The severity of stroke was more pronounced in the COVID-19 group based on the ASPECTS, NIHSS score at presentation, and the number of involved vessels. Although the NIHSS score was not significantly different between both groups 24 hours post-thrombectomy, this is because patients who were COVID-negative and presented with strokes were significantly older and had several comorbidities. On the other hand, patients with COVID-induced strokes were significantly younger with less comorbidities. Thus, after thrombectomy, NIHSS was affected by the severity of the stroke in patients with COVID and by the comorbidities in patients who were COVID-negative. The get with the guidelines (GWTG)-Stroke analysis reported similar findings after reviewing 1143 patients diagnosed with COVID-19: a higher NIHSS score at presentation and more LVOs.[35] In our study, stroke care during the pandemic was not compromised as demonstrated by the rate of tPA administration, which was similar between both groups, whereas another study reported a relative global decline in IV thrombolysis during the first wave of the COVID-19 pandemic.[56] The interval from symptom onset to hospital presentation was shorter in the COVID-19 group. The only prolonged time metric in the COVID-19 group was time to arterial access, by 24 minutes, which can be attributed to the workflow during the pandemic. Similar conclusions regarding stroke care during the pandemic were reported by a group from Switzerland, Spain, and the GWTG-Stroke consortium. They did not find any significant difference in the rate of IV-tPA or MT procedures between patients with COVID-19 and non–COVID-19 patients. Contrary to our finding, the Switzerland and Spain groups did not experience a delay in admission to arterial access[44,45] while the GWTG-Stroke consortium reported a delay in admission to arterial access by a difference of 24 minutes, similar to our cohort.[35]

The complexity of the MT procedure is influenced by several factors, including clot burden and consistency. Complexity can be assessed by direct methods, such as filling a questionnaire after each case or simply providing a score, or by indirect methods based on the duration of the procedure, number of vessels involved, number of passes, achieving either complete or favorable revascularization, or technical complications. The COVID-19 group had a higher number of involved vessels, a similar number of passes, longer procedure duration by 11 minutes, and a lower proportion of complete revascularization. Patients with COVID-19 had a lower likelihood of achieving mTICI 3 by 60%, whereas mTICI 2b/3 reperfusion was similar between the 2 groups. Such outcomes, particularly sICH and favorable revascularization outcomes, have been reported in previous COVID-19 series[43-45] and are in line with historic MT data.[57]

Finally, the unfavorable functional outcomes at discharge and follow-up were observed at a significantly lower proportion in the COVID-19 group. Moreover, mortality was more frequent as of 40%, and COVID-19 was associated with 2.5-fold poor outcomes. The mortality rate, when compared with prior published data, is significantly higher in this study. Similarly, the GWTG-Stroke consortium and the Global COVID-19 Stroke Registry demonstrated that COVID-19 was an independent predictor of poor outcomes and death.[33,35] Despite a more extended hospital stay in the COVID-19 group by ~10 days, the rate of sICH and NIHSS score at 24 hours post-thrombectomy were not significantly different. Poor outcomes have been reported in other pathologies occurring in the setting of COVID-19.

Limitations

Our article has strength and limitations. The main limitation of this study is its' retrospective design and the absence of randomization. In addition, there were significant differences in baseline characteristics between both cohorts such as age, sex, comorbidities, and baseline functional status. The period of treatment was also different between both cohorts. Finally, our study lacked weighted data analysis to account for volume contribution by each center. The strength of the article is the relatively large sample size, the international experience, and the comparative analysis performed.

CONCLUSION

COVID-19 is an independent predictor of poor outcomes and incomplete revascularization in patients with stroke due to a LVO. Patients are younger, tend to have less cerebrovascular risk factors, and suffer from higher morbidity/mortality rates.

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